TITLE PAGE

Section III: Health, Disease & Physical Activity

Appetite and energy intake following a bout of circuit resistance training in chronic hemiparetic stroke patients: a preliminary randomized controlled trial

Running head: Acute effects of CRT on appetite and energy intake

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ABSTRACT

Purpose: The main aim of this study was to investigate the effects of circuit resistance training (CRT) on post-exercise appetite and energy intake in chronic hemiparetic stroke patients. A secondary aim was to evaluate the reproducibility of these effects.

Methods: Seven participants met the eligibility criteria and, in a randomized order, participated in a non-exercise control session (CTL) and two bouts of CRT. The CRT involved 10 exercises with 3 sets of 15-repetition maximum per exercise, performed using a vertical loading approach, with each set interspersed with 45 s of walking. Expired gases were collected 10 min before, during, and for 40 min after CTL and CRT to calculate the net energy cost of the exercise and the relative energy intake post-CTL/CRT. Hunger, fullness, desire to eat, and energy intake were assessed at baseline and for 12 h after CTL and CRT.

Results: Compared to CTL, hunger, desire to eat ($P < 0.001$), and relative energy intake ($P < 0.05$) were significantly lower after CRT, whereas the perception of fullness was significantly higher ($P < 0.001$). Significant differences between CTL and CRT were observed only for the first 9 h of the post-exercise period for hunger, fullness, and desire to eat ($P < 0.05$). No significant differences in appetite or relative energy intake were observed between the two bouts of CRT.

Conclusions: A bout of CRT elicited decreased post-exercise appetite and relative energy intake in chronic hemiparetic stroke patients. Decreased appetite perceptions lasted for around 9 h and were reproducible.

Keywords: appetite, circuit-based exercise, indirect calorimetry, metabolism, resistance training.

INTRODUCTION

Stroke is characterized by a neurological deficit attributed to an acute focal injury of the central nervous system by a vascular cause, including cerebral infarction, intracerebral hemorrhage, and subarachnoid hemorrhage [1]. Data from the 2019 Global Burden of Diseases, Injuries, and Risk Factors Study indicated that globally there were 101 million prevalent cases of stroke and an associated 6.55 million deaths [2]. A large percentage of people survive a stroke and live with resulting sequelae, the most common of which is neuromuscular dysfunction due to decreased activity of descending corticospinal pathways that control the activity of motor neurons [3]. This causes paresis, paralysis, spasticity, sensory-perceptual dysfunction, and debilitating secondary effects such as loss of muscle mass and strength, impaired oxidative metabolism, and low exercise capacity [4]. This culminates in a greater sense of weakness associated with early fatigue and higher amounts of sedentary behavior than age-matched healthy controls [5], which heighten the risk for stroke recurrence [6].

Furthermore, the increased fat mass and reduced fat-free mass observed in many chronic stroke patients are associated with a 10-20% reduction in resting metabolic rate (RMR) [7,8], which accounts for the largest proportion of the total daily energy cost required to maintain the body's integrated systems and homeostasis [9]. In a prospective study involving 1,139 stroke patients, Redfern, McKevitt [10] reported an obesity prevalence of 36% within the first 12-months after a stroke. Although the '*obesity paradox*' supports the notion that the presence of obesity reduces the risk of recurrent stroke compared to non-obese individuals [11], obese stroke patients are more susceptible to cardiovascular risk factors, including hypertension, dyslipidemia, type 2 diabetes mellitus, metabolic syndrome, and depression [6]. According to the findings of Towfighi and Ovbiagele [12], higher body mass index (BMI) after stroke is associated with a greater risk of all-cause and cardiovascular mortality among younger individuals, who may derive greater benefit from more vigorous efforts to monitor and treat obesity.

Regular physical exercise is regarded as important for controlling cardiovascular risk factors, and for promoting improvements in muscle strength, cardiorespiratory fitness, and weight management [6]. Consequently, recommendations for exercise prescription have been developed to guide health professionals working in stroke rehabilitation [6,13]. Recommendations state stroke patients should aim to engage in aerobic exercise on 3-5 d/wk and muscular strength and endurance training on 2-3 d/wk. In this context, circuit resistance training (CRT) has emerged as an effective and time-efficient strategy to improve strength of the lower and upper limbs, cardiorespiratory fitness, and body composition [14].

In regards weight management, it is well established that weight loss or gain is related to an imbalance between total energy intake and the total energy expenditure resulting from the RMR, diet-induced thermogenesis, and physical activity [15]. The interplay between exercise, appetite, and energy balance has been a focus of research in recent years. One notable issue proposed by Epstein and Wing [16] over 4 decades ago is that '*exercise may stimulate the appetite so that persons who exercise increase their eating and do not lose as much weight as expected*'. Although findings of cross-sectional studies on this issue have been mixed, observing either increased energy intakes post-exercise [17] or anorexic responses [18], a meta-analysis by Schubert, Desbrow [19] concluded a single bout of exercise does not alter energy intake in the subsequent hours when compared to a non-exercise control day. This suggests exercise-related energy expenditure is not compensated by increased post-exercise energy intake and, therefore, a bout of exercise should create an energy deficit with an associated positive impact on long-term weight management from a long-term exercise program. Findings from the meta-analysis, however, also indicate that less fit individuals are more likely to experience a post-exercise anorexic effect, at least in the initial hours following a bout of exercise [19]. Stroke patients are characterized by very low cardiorespiratory fitness [6] and, therefore, may be particularly susceptible to a post-exercise anorexic effect that increases weight loss beyond that resulting from the energy expenditure associated with exercise. Moreover, a high prevalence of sarcopenia [20], poor nutritional status [21], and loss of appetite [22] have been reported among stroke patients, and a post-exercise anorexic effect has the potential to exacerbate these issues.

Considering the lack of studies examining post-exercise appetite and energy intakes in stroke patients, two questions arise: (i) To what extent does a bout of CRT alter post-exercise appetite and energy intake in stroke patients? and (ii) How reproducible are these responses? The main aim of the present study therefore was to investigate the appetite and energy intake responses for 12 h after a bout of CRT in chronic hemiparetic stroke patients. A second aim was to evaluate the reproducibility of these responses. We hypothesized that CRT would elicit a short-term suppression of appetite and energy intake but trigger a partial compensation in energy intake over a longer period (i.e., 12 h) and that these responses would be reproducible.

MATERIALS AND METHODS

Participants

Potentially eligible participants were recruited from the University Hospital Pedro Ernesto and Piquet Carneiro Polyclinic of the State University of Rio de Janeiro. The following inclusion criteria were applied: a) chronic stroke (≥ 6 months) with right or left hemiparesis; b) able to walk without supervision; c) enrolled in a neuro-motor rehabilitation program; d) a score above 36 on the Berg balance scale [23]; e) a minimum score of 50 on the Fugl-Meyer scale; and f) not dieting or exhibiting any extreme dietary habits, including disinhibited and restrained eating tendencies. Exclusion criteria included: a) current smoker; b) uncontrolled hypertension; c) patients with clinical manifestations of hyper or hypothyroidism; d) acute or chronic hepatic disease; e) patients with a history of angina or tests compatible with myocardial ischemia; f) previous history of acute myocardial infarction and/or myocardial revascularization; g) clinical signs of heart failure, symptomatic cardiac arrhythmia, or clinically significant valve disease; h) history of drug or alcohol abuse; i) history of psychiatric or neurological disease other than stroke; and j) severe aphasia or a cognitive-communication deficit.

Eighteen people initially volunteered to participate in the study, with 11 of these excluded due to the presence of the following: heart failure ($n = 3$), cognitive impairment ($n = 2$), kidney disease ($n = 1$), uncontrolled hypertension ($n = 1$), smoking ($n = 1$), and voluntary waiver due to lack of time ($n = 3$). Finally, our convenience sample composed of seven participants (4 males and 3 females; 4 with right and 3 with left hemiparesis) were therefore considered eligible after the initial screening. They were informed of the requirements, benefits, and potential risks and discomforts of participation, and subsequently provided informed consent prior to the commencement of the study. Figure 1 shows the flowchart for the study. The experimental procedures adhered to the ethical guidelines outlined in the Declaration of Helsinki and the study gained approval from the Pedro Ernesto University Hospital at Rio de Janeiro State University institutional ethics committee (CAAE: 30464819.0.0000.5259). This clinical trial was registered at a World Health Organization accredited office (Brazilian Clinical Trials Registry – ReBec, protocol RBR-4y7yyfs, available at https://ensaiosclinicos.gov.br) and conforms to the Consolidated Standards of Reporting Trials (CONSORT) 2010 [24]. Table 1 describes participant characteristics.

INSERT FIGURE 1 AND TABLE 1

Preliminary testing

Prior to the experimental trials, participants visited the laboratory over 3 weeks to undergo health screening, preliminary measurements (i.e., anthropometry, functional motor performance, cognitive status and RMR), familiarization (i.e., visual analog scales to assess appetite, food diary to record energy intakes, and exercises included in the CRT), and test-retest reliability of 15-repetition maximum (15-RM) tests.

Body mass and height were assessed respectively by digital balance scales (Welmy^{TM}, São Paulo, Brazil) and a stadiometer graded in millimeters (American Medical do Brazil^{TM}, São Paulo, Brazil). BMI was subsequently calculated as the body mass (kg) divided by height (m^2). Waist circumference was taken midway between the lowest rib and the top of the iliac crest. Hip circumference was taken at the widest diameter of the buttocks. Waist-hip ratio was calculated by dividing waist circumference by hip circumference.

Cognitive mental status was assessed using the Mini-Mental State Exam [25]. Briefly, this consists of a two-section exam, as follows: (i) only vocal responses are required and involves orientation, memory, and attention; and (ii) more complex tasks, such as naming objects, following verbal commands, writing a sentence spontaneously, and copying a polygon. The maximum scores from the first and second sections are 21 and 9, respectively, totaling 30 points.

The Fugl-Meyer scale was applied to assess the degree of motor impairment of participants through abnormal synergic voluntary movements in the motor function domain [26]. Scale scores range from 0 to 100 points (< 50 points indicates severe motor impairment, 50-84 represents marked impairment, 85-95 is moderate, and 96-99 is slight). Static and dynamic balance were assessed using the Berg scale [27], in which a maximal of 56 points could be achieved for items scored on 0-4 point scale.

Physical activity level was assessed by the International Physical Activity Questionnaire - Short Form (IPAQ-SF), which comprises seven questions to capture average daily time spent in four different intensity levels: a) vigorous-intensity activity; b) moderate-intensity activity; c) walking; and d) sitting. For all activities, the number of days *per* week and minutes *per* day the participant continually performed the activity for ≥10 min for the last seven days was recorded. Total daily physical activity was calculated by adding the product of reported time within each item by a metabolic equivalent value specific to each category of physical activity [28].

RMR was determined as follows for the purpose of estimating daily energy requirements in accordance with the recommendations of Compher et al. [29]: abstention of physical exercise, alcohol, soft drinks and caffeine in the 24 h preceding the assessment, overnight fasting prior to the assessment (~12 h of fasting), and minimum effort when travelling to the laboratory. In the laboratory, the participants laid in a calm environment for an acclimation period of 10-min, after which the RMR was measured for 30-min in a supine position. The RMR was taken as the average of the last 5 min of steady-state data (i.e. coefficient of variation ≤10% during 5 min), since this time period has been previously shown to elicit a steady-state response and high test-retest reliability [30].

Fifteen-repetition maximum (15-RM) tests were performed to determine the training loads for each resistance exercise, using the standard procedures proposed by the ACSM [31]. The 15-RM tests were repeated after a 30 min rest to establish the reproducibility of the load. Where the loads varied more than 5% in the two 15-RM tests, there was a further 30 min rest period, and the test was repeated.

Participants were asked to maintain their normal diet throughout the study, which was verified by 24-h dietary recall collected during nonconsecutive 3-day diet records (2 weekdays, 1 weekend day). A nutritionist explained to each participant how to complete the record, which was reviewed during collection. Dietary records were analyzed using a computer-based nutritional analysis program (nutriDieta software, DF Médica®, Brazil) to determine the habitual energy and macronutrient intakes of the participants.

Study design

The entire trial process occurred from January 2018 to December 2020, when the last eligible participant concluded all procedures. Figure 2 illustrates the timing of each assessment performed during each of the three experimental trials. The study incorporated a computer-generated randomized, counter-balanced, controlled cross-over design, including the following: i) a non-exercise control session (CTL); ii) 1st bout of CRT; and iii) 2nd bout of CRT. ACM generated the random allocation sequence, VABC enrolled participants, and GFF assigned participants to the intervention. Participants were only informed about which session would be performed when they arrived at the laboratory. To avoid any carry-over effects, each experimental trial was separated by 48 to 72 h and participants were instructed not to engage in any form of physical exercise in the 24 h preceding each experimental trial. Participants also were instructed to abstain from alcohol, soft drinks, and caffeine in the 24 h preceding each experimental trial and to replicate their dietary intake recorded during the preliminary testing. The research team contacted the participants via telephone 48 h before each trial to ensure the consistency of energy intake for the 24 h prior to experimental trials. The CTL session and bouts of CRT were conducted in a thermoneutral environment (i.e., 21-24ºC and relative humidity between 50-70%). No changes to the experimental procedures occurred after trial commencement.

INSERT FIGURE 2

On the day of the trials, participants consumed a standardized breakfast at home at 6:30 a.m. prior to arriving in the laboratory. Participants were asked to choose from the following food items: white bread, brown bread, toasted wheatgerm, cream cracker biscuit, margarine, cream cheese, ricotta cheese, Minas frescal cheese, boiled chicken egg, melon, tomato, cucumber, skimmed UHT milk, skimmed powdered milk, and whole long-life milk. Participants also were asked to replicate the food ingested in the morning of the first experimental trial on the mornings of subsequent trials. Dietary analysis showed that breakfast, on average, represented 25% of the estimated daily energy needs for a given participant during a non-exercise day. Average macronutrient content was 56% carbohydrate, 20% protein, and 24% fat. Participants then undertook *laboratory-phase* monitoring between 08:00 and 10:00 a.m., consisting of determination of energy expenditure immediately before, during, and for 40-min after the CTL or CRT, and appetite immediately before and after CTL and CRT. Upon leaving the laboratory, *ambulatory-phase* monitoring was carried out for the remainder of the 12-h post-CTL/CRT period. This involved determination of appetite and energy intake.

The CRT involved 10 exercises with 3 sets of 15-RM per exercise, performed using a vertical loading approach. The exercises were chosen to improve functional capacity for carrying out typical activities of daily living performed by individuals post-stroke (e.g., pull and push, sitting and rising, walking up and down stairs) [6] and to enable the reproducibility of the protocol in regular gyms. For this, the exercises were divided into functional body weight exercises (i.e., box step-up and squat) and machine-based exercises with external workloads [i.e., leg press, seated row, knee extension, horizontal chest press, knee flexion, shoulder press, hip abduction, and biceps curl (TechnoGym, Selection Line, Cesena, Italy)]. There was an active walking interval of 45 s between sets of resistance training exercises. The walking bouts were performed at a self-selected pace. Participants were instructed to walk at comfortable speeds. The CRT was preceded by a warm-up consisting of 1 set of 15 repetitions at 50% of 15-RM in leg press and seated row, with a 45 s walk after each exercise, totaling ~5 min of warm-up. The CTL consisted of 20 min of seated rest and the participants were monitored with the same instruments used in the bouts of CRT. Within 2 min of completing the CTL and bouts of CRT, participants were placed in a supine position for a recovery period of 40 min. Figure 3 illustrates exercises included in the CRT.

INSERT FIGURE 3

Energy cost of experimental trials

Pulmonary gas exchange was determined at baseline, during, and for 40-min after CTL and CRT using a VO2000 telemetry system (Medical Graphics®, Saint Louis, USA) and a silicone oronasal mask (Hans Rudolph^{TM}, Kansas, MO, USA). The gas exchange variables were 30-s stationary time-averaged, which provided a good compromise between removing noise in the data while maintaining the underlying trend [32]. Prior to testing, the gas analyzers were calibrated according to the manufacturer's instructions using a certified standard mixture of oxygen (17.01%) and carbon dioxide (5.00%), balanced with nitrogen (AGA®, Rio de Janeiro, RJ, Brazil). The total energy cost of each experimental trial was estimated by adding the energy expended during the experimental trial to the net recovery energy cost. The net energy recovery cost was calculated by subtracting the average value in the last 5-min of the baseline assessment from the average energy expended during the 40 min after CTL or CRT.

Appetite, energy intake and relative energy intake

Appetite perceptions, consisting of hunger, fullness, and desire to eat, were assessed using 100 mm visual analogue scales anchored at each end with the statements "*not at all*" and "*extremely*" [33]. Each perception was recorded at baseline, after 40 min of recovery in the *laboratory-phase*, and at 3, 6, 9, and 12 h post-experimental trials in the *ambulatory-phase*, immediately before *ad libitum* energy intake. Participants were instructed to eat until '*comfortably full*' and informed that additional food was available if desired. Food and fluid intake were recorded throughout via dietary recall according to the nutritionist's advice and used to estimate energy and macronutrient intake during the 24 h immediately following each trial (nutriDieta software, DF Médica®, Brazil). Relative energy intake was estimated by subtracting the energy intake from the total energy cost expended for either CTL or CRT. No changes to outcomes occurred after trial commencement.

Statistical analyses

All statistical analyses were performed using IBM SPSS® version 23 (SPSS^{TM} Inc., Chicago, IL, USA). Descriptive sample data are presented as means ± standard deviations (SDs) for normally distributed data and the median and interquartile range (IQR) otherwise. Marginal models via the SPSS MIXED procedure were used to analyze the effects of Condition (i.e., CTL and 1st and 2nd bouts of CRT) and Time (baseline and 40 min, 3, 6, 9, and 12 h post-CLT/CRT)] on appetite perceptions, and the effect of Condition on total energy cost, and absolute and relative energy intakes. The best fitting covariance structure was identified as that which minimized the Hurvich and Tsai's criterion value. Where there was a statistically significant main effect or interaction effect, post hoc pairwise comparisons with Sidak-adjusted P values were obtained. A two-tailed P value < 0.05 was accepted as statistically significant. Test-retest reliability of main outcomes assessed from the 1st and 2nd bouts of CRT were evaluated by the intraclass correlation coefficient (ICC), which was calculated as a one-way random effects model [34]. The level of reliability according to the ICC was interpreted as follows: low, <0.40; moderate, 0.40 to 0.75; and high, > 0.75.

RESULTS

The median (IQR) 24-h energy intake during preliminary testing was 5336 (4987) *kJ*, with macronutrient contents of 49 (40) % carbohydrate, 28 (22) % fat, and 24 (21) % protein. Figure 4 displays the mean ± SD difference (diff) between the 1st and 2nd bouts of CRT *vs*. CTL and the ICCs for the two bouts of CRT, at baseline and for 12-h post-CTL/CRT. A significant main effect for Condition was observed for hunger (F = 35.6, $P < 0.001$), fullness (F = 27.9, $P < 0.001$), and desire to eat (F = 77.9, $P < 0.001$). Hunger and desire to eat were significantly lower during recovery from both bouts of CRT compared to CTL (1st bout of CRT *vs*. CTL: mean diff = -11.2 and -17.4 mm, respectively, $P < 0.001$; 2nd bout of CRT *vs*. CTL: mean diff = -9.7 and -15.6 mm, respectively, $P < 0.001$). Fullness was significantly higher during recovery from CRT compared to CTL (1st and 2nd bouts of CRT *vs*. CTL: mean diff = 12.2 and 14.1 mm, respectively, $P < 0.001$). A significant Condition x Time interaction revealed that the differences between CTL and CRT decreased over time for hunger (F = 3.7, $P < 0.001$), fullness (F = 2.2, $P = 0.024$), and desire to eat (F = 9.6, $P < 0.001$). Post hoc pairwise comparisons showed, for example, that for each of the three perceptions of appetite, significant differences between CTL and CRT were only observed until 9-h post-exercise. The largest differences between CTL and the 1st and 2nd bouts of CRT were observed in the first 40-min of recovery (Δ hunger: -17.9 ± 13.2 and -16.6 ± 13.0 mm, respectively; Δ desire to eat: -29.6 ± 11.1 and -27.8 ± 14.0 mm, respectively), or at 3-h of recovery (Δ fullness: -19.9 ± 11.2 and -21.7 ± 6.5 mm, respectively). At baseline there were no significant differences in perceptions of appetite between conditions ($P \geq 0.05$). No significant differences between the 1st and 2nd bouts of CRT were observed for all perceptions of appetite ($P \geq 0.05$) and ICCs ranged from 0.47 to 0.93.

INSERT FIGURE 4

Figure 5 shows the mean ± SD total energy cost, and absolute and relative energy intakes after CTL and the 1st and 2nd bouts of CRT. A significant effect for Condition was observed for total energy cost (F = 68.1, $P < 0.001$) and relative energy intake (F = 4.5, $P = 0.035$). No statistically significant difference in total energy cost was observed between the two bouts of CRT (mean diff = 40 *kJ*, $P = 0.868$), however, the 1st and 2nd bouts of CRT were 552 and 592 *kJ* higher than CTL, respectively ($P < 0.001$). Post hoc analyses also showed a significantly lower relative energy intake during the 1st and 2nd bouts of CRT than during

CTL (mean diff = -1,338 and -1,175 *kJ*, respectively, $P < 0.05$). As depicted in Figure 5, no difference in absolute energy intake was observed across conditions. There were no adverse events to report.

INSERT FIGURE 5

DISCUSSION

The main aim of the present study was to investigate the effects of CRT on post-exercise appetite and energy intake in chronic hemiparetic stroke patients. A secondary aim was to evaluate the reproducibility of these responses. To our knowledge, this is the first study to investigate appetite and energy intake following acute CRT in chronic hemiparetic stroke patients. The main findings were: (a) hunger and desire to eat were significantly lower during the first 9 hours of recovery from CRT compared to CTL, while fullness was significantly higher, resulting in a significantly lower relative energy intake; and (b) no significant differences between the 1st and 2nd bouts of CRT were observed for appetite or energy intake.

Our primary hypothesis was confirmed, evidencing decreased hunger and desire to eat and increased fullness after CRT ($P < 0.001$). It is claimed that decreased appetite is to some extent mediated by hormonal changes, such as the suppression of acylated ghrelin levels, and increased perceptions of satiety such as fullness are partially due to a rise in levels of peptide YY and glucagon-like peptide 1 [35]. Our findings partially agree with recent findings from Johnson, Mistry [36], who reported decreased appetite after a bout of resistance exercise compared to CTL in older adults without a history of stroke ($P = 0.007$). However, no difference in energy intake was observed 2-h after resistance exercise ($P = 0.865$), while our study showed lower relative energy intake for 9 hours after CRT *vs*. CTL ($P \leq 0.05$). Differences between study findings may have been due to the present study investigating stroke patients compared to the apparently healthy elderly participants used in the study by Johnson, Mistry [36] and the differences in resistance training protocols. Our study used circuit resistance training, whereas Johnson, Mistry [36] incorporated traditional resistance training consisting of two sets of 10-15 repetitions of each exercise at 40-50% at estimated 1-repetition maximum, with 2 min of rest between each set. Moreover, Johnson, Mistry [36] limited their analyses to 5 h post-intervention, while our study investigated the whole awake period after CTL and CRT (12 h of analyses).

Some methodological aspects must be considered regarding energy intake. Our findings revealed that absolute energy intake after CRT did not differ from CTL; however, the relative energy intake after CRT was lower than after CTL ($P \leq 0.05$), meaning that no compensatory increase in absolute energy intake after CRT occurred. Relative energy intake takes into account the energy intake after the bout of CRT and also considers the energy expenditure associated with the exercise [19], thereby providing insight into energy balance, which was negative in the present study. Analysing only absolute data could lead to misinterpretation of the phenomenon. Accordingly, a meta-analysis reviewed the deficit in energy intake produced by exercise and whether this deficit is further compensated [19]. Twenty-nine studies were included with a median of 11 participants per study (range from 7 to 21). Exercise had a trivial non-significant effect on absolute energy intake (effect size = 0.14, 95% CI: -0.005 to 0.29), but a large significant effect on relative energy intake (effect size = -1.35, 95% CI: -1.64 to -1.05). The authors concluded that exercise promotes an energy deficit that is not subsequently fully compensated by increased energy intake. Our results therefore agree with the meta-analysis, although their findings did not include CRT or stroke patients.

Stroke patients often present with dysphagia [21], loss of appetite [22], reduced energy intake [37], nutrition deficits [37], and considerable risk of developing sarcopenia [20]. One could therefore question whether CRT would be a favorable training strategy for these patients, due to the post-exercise decrease in appetite and relative energy intake, and the associated negative energy balance that could lead to long-term weight loss. This is considered risky for these patients [22] as obesity and overweight improves survival in stroke patients [38]. This is a notable issue since CRT improves strength and functional performance in chronic stroke patients [39] and is recommended in the joint scientific statement of the American Heart Association and American Stroke Association [6]. This creates the obesity paradox, as obesity is an independent risk factor for cardiovascular disease and mortality [40]. The lack of understanding of this topic highlights the urgent need for research to elucidate the role of exercise on appetite regulation and weight management in chronic hemiparetic stroke patients and how these impact on long-term energy balance, cardiovascular risk, and mortality.

Our findings show that the anorexic response to bouts of CRT lasted 9 h into recovery, returning to control levels thereafter, with peak appetite suppression occurring withing the first hour. This highlights the transient nature of the anorexic response to CRT. Another aspect that should be considered when interpreting our findings is that our sample was composed on average by overweight stroke patients (BMI = 26.6 ± 3.7 kg/m^2). A transient energy deficit therefore does not seem to be an issue for our participants, considering the evidence that there is better survival and non-fatal functional outcomes for overweight and obese stroke patients [22]. Physical activity recommendations for stroke patients state that CRT should be performed 2-3 days per week [6]. If performed on alternate days (e.g., Monday, Wednesday, Friday), it is feasible that the 48-h interval between bouts of CRT would be sufficient to allow energy balance over the week to prevent muscle mass loss and improve functional independence, especially if accompanied by a nutritional intervention as part of a multi-modal rehabilitation program [41]. However, caution is needed when prescribing CRT to normal and underweight patients and studies are required to provide a better comprehension of this topic before evidence-based guidelines can be developed.

Another important finding from our study relates to the reproducibility of hunger, desire to eat, and fullness after CRT. Confirming our secondary hypothesis, none of the analysed variables were significantly different from each after the two bouts of CRT, and the level of agreement was moderate-to-high throughout the experimental period. Laan, Leidy [42] investigated the reproducibility of appetite responses to resistance exercise and showed appetite was reproducible at pre- and post-exercise. They were not able to elicit significant changes in post-exercise appetite when compared to control, however, while we observed an anorexic response. Those authors investigated young active adults for a 105-min recovery time, which may help explain differences between research findings. Additionally, their resistance exercise protocol was not performed in a circuit fashion and was composed of only 5 exercises, thereby not meeting the guidelines of the ACSM [31] for resistance training (i.e., 8-10 exercises involving major muscle groups).

Lastly, the present study has several strengths that deserve attention: (i) this is the first study to investigate appetite and energy intake in response to a bout of exercise in chronic hemiparetic stroke patients; (ii) the proposed exercise protocol (i.e. CRT) involved both strength and cardiorespiratory components, and was monitored by indirect calorimetry, allowing the assessment of the energy cost of the exercise; (iii) beyond the laboratory assessments, we analysed the ambulatory responses during the entire awake period (12-h), which was fundamental in determining the duration of the anorexic response (i.e., 9 h); and (iv) we replicated the bout of CRT, providing reproducibility data for our findings. However, some limitations must be acknowledged: (i) our convenience sample of seven participants was relatively small and no prospective power calculation was conducted; (ii) the female participants were limited to overweight patients; and (iii) we were unable to analyze blood samples to investigate the possible mechanisms underlying the changes in appetite in response to CRT (e.g., acylated ghrelin, peptide YY, and glucagon-like peptide 1). Further research is needed to elucidate the acute appetite responses of stroke patients to other exercise modalities (e.g., aerobic exercise or resistance exercise alone). There is also a need for randomized controlled clinical trials to investigate chronic responses to exercise interventions in regards long-term energy balance, cardiovascular risk factors, and mortality.

In conclusion, a single bout of CRT decreases appetite and relative energy intake in stroke patients, with no compensatory increases in absolute energy intake. The decreased appetite in response to CRT seems to be transient, lasting around 9 h. In addition, repeated bouts of CRT on two different days provided similar appetite responses and energy intakes in chronic hemiparetic stroke patients.

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Table 1. Characteristics of the study participants.

Variable	**Mean ± SD** **Total**	**Mean ± SD** **Male**	**Mean ± SD** **Female**
Sample	7	4	3
Age (years)	58 ± 12	53 ± 11	64 ± 11
Time after stroke (months)	91 ± 55	119 ± 52	53 ± 34
Body mass (kg)	69.2 ± 8.4	68.6 ± 11.1	70.0 ± 4.9
Height (cm)	161.9 ± 10.9	167.3 ± 11.4	154.7 ± 5.5
Body mass index (kg/m^2)	26.6 ± 3.7	24.5 ± 3.1	29.3 ± 2.6
Waist circumference (cm)	89.5 ± 12.1	80.7 ± 2.8	98.3 ± 11.1
Hip circumference (cm)	96.7 ± 11.1	96.3 ± 5.0	97.0 ± 16.8
Waist-hip ratio	0.94 ± 0.16	0.84 ± 0.02	1.03 ± 0.20
International physical activity questionnaire (MET-min/week)	796 ± 258	851 ± 346	722 ± 76
Fugl-Meyer´s functional scale (0-100)	87 ± 5	85 ± 7	90 ± 3
Berg´s balance scale (0-56)	55 ± 1	55 ± 1	55 ± 2
Mini-mental State Exam (0-30)	27.2 ± 1.8	27.3 ± 2.3	27.0 ± 1.7
Resting metabolic rate (kcal/day)	1,220 ± 290	1,206 ± 409	1,238 ± 27

FIGURES

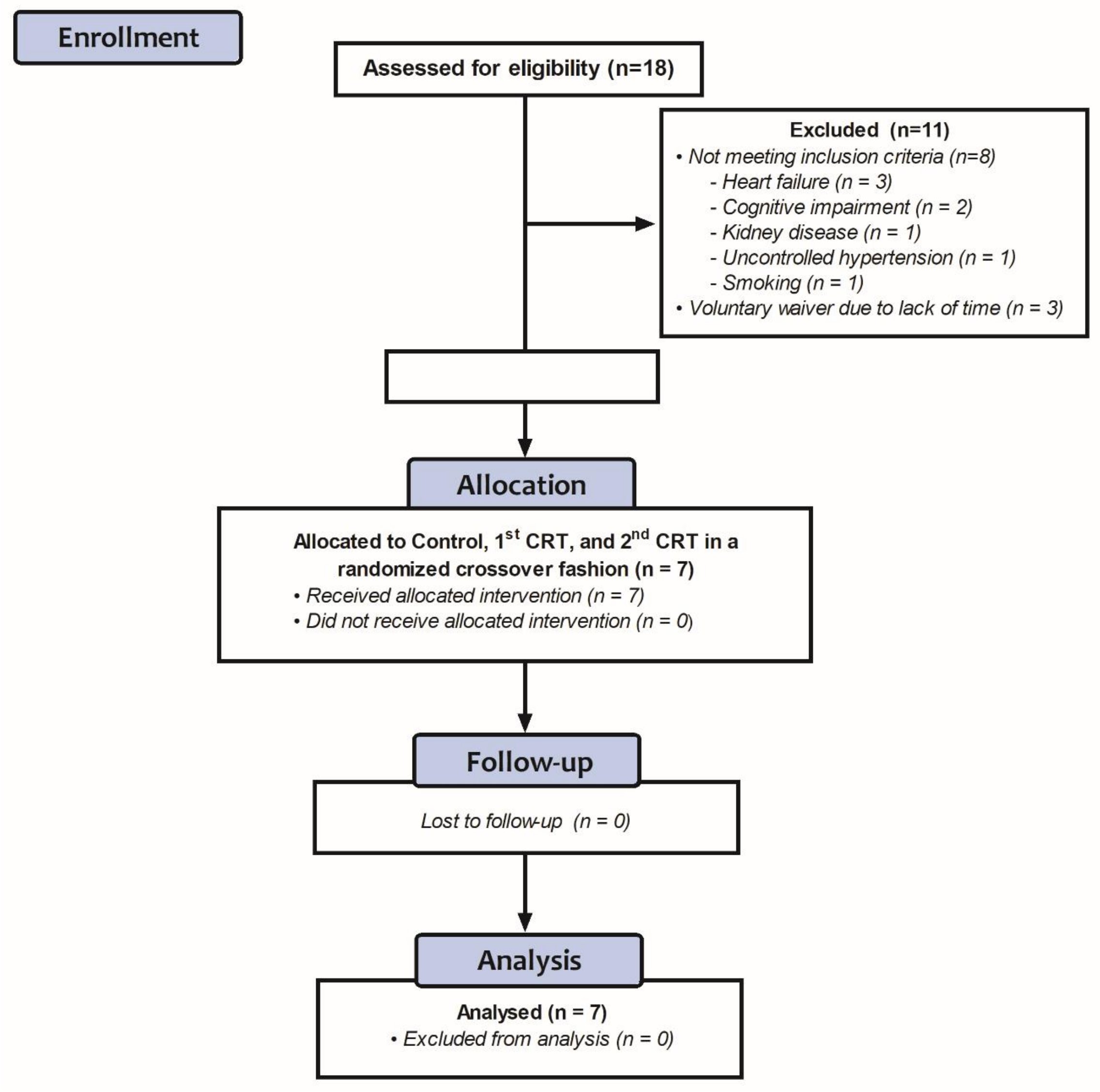

Figure 1: Flowchart for the study.

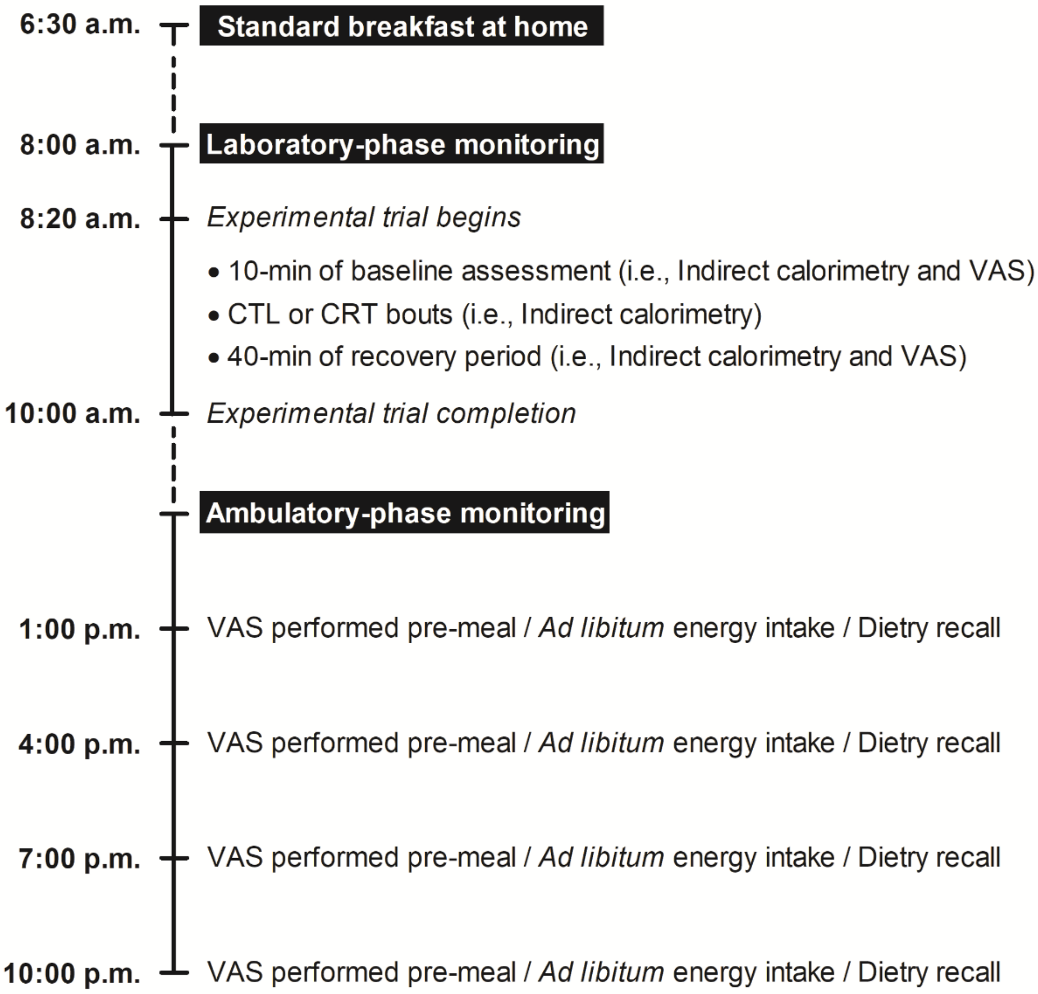

Figure 2. Overview of the study design. VAS: visual analogue scale; CTL: non-exercise control session; CRT: circuit resistance training.

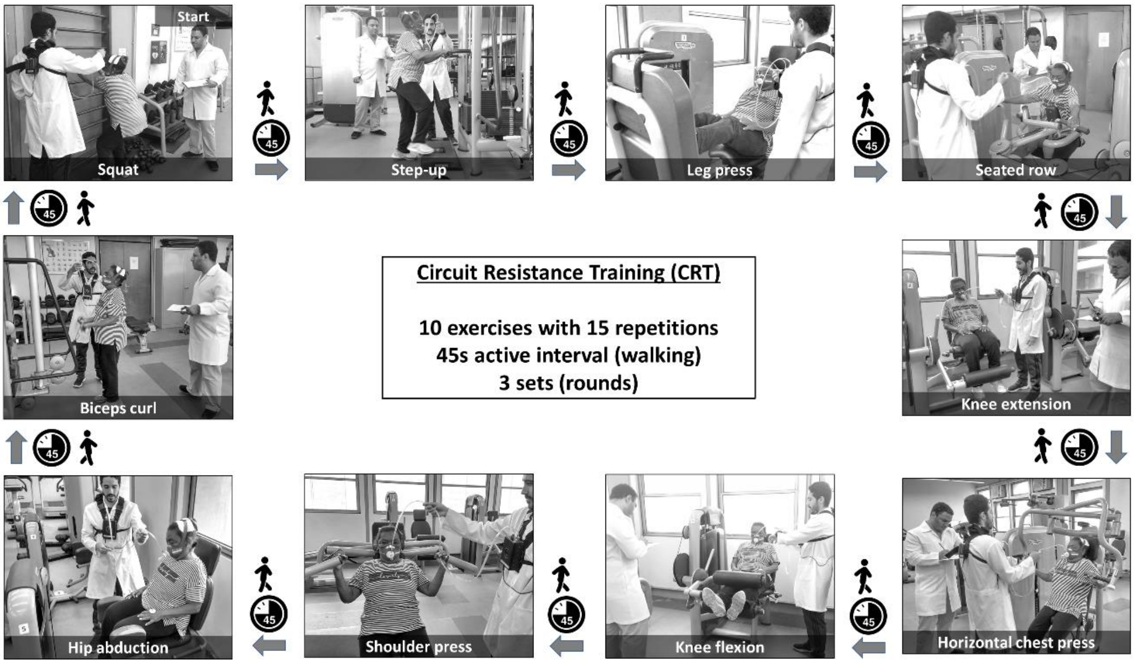

Figure 3. Illustration of exercises included in the circuit resistance training (CRT).

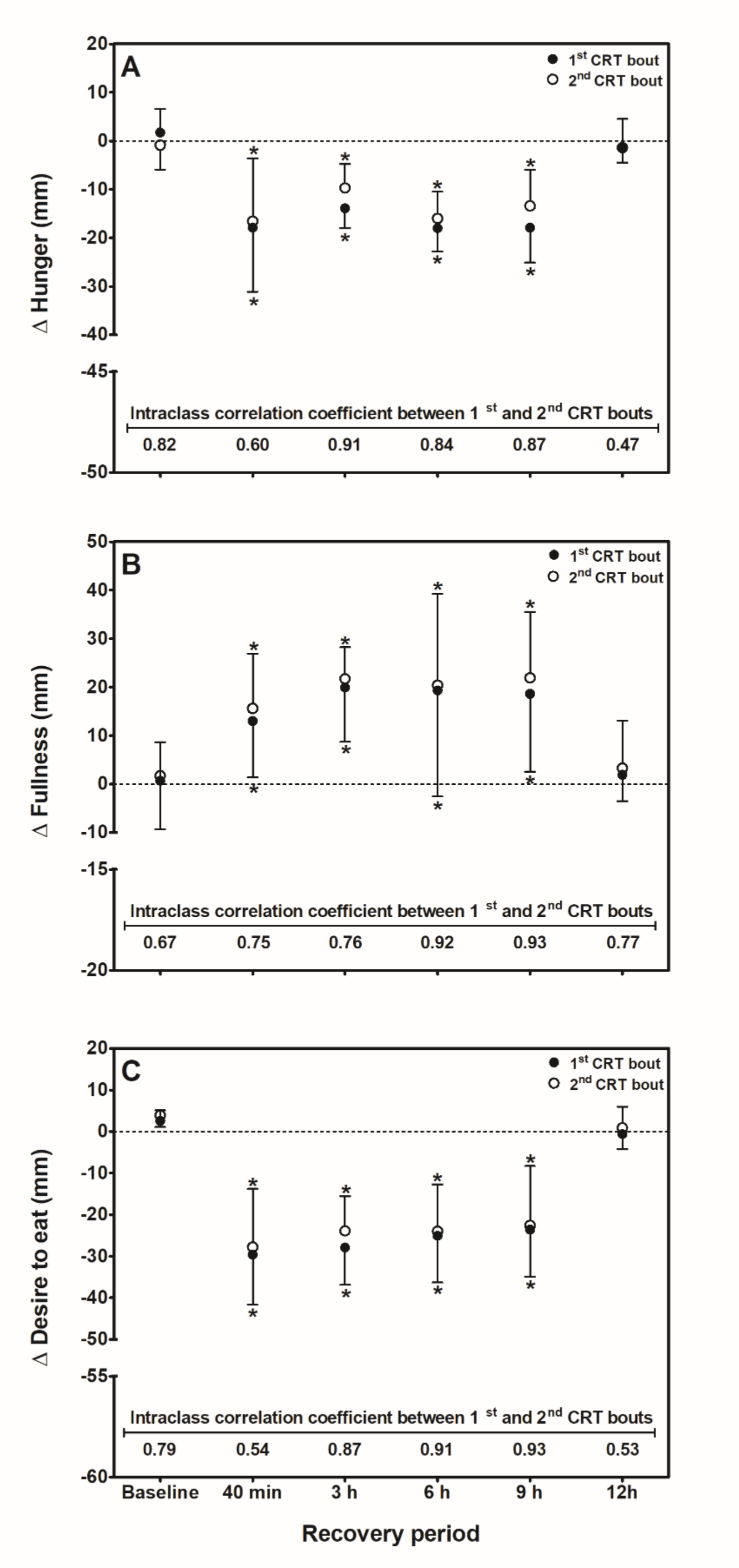

Figure 4. Mean ± SD difference (Δ) in hunger (A), fullness (B) and desire to eat (C) between the 1st and 2nd bouts of CRT *vs*. CTL at baseline and over the 12 h monitoring period. CRT: circuit resistance training; CTL: non-exercise control session; *: Significantly different to CTL ($P < 0.05$).

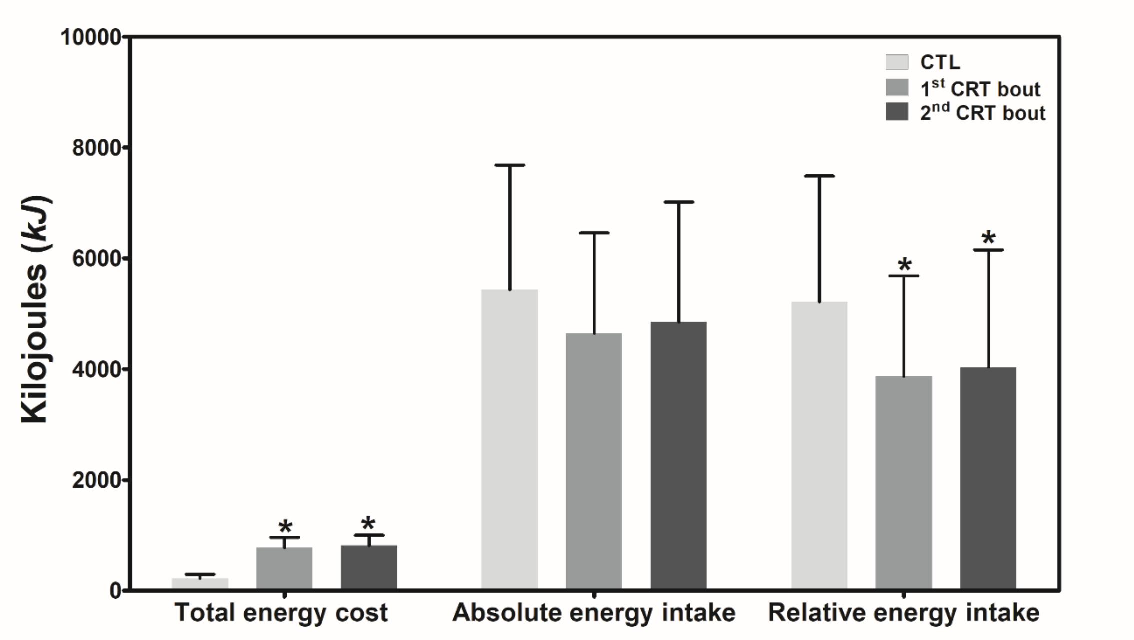

Figure 5. Mean ± SD total energy cost, and absolute and relative energy intakes after CTL and the 1st and 2nd bouts of CRT. CRT: circuit resistance training; CTL: non-exercise control session; *: Significantly different to CTL ($P < 0.05$).