## "No Pain, More Gain"? Affect and Adherence to Exercise in Migraine Patients: A Prospective Cohort Study

"No Pain, More Gain"? Resposta Afetiva e Aderência ao Exercício em Pacientes com Migrânea: Um Estudo Prospectivo

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### ABSTRACT

Objectives: To compare the affective and perceptual responses to a standardized exercise session between episodic migraine patients and nonheadache persons, and its influence on adherence to an 12-week exercise training program. Methods: In a secondary analyses of a prospective cohort enrolled in a clinical trial, we assessed the affective response at rest, at 15th min of exercise, and immediately after an acute 40-min exercise session previously the training program. All measurements were undertaken in headache-free days. Participants were subsequently randomly assigned to a 12-week aerobic exercise-training program, or to a waitlist. In a multiple linear regression model, variables tested as possible predictors of adherence were body mass index, cardiorespiratory fitness, and the perceived exertion and affect scores elicited in the previous exercise session. Results: Fifty-four participants were analyzed for acute exercise session data (mean3SD age: 37.37311.5; mean3SD BMI: 26.734.5). Patients (N=28) and controls (N=26) showed no differences in anthropometric characteristics and cardiorespiratory fitness. Compared to controls, migraine patients showed reduced affective response during and after exercise, but showed no differences in perceived exertion. Twentyfive participants (patients: N=13; controls: N=13) concluded the 12-week exercise-training program. Adherence was lower in migraine group (p = 0.1, d = 0.641). Multiple linear regression analysis showed post-exercise affect score as the only predictor variable of adherence to the exercise-training program ( $\beta$  =0.405, p = 0.040). **Conclusions:** This study indicates that migraine patients have lower affective response to exercise, which was associated with adherence to the training program.

**Keywords:** Psychology; Headache Disorders; Healthy Lifestyle; Sedentary Behavior; Exercise.

### RESUMO

Objetivos: Comparar as respostas de valência afetiva e percepção do esforço entre pessoas com migrânea e sem cefaleias durante uma sessão de exercício padronizada e sua influência na aderência a um programa de 12 semanas de treinamento aeróbio. Métodos: Em análise secundária de uma coorte prospectiva de um estudo clínico, controlado e randomizado, avaliamos a resposta afetiva basal, no 15º minuto de exercício e imediatamente após uma sessão aguda de exercício aeróbio previamente ao programa de treinamento aeróbio. Todas as mensurações foram conduzidas interictalmente. Um modelo de regressão linear múltipla testou as variáveis basais de IMC, aptidão cardiorrespiratória e percepção do esforço e escores afetivos da sessão aguda de exercício como preditoras de aderência ao programa. Resultados: Cinquenta e quatro participantes foram avaliados (média3DP idade: 37,37311,5; média3DP IMC: 26,734,5). Pacientes (N=28) e controles (N=26) não apresentaram diferenças nas características antropométricas e aptidão cardiorrespiratória. Comparado aos controles, pacientes com migrânea exibiram uma resposta afetiva reduzida durante e após a sessão de exercício aguda, mas sem diferenças significativa na percepção do esforço. Vinte e cinco participantes (pacientes: N=13; controles: N=12) concluíram o protocolo de treinamento aeróbio. Aderência foi menor no grupo de pacientes (p = 0,1, d = 0,641). A análise de regressão mostrou a resposta afetiva após a sessão aguda de exercício como única variável preditora de aderência ( $\beta = 0.405, p = 0.040$ ). **Conclusão:** Esse estudo sugere que pacientes com migrânea apresentam uma resposta afetiva reduzida ao exercício, a qual está associada a menor aderências ao programa de treinamento aeróbio.

**Descritores:** Psicologia; Distúrbios da dor de cabeça; Estilo de vida saudável; Comportamento Sedentário; Exercício.

## INTRODUCTION

Even though regular aerobic exercise has been shown effective for migraine prevention (1-4), as a chronic pain condition, migraine may represent an obstacle to physical activity participation. Epidemiological data have shown increased risk for having migraine among individuals in the lowest quintile of cardiorespiratory fitness level (5) and a negative association between migraine prevalence and physical activity levels (6-10). Migraine attacks per se can hinder physical activity participation, and physical activity is considered a trigger factor for around 50-60 % of patients, while 75.6 % and 84.2 % of patients believe that moderate and vigorous exercise can worsen attacks, respectively (11,12). Thus, the prevailing argument to explain this negative relationship between physical activity and migraine has been ascribed to fearavoidance behavior or kinesiophobia (6-12).

Alternatively, another explanation for this negative association between physical activity and migraine might lie in the affective response to exercise. Affective response to exercise refers to a basic affect domain, or the pleasure/displeasure one may feel when exercising, and it has been established as a determinant factor of future adherence to physical activity participation (13,14). Its theoretical framework encompasses the rewarding, self-reinforcing (hedonic) component of the physical activity behavior (15-17). Exercise performed in the positive valence is associated with higher adherence, whereas exercise eliciting negative responses are more likely to be discontinued (15-17). The affective response to exercise is believed to be operationalized under the so-called dual-mode theory (16-18). This theory proposes a dimensional, rather than categorical, measure of affect, which in its turn depends on whether the exercise is performed below, at, or above the ventilatory threshold (16-18). The ventilatory threshold represents a ventilatory parameter that indicates the cardiometabolic turning point marking the transition from aerobic to anaerobic energy metabolism, above which by-products from anaerobic metabolism (e.g., CO<sub>2</sub>, protons, etc.) build-up in the working skeletal muscles, contributing to metabolic acidosis, hyperventilation, limb pain, and early fatigue (16-18). Overall, the affective response is stable and kept on positive valence when the exercise is performed slightly below the ventilatory threshold (or mild to moderate exercise), it largely varies among individuals at the ventilatory threshold (moderate exercise), and decreases to negative valence as exercise intensity surpasses the ventilatory threshold (e.g., vigorous exercise) (18).

Affective response to exercise has never been patients. assessed in migraine Understanding psychological factors related to physical activity behavior in people with migraine has become particularly relevant, since accumulating evidence points to increased risk for mental and cardiovascular diseases in this population (19-22), which in turn can be reduced by regular physical activity (23). Thus, we wondered whether migraine patients would exhibit altered affective response to a single bout of exercise (i.e., acute session) performed at the ventilatory threshold (moderate intensity) compared to non-headache individuals, and whether this previous measure of affect would predict adherence to a subsequent aerobic exercise-training program performed at the same exercise intensity. We hypothesized that individuals with migraine would rate lower affective scores in the exercise session compared to non-headache individuals, and the affective response to exercise would be positively associated with future adherence to the exercise-training program.

## **METHODS**

This is a prospective cohort study using secondary, post hoc analyses of affect and perceptual measures during an exercise session, and their influence in adherence to future exercise participation in a supervised exercise training program. Data were retrieved from patients enrolled in a clinical trial registered in the National Institute of Health (www.ClinicalTrials.gov) under #NCT01972607, and part of the clinical trial results has been published elsewhere (2). The study protocol complied with the Good Clinical Practice Principles and the Helsinki Declaration, and was approved by the Research Ethics Committee of the Federal University of São Paulo/Brazil, registered under #08152011.

### **Participants**

Participants were recruited from São Paulo Hospital's Headache Unit and a tertiary clinic, The inclusion criteria were: individuals aged 20 to 60 years, of both sexes, physically inactive (defined as  $\leq 1 \text{ day/week}$ of leisure-time physical activity the previous 12 months), non-headache individuals and patients with episodic migraine (having 1-14 attacks per month), including migraine without aura, migraine with aura, or presenting both migraine subtypes, according to the 2nd edition of the International Classification of Headache Disorders (24). Exclusion criteria were: taking any prescribed preventive medication, except abortive medication during migraine attacks, taking dietary supplements, pregnancy, clinical history of cardiovascular, pulmonary, metabolic, rheumatic, musculoskeletal, and others neurological diseases, including other headaches. All participants had a neurological and cardiac (electrocardiographic) examination before inclusion in study and gave signed informed consent.

After being screened for inclusion in the study by two headache-trained neurologists (authors RTR and MFPP), all participants were given a headache diary and were examined every 4 weeks (clinical visits) until the end of the study for checking headache status (paperbased headache diaries). Participants who self-reported never having migraine, without any headache in the past 3 months, and did not present any headache in their diaries, were considered as controls.

### **Procedures and Measures**

The cardiopulmonary exercise tests, affect measures, and the aerobic exercise-training program were

conducted at the Center for Studies in Psychobiology and Exercise, a University-based center, on two separated experimental visits. About 1-2 weeks after the screening visit, participants were scheduled for the cardiorespiratory fitness assessment. Around a week later, participants performed an acute, 40-min aerobic exercise session for assessment of the affective response. Figure 1 summarizes the study's design. All measurements were undertaken between 8:00AM and 11:00AM, interictally. All women were assessed within the follicular period of the menstrual cycle for the affective response.

After the acute exercise session, researcher ABO randomly assigned participants (simple randomization, 1:1 assignment rate) to receive a 12-week aerobic exercise-training program or enter a waitlist. An online software generated random numbers, previously attributed as follows: odd numbers = exercise-training program, even numbers = waitlist.

#### **Cardiorespiratory Fitness Assessment**

Participants underwent a maximal cardiopulmonary exercise test on a treadmill (Centurion 300, MICROMED, Brasília, DF, Brazil) with ramp protocol for determination of peak oxygen uptake (VO<sub>2Peak</sub>), a gold-standard measure of cardiorespiratory fitness, and the ventilatory threshold, an amply used cardiometabolic parameter of submaximal exercise intensity. The ventilatory threshold consist of a ventilatory indicator reflecting the skeletal muscle energy metabolism, which set the turning point of exercise intensity above which the metabolic acidosis from anaerobic metabolism supplementation cannot be buffered (25). Determination criteria for VO<sub>2Peak</sub> consisted of meeting at least two of the following criteria: 1) to reach the maximal age-predicted heart rate (220-age); 2) respiratory exchange ratio > 1.1; 3) rate of perceived exertion (RPE)  $\geq$  18. The ventilatory threshold was determined adopting the ventilatory equivalents method, defined as the stage where the first rise in the ventilatory equivalent of O2 (VE/VO2) occurs without concurrent rise in the ventilatory equivalent of CO2 (VE/ VCO2) (25). Tests were conducted by a cardiologist and exercise physiologist, not informed about participants assignment and independent of the study.

# Affective Response and Perceived Exertion Assessment

Participants were informed that they would perform a moderate aerobic exercise session according to the current guidelines for exercise prescription. They were also aware that the main goal at this visit was to assess psychological aspects of exercise.

The exercise session consisted of 40 minutes of moderate walking/jogging on treadmill (depending on participant's initial fitness level), composed by 5 minutes of warm-up, 30 minutes inside the aimed intensity, and 5 minutes of cool down period. Intensity was set at the work rate (m.min<sup>-1</sup>), rate of perceived exertion (RPE), and heart rate (HR) corresponding to the ventilatory threshold. The HR was monitored by a heart rate monitor(Polar® Electro, model F5, Finland) and the RPE was assessed by the 20-point Borg's scale (26). The RPE score measured at the last minute of the exercise session was used in the analyses.

Feeling Scale (FS) was used as a measure of affect. FS is a bipolar, Likert-type scale amply used as a broad dimension of pleasure/displeasure (basic affect) during exercise (27). It is composed by 11 points ranging from +5 to -5, with anchors at zero ("Neutral") and at each odd integer, from "Very Good" (+5) to "Very Bad" (-5). The affective response was assessed by two experienced exercise physiologists (ABO, DLG), randomly assigned (coin flipping) to conduct each experiment. FS was employed at three time points: at rest, just before the exercise initiates (FSREST), at the 15th minute of exercise (FSEXE), and immediately after the exercise cessation (FSPOST). Conversation was limited to answering participants' questions regarding the protocol, and participants were not allowed to listen to music, or to use any portable electronics. Participants experiencing migraine attacks during the exercise sessions were excluded from the analysis.

### **Aerobic Exercise-Training Protocol**

Exercise sessions reproduced the acute exercise session protocol with regard duration and intensity, and were delivered 3 times per week. All exercise sessions were supervised by exercise physiologists (ABO, DLG, and MTM).

### **Statistical Analyses**

Differences between migraine and control groups for anthropometric variables, cardiopulmonary fitness, and adherence for the exercise-training groups were analyzed by independent t-test. Comparisons between groups for affective response were analyzed by repeated-measures ANOVA,with 2 groups x 3 time points (FSREST, FSEXE, and FSPOST); Bonferroni's adjustments were computed for the confidence intervals of multiple pairwise comparisons. If

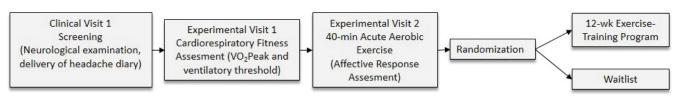


Figure 1. Study's design.

the assumption of sphericity was violated in the repeatedmeasures ANOVAs, the degrees of freedom were adjusted by Greeenhouse-Geisser's correction.

A multiple linear regression model was applied to test the predictors of adherence to exercise (dependent variable). Adherence was defined as the percentage of attendance to the exercise protocol sessions. Predictors variables were, body mass index (BMI),  $VO_{2Peak}$ , RPE, FSREST, FSEXE, and FSPOST. A stepwise method for variables selection was employed in the regression model. Analyses were computed by the SPSS software (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY), and graphs were designed by GraphPad Prism® software (GraphPad Software Inc., Version 5.0, San Diego, CA). A p < 0.05 was considered statistically significant.

## RESULTS

Participants' flow in the study is shown in Figure 2. Fifty-four participants (Male: N = 10, Female: N = 44; mean3SD age: 37.37311.5 and BMI: 26.734.5) were included in the analyses. Migraine (n = 28) and control (n = 26) groups were homogenous regarding sex, age, BMI, cardiorespiratory fitness, as well as there were no difference between groups for the cardiorespiratory data and work rate elicited at the ventilatory threshold (both ~ 55 % of maximal cardiorespiratory fitness, and ~70 % of maximal heart rate) (Table 1).

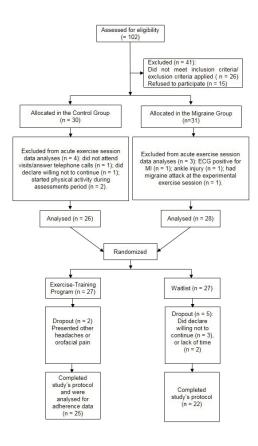


Figure 2. Participants' flow in the study.

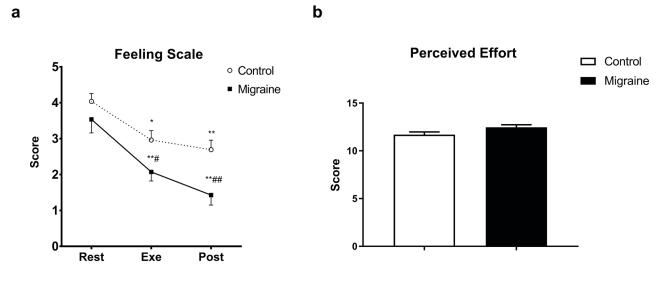
**Table 1.** Participants` anthropometrical, clinical, andcardiorespiratory data.

caraiorespiratory datai			
Variables	Migraine	Control	
Variables	(N=28)	(n=26)	
Anthropometric Data			
Sex (%)			
Male	5(17.9)	5(19.2)	
Female	23(82.1)	21(80.8)	
Age (years)	38.6±12.4	35.9±10.5	
Body Weight (kg)	72.1±16.0	69.7±11.7	
Height (m)	1.62±0.08	1.63±0.08	
BMI (kg/m²)	26.9±5.0	26.4±3.9	
Clinical Data			
Living w/ Disease (yrs)	17.6±11.1	0	
Days with Headaches (/month)	9.5±6.0	0	
Migraine Frequency (/month)	8.6±6.0	0	
Pain Intensity (0-3)	1.58±0.3	0	
Cardiopulmonary Data			
At Peak			
VO <sub>2Peak</sub> (mL.kg.min <sup>-2</sup> )	31.8±6.7	32.5±7.5	
HR (b.p.m)	181.7±15.1	182.8±9.5	
HR (% age predicted)	100.3±6.6	99.5±4.8	
WR (watts)	110.0±32.5	116.2±34.5	
RPE	19.4±0.9	19.3±0.9	
At the Ventilatory Threshold			
VO <sub>2</sub> (% VO <sub>2Peak</sub> )	55.2±9.4	55.4±7.3	
HR (b.p.m)	127.7±17.7	125.1±15.6	
WR (watts)	66.1±20.2	64.2±16.6	
RPE	10.3±2.5	10.1±2.3	

 $\rm VO_{2Peak}$ : Peak oxygen uptake. HR: Heart rate. WR: Work rate. RPE: Rate of perceived effort.

For the affective response to acute exercise, repeated-measures ANOVA of FS showed a main effect of time [F(1, 52) = 37.5; p < 0.001;  $\eta^2$  = 0.64], a main effect of group [F(1, 52) = 10.6; p < 0.002;  $\eta^2 =$ 0.41], and interaction [F(2, 104) = 5.9; p < 0.048;  $n^2 =$ 0.2] (Fig. 3a). Multiple pairwise comparisons showed no differences between migraine and control groups for FSREST (mean3SD = 3.531.9 vs 431.1, respectively, p = 0.262), while there was a significant progressive decline from FSREST to FSPOST for both groups (Fig. 3a). The migraine group had a steeper decline, which was significantly lower than control group for FSEXE (mean3SD = 2.031.3 vs 2.931.3, p < 0.031, respectively) and FSPOST (mean3SD = 1.431.4 vs 2.731.3, p = 0.001, respectively) (Fig. 2a). The RPE at the end of the exercise session was not different between control and migraine groups (mean3SD = 11.631.4 vs 12.431.4, p > 0.05, d = 0.1, respectively) (Fig. 3b).

For the adherence data, twenty-five (migraine: n = 13; control: n = 12) completed the exercise-training program and were analyzed in the regression model. There was no difference between groups for adherence



**Figure 3.** Affective response (a) and perceived effort (b) of a 40-min. aerobic exercise session; Data are expressed as mean $\pm$ SE. \*: p < 0.05 vs REST; \*: p < 0.01 vs REST; #: p < 0.05 vs Control; ##: p < 0.01 vs Control; Multiple pairwise comparisons of repeated-measure ANOVA.

to the exercise program [55.9318.4 % vs 66.4313.0 %, respectively; t(23) = 1.6, p = 0.1, d=0.64], although a large effect size was observed.

In the whole exercise-training cohort, multiple linear regression analysis showed FSPOST the only predictor variable of adherence to subsequent exercise-training program ( $\beta$  = 0.405, *p* = 0.04). Based on the adjusted R<sup>2</sup> data of our model, 12.9 % of variance in adherence was explained by FSPOST. Also, the coefficients of this model showed that, if all the other variables were kept constant, every 1-point drop in the FS score resulted in 4.2 % drop in adherence.

In order to further explore whether adherence could be affected by migraine attacks frequency, we used Pearson's correlations test (as these variables presented normal distribution) for analyses between clinical variables and adherence in the exercise-training migraine cohort. There were no significant correlations between adherence and changes in pre-post values ( $\Delta$  values) for days with migraine (r = -0.01, *p* = 0.981), or migraine frequency (r = -0.18, *p* = 0.544) (Table 2). Neither there were correlations between clinical and affective variables.

## DISCUSSION

Our study shows for the first time a reduced affective response to aerobic exercise, both during and after an acute exercise session, in individuals with migraine compared to non-headache individuals. Also, we provided further evidence to the idea considering the affective response to exercise captured by the feeling scale as a potential determinant factor of physical activity behavior (14-17), by showing a predictive value of post-exercise affect on future adherence to an exercise program. Although physical activity behavior is determined by a myriad of social, cultural, and affective-cognitive factors, the affective response to exercise is a relevant and well-established topic in behavioral research, since it is associated with physical activity participation, and its public health implications in terms of management and prevention of mental and cardiovascular diseases (14-17). Indeed, in recognition of the relevance of affective response on future exercise participation, current exercise prescription guidelines have included the feeling scale as a complementary parameter of exercise intensity (28).

We recognize that physical activity behavior is complex, and in migraine patients, attack-related pain per se can hinder physical activity participation and contribute to fear-avoidance behavior/kinesiophobia (11-13). In fact, anxiety-related processes seem to play a relevant role in physical activity behavior in this population. For example, in a cohort of 100 patients, Farris et al (2019) showed that intentional avoidance of physical activity is prevalent in up to 78 % of patients, and it positively correlates with migraine frequency (11). Still in this study, over 70 % of patients reported avoiding both moderate and vigorous exercise on average 3 times *per* week in the previous month, indicating that intentional avoidance constitutes a relevant factor contributing to lower physical activity in this population (11). In another analysis, the same group found that physical activity avoidance is influenced by anxiety sensitivity, and higher anxiety score were associated with a significant increase in the odds of PA avoidance at both moderate and vigorous intensities, with stronger associations between the domains physical concerns and vigorous exercise avoidance (up to 7.5-fold increase) (12). Although we did not inquire our patients about their believes/perceptions of exercise as a trigger, or anxiety sensitivity scores, migraine frequency or days with migraine had no correlation with adherence

		Adherence to Exercise	Migraine Days	Migraine Frequency	∆ Migraine Days	∆ Migraine Frequency
Adherence	-	-				
	-					
Migraine Days	r	35	-			
	р	.23				
Migraine Frequency	r	37	.86	-		
	р	.20	<.001			
$\Delta$ Migraine Days	r	00	.36	.30	-	
	р	.98	.22	.31		
∆ Migraine Frequency	r	18	.17	.20	.88	-
	р	.54	.57	.49	<.001	

Table 2. Correlations between adherence and migraine clinical data.

to the training program or affective response, and our sample was composed by patients voluntarily interested in exercise who did not report any attack attributed to physical exercise (based on headache diaries data). As such, the results found here add a new perspective in understanding the negative relationship between migraine and physical activity levels, which to date has been unanimously ascribed to fear-avoidance/anxiety mechanisms. The affect-based process contemplates the hedonic, self-reinforcing properties of physical activity (14-18), which are thought to be mediated by common neurophysiological mechanisms disrupted in migraine pathophysiology, such as monoaminergic, opioidergic, and endocannabinoidergic signaling (2,4). Therefore, it is likely that altered affective processes occurring during the physical exercise session could also influence this negative relationship between migraine and physical activity. This merits further investigation.

Lastly, but not least, anxiety-related processes may eventually underlie the negative affect-exercise adherence relationship, as anxiety sensitivity has shown to moderate the affective response to exercise in other clinical populations (29). Farris's group showed that in low-active smokers seeking treatment for smoking cessation, anxiety sensitivity negatively associated with physical activity enjoyment scale (PACES) and correlated with anxiety and mood in the 1-mile walk test (29). The authors ponder that anxiety sensitivity may attenuate positive physical feelings (enjoyable feelings) elicited by physical activity, exacerbate the forcasting of negative affective and physical outcomes, resulting in affective states that contribute to avoidance behavior (29).

With regard the exercise intensity and its implication on the affect-adherence relationship, a consistent line of evidence suggests a negative association between vigorous exercise and long-term adherence to physical activity (14-18). These authors criticize the "no pain, no gain" pop culture, arguing that in terms of public health, pursuing higher exercise intensity may be detrimental for assuring long-term adherence to physical activity participation. Exercise performed at the ventilatory threshold, as used here, prevents the build-up of byproducts and metabolites from anaerobic metabolism, and hence hyperventilation, limb pain, and early fatigue (19). It also promotes cardiorespiratory fitness and is a standardized cardiometabolic parameter of exercise intensity. Nonetheless, affective response at this intensity largely varies in the population (19). On the other hand, as vigorous exercise may also promote specific therapeutic effects, recent work has aimed at manipulating exercise prescription in order to conceive vigorous exercise with positive affect, and hence, promote long-term adherence to high intensity exercise (30). These authors have employed repeated, short high-intensity bouts of exercise (also known as high intensity interval training, or "HIIT") (30). In the context of migraine, data from clinical trials have shown preventive effects with either moderate (i.e., at the ventilatory threshold) (2-4), or vigorous exercise performed as HIIT ( $\geq$  90% of maximal HR) (31). In the later study, vigorous exercise performed with the HIIT approach promoted superior clinical effects on migraine frequency, cardiorespiratory fitness, and retinal blood vessels dilation, suggesting greater clinical and cardiovascular effects compared to moderate exercise (31). Because to date there is no study comparing long-term adherence between vigorous vs moderate exercise in migraine patients, these data underscore the need for further studies aiming at investigating psychological and physiological outcomes from different exercise prescriptions in migraine trials, and developing new strategies to increase the affective component of physical activity.

The affective response and adherence to exercise should be further investigated in people with migraine. As outlined by Farris et al (2019), clinicians should aim at managing the subjective appraisal of bodily sensations by incorporating psychoeducation strategies to reinforce the clinical benefits of regular physical activity (2-3), adjusting current exercise prescriptions frames to fit gradual exposure approaches (i.e., desensitization), and by comparing beliefs of migraine trigger effects of physical activity with objective data (12). We propose for the newbie patient that is physically inactive or lowactive (i.e., those not meeting the minimum amount of physical activity recommended by health and exercise guidelines), practitioners should preconize a reduced session time for aerobic exercise (e.g., up to 20 minutes), with gradual, progressive load increment until targeted perceptual (e.g., keep between 11 and 13 on 20-point Borg's scale, the verbal anchors "Light" and "Somewhat hard", respectively), affective (e.g., no lower than +1 on feeling scale, the verbal anchor "Good"), and cardiovascular parameters (e.g., not above ventilatory threshold, or ~70 % of maximal age-predicted HR). Other exercise prescription approaches (e.g., HIIT) should be also tested in this population to establish safe, enjoyable, and realistic exercise routines that assure adherence.

One should be aware of several limitations in this study while interpreting these findings. This study found a large effect size for the affect variables outcome, but the small sample size yielded underpowered data ( $\beta$  = 0.73), and limit extrapolation from the regression model. From clinical practice, we perceive that migraine patients interested in participating in studies with physical exercise represent a minority of this population, and this may constitute selection bias. Additionally, based on headache diaries checking, physical activity was not a trigger among the patients of this study, most participants were women, and there were some restrictive inclusion criteria. All these factors limit the generalizability of our results. Importantly, the expectation towards improvement in headaches through exercise training might have rendered patients more motivated than control individuals. Yet, if this was true, our results would be underestimated. Another limitation concerns to performance bias, as the experimenters that conducted the exercise sessions were not blinded to participants' conditions. This could have resulted in unequal attention delivered by the experimenters to the participants, influencing the affect scores. Lastly, although the exercise protocol tried to reproduce a regular aerobic exercise session, it is not possible to exclude the influence of factors related to the laboratory/experimental settings.

The strengths of this study are the prospective design, the use of gold-standard measure of cardiorespiratory fitness, and standardized exercise testing and prescription based on ventilatory threshold, which allowed us to compare subjective psychological parameters in response to an objective, physiologic stimulus.

## CONCLUSIONS

In conclusion, the affective response to an aerobic exercise of equivalent physiological intensity is reduced in migraine patients compared to non-headache individuals, and predicted adherence to future participation in an exercise-training program. Interventions with physical activity/exercise should adopt the feeling scale as a complementary parameter of exercise intensity and exploit activities that elicit higher affective responses.

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