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RESEARCH ARTICLE

Dynamics of pleasure–displeasure at the limit of exercise tolerance: conceptualizing the sense of exertional physical fatigue as an affective response

Mark E. Hartman[1,2], Panteleimon Ekkekakis[2,*], Nathan D. Dicks[3] and Robert W. Pettitt[4]

ABSTRACT

The search for variables involved in the regulation and termination of exercise performance has led to integrative models that attribute a central role to the brain and utilize an array of psychological terms (e.g. sensation, perception, discomfort, tolerance). We propose that theorizing about exercise regulation would benefit from establishing cross-disciplinary bridges to research fields, such as affective psychology and neuroscience, in which changes along the dimension of pleasure–displeasure are considered the main channel via which homeostatic perturbations enter consciousness and dictate corrective action (slowing down or stopping). We hypothesized that ratings of pleasure–displeasure would respond to the severity of homeostatic perturbation and would be related to time to exhaustion during exercise performed at an unsustainable intensity. In a within-subjects experiment (N=15, 13 men and 2 women, age 23.4±2.2 years; maximal oxygen uptake 46.0 ±8.0 ml kg^{-1} min^{-1}), we compared the slope of ratings of pleasure–displeasure (acquired every 1 min) during cycling exercise at a power output 10% above critical power until volitional termination under glycogen-loaded and glycogen-depleted conditions. As hypothesized, ratings of pleasure–displeasure declined more steeply under glycogen depletion (P=0.009, d=0.70) and correlated closely with time to exhaustion under both glycogen-loaded (r=0.85; P<0.001) and glycogen-depleted conditions (r=0.83; P<0.001). We conclude that in exercise, as in other domains, changes in pleasure–displeasure may be the main channel via which homeostatic perturbations enter consciousness. This proposal may have important implications for conceptualizing and identifying the neurobiological mechanisms of the sense of exertional physical fatigue.

KEY WORDS: Homeostasis, Perceived exertion, Oxygen uptake kinetics, Slow component

INTRODUCTION

Identifying the factors that regulate and limit exercise performance would have significant implications not only for academic disciplines, such as integrative biology (Irschick and Higham, 2016) and exercise science (Gabriel and Zierath, 2017), but also for many types of athletic competition and, crucially, for the treatment of clinical conditions characterized by reduced exercise capacity and, consequently, reduced quality of life. Given the high stakes, the search has been long and vigorous but has yet to yield signs of substantive progress.

In the 1930s, Lehmann et al. (1939) gave three young men methamphetamine (a strong centrally acting stimulant then sold legally in tablet form) and found that, although the drug had minimal cardiovascular and metabolic effects, their endurance performance was extended substantially. This observation led the authors to propose that, when individuals decide to discontinue the exercise in the absence of the drug, there is always an energy reserve that is left unused. Thus, they postulated that the point at which exercise terminates is 'never an absolute fixed amount of work' (Lehmann et al., 1939, p. 690); instead, exercise is stopped when the balance between positive factors (such as determination and willpower) and negative factors (such as muscle pain and fatigue) tips toward the latter. Lehmann et al. (1939) considered the energy reserve a safety buffer, noting that by abolishing the subjective barrier (i.e. interfering with the balance between the positive and negative factors), the drug can pose a risk.

Since then, the search for the factors that regulate and limit exercise performance has proceeded in various directions, with some researchers concentrating on processes within the working muscles and others taking a broader, integrative view akin to the perspective adopted by Lehmann et al. (1939). Synthesis of the various perspectives into a unifying model, however, has been elusive. Some authors have questioned whether the brain plays an important role in the regulation of exercise performance (Weir et al., 2006), have rejected the notion that evolution could have favored a mechanism that would leave energy reserves unused (Shephard, 2009), and have insisted that, given good health, youth and familiarity with strenuous exercise, the termination of exercise is 'purely "physical" and can be understood through bioenergetic, muscle metabolite/substrate, and neuromuscular considerations' (Burnley and Jones, 2018, p. 10).

Other authors have espoused models in which exercise performance is regulated by the brain, asserting that the brain constantly monitors the totality of peripheral physiological functions, generates subjective states that reflect the condition of the body, and terminates exercise before homeostatic perturbation can cause irreparable harm by eliciting a sense that continuation would be intolerable (Jones and Killian, 2000; Taylor et al., 2016). For example, Gandevia (2001) acknowledged that, among other factors, exercise terminates when 'a "sensory" or tolerance limit' is exceeded, defined as the point at which 'the consequences of continuing the task become sufficiently unattractive' (Gandevia, 2001, p. 1766). According to Gandevia (2001), the brain will 'act to

[1]Viola Holbrook Human Performance Laboratory, Minnesota State University, Mankato, MN 56001, USA. [2]Department of Kinesiology, Iowa State University, Ames, IA 50011, USA. [3]Department of Health, Nutrition, and Exercise Sciences, North Dakota State University, Fargo, ND 58102, USA. [4]Office of Research and Sponsored Projects, Rocky Mountain University of Health Professions, Provo, UT 84606, USA.

*Author for correspondence (ekkekaki@iastate.edu)

P.E., 0000-0003-4260-4702

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"protect" the muscle … at the expense of truly maximal performance' (Gandevia, 2001, pp. 1771-1772) and, therefore, 'exercise stops when the muscle has not fatigued sufficiently at a peripheral level to limit the performance of the task' (Gandevia, 2001, p. 1772). Echoing the rationale suggested six decades earlier by Lehmann et al. (1939), Gandevia (2001) speculated that this premature termination likely confers an 'evolutionary advantage' as the continuation of exercise would put the muscle in a 'catastrophic state' from which recovery would be 'delayed or impossible' (Gandevia, 2001, p. 1772).

In recent years, authors have implicated 'conscious sensations of muscle discomfort and fatigue' (Taylor et al., 2016, p. 2304) in exercise performance, have postulated a 'sensory tolerance limit' as a key regulator of exercise intensity (Hureau et al., 2018), have likened bodily sensations to a 'safety switch' that can be overridden by centrally acting drugs (Meeusen and Roelands, 2018), and have asserted that, by manipulating bodily afferents, the brain can 'allow' or 'tolerate' a higher work output from the muscles (Amann and Dempsey, 2016). However, the brain mechanisms involved in linking interoceptive afferents to subjective states (e.g. discomfort, sensation, tolerance) and ultimately to the regulation of exercise performance are presumed to remain largely 'unknown' (Amann, 2012, p. 834).

The absence of connections between the study of exercise regulation and the study of affect-related subjective states may be attributed to the fact that, until now, researchers have focused on a different construct, namely ratings of perceived exertion (Borg, 1998). Ratings of perceived exertion have been accepted as a reportedly 'suitable means to quantify an individual's relative "proximity" to the sensory tolerance limit' (Hureau et al., 2018, p. 17). This convention likely draws from the 50 year history of the concept of perceived exertion in exercise science. We propose that research on the regulation of exercise performance may gain additional insights by (a) considering changes along the dimension of pleasure–displeasure as a subjective indicator of homeostatic perturbations and (b) turning to the knowledge base of affective psychology and neuroscience, fields that have long histories of investigating the psychological processes, neuroanatomical substrates and neurophysiological mechanisms involved in converting interoceptive afferents to such subjective states as discomfort, sensation and tolerance.

Considering affective states as regulators of exercise performance has several advantages. In the rationale proposed by Lehmann et al. (1939) and echoed by contemporary authors who espouse similar views (Gandevia, 2001; Hureau et al., 2018; Jones and Killian, 2000), exercise is stopped when the positives associated with continuation (e.g. future pride, praise, rewards) are outnumbered or overpowered by the negatives (e.g. current displeasure, exhaustion, pain). Pleasure–displeasure is supremely positioned to serve as the 'common currency' (Berridge and Kringelbach, 2015; Cabanac, 1992) that would enable the conversion of these heterogeneous considerations to a common scale, so they can be compared. This addresses the problem of the 'final common path' first identified by Sherrington (1906) regarding the neural control of a single muscle and later generalized by McFarland and Sibly (1975) to whole-body behavior. At the level of the single muscle, this problem lies in the fact that, while the muscle may be subject to multiple, possibly antagonistic, reflexes, it can only 'do' one thing at a time (i.e. contract or relax). Therefore, some upstream 'node' in the nervous system, which functions on the basis of a specific decision rule, must integrate the various inputs, compare them in terms of one or more features (e.g. their intensity), and assign priority to one action over others. In the more complex case of whole-body behavior, the organism may need to satisfy multiple, possibly incompatible, objectives but can enact only one behavior at a time. For such a system to function, it is again necessary to interject a 'node' that gives access to the final common path (the movement of the body) only to the objective ranked most highly on a common scale. That pleasure–displeasure can serve as the 'common currency' in regulating exercise (e.g. balancing the need to decrease intensity to avoid fatigue with the need to increase intensity to keep warm in a cold environment) has been demonstrated since the early 1980s (Cabanac and LeBlanc, 1983).

Additionally, pleasure–displeasure is theorized to be the channel via which homeostatic perturbations enter consciousness and dictate corrective action (Damasio and Carvalho, 2013; Strigo and Craig, 2016). Unlike perceptions of exertion, which increase linearly with exercise intensity, ratings of pleasure–displeasure exhibit a quadratic decline above the gas exchange threshold, a pattern that becomes homogeneously precipitous as intensity approaches maximal capacity, mirroring the severity of homeostatic perturbation (Ekkekakis et al., 2005, 2011).

Interestingly, just like research examining the factors involved in the regulation and termination of exercise has overlooked affective states, affective psychology and neuroscience investigating the links between homeostatic perturbations and affect have overlooked exercise. Authors who have considered affect as a primordial element of consciousness linked to the maintenance of homeostasis have devoted little (Panksepp, 2005) or no attention to exercise (Denton et al., 2009), despite its vital role in hominid evolution (Bramble and Lieberman, 2004), focusing instead on other human universals, such as hunger and thirst.

The present study

In high-intensity, constant-load exercise, power (P) and the time limit of exercise tolerance (t_{LIM}) exhibit a well-characterized hyperbolic relationship described by the formula $(P-CP)t=W'$, where CP is the level of 'critical power' (the highest rate of work that is sustainable over a long time without causing the energetic system to 'max out') and W' is the curvature constant, which represents the amount of work that can be performed above CP (Moritani et al., 1981; Whipp et al., 1982a,b). Physiologically, W' is theorized to correspond to the finite amount of energy that can be utilized above CP, namely energy from phosphate sources (primarily phosphocreatine), glycogen available for anaerobic glycolysis and a limited oxygen store (bound to myoglobin and hemoglobin in venous blood). The severity of homeostatic perturbation is presumed to be a joint function of the gradual depletion of these energy resources and the accumulation of metabolites, such as hydrogen ions, inorganic phosphate, adenosine diphosphate and extracellular potassium (Gregory et al., 2015; Light et al., 2008; Pollak et al., 2014). Above CP, as the energy resources are depleted and the levels of metabolites rise, the so-called 'slow component' of oxygen uptake, likely the result of the recruitment of less efficient fast-twitch (type II) muscle fibers, drives oxygen uptake to its peak value (Jones et al., 2010, 2011). Although the hyperbolic model of the $P-t_{LIM}$ relationship fits empirical data well, there is still considerable individual variability in W' and, therefore, t_{LIM} even among samples of participants that are homogeneous with respect to training history and maximal exercise capacity, such that the point of exercise termination is best described as the 'limit of tolerance' rather than the maximal physiological limit of exercise capacity (Jones et al., 2010). Researchers have demonstrated that, at the point at which participants choose to terminate exercise, there is still a

'large functional reserve' (Morales-Alamo et al., 2015, p. 4642) as anaerobic glycolysis continues and the rate of ATP resynthesis still exceeds the rate of consumption.

The primary aim of the present study was to investigate the utility of ratings of pleasure–displeasure as an indicator of the severity of the homeostatic perturbation near the limit of exercise tolerance. To this end, we examined the association between the rate of change (defined as the slope over time) in ratings of pleasure–displeasure during exercise performed above CP with the time to exhaustion (t_{LIM}) and the amount of work performed (W'). To assess the robustness of this association, we experimentally varied the degree of homeostatic perturbation by manipulating the glycogen stores, creating a glycogen-depleted (GD) and a glycogen-loaded (GL) condition. Glycogen depletion is known to result in shorter t_{LIM} (Bergström et al., 1967; Gollnick et al., 1974; Miura et al., 2000). We theorized that ratings of pleasure–displeasure would track the severity of the homeostatic perturbation and exhibit a close correspondence to the impairment in exercise performance. Therefore, our first hypothesis was that the rate of decline in ratings of pleasure–displeasure would be steeper in GD than in GL. Our second, related, hypothesis was that the slopes of ratings of pleasure–displeasure would correlate with time to exhaustion (t_{LIM}) during exercise above CP. For simplicity, possible allostatic and rheostatic patterns were not considered.

A secondary aim was to examine the relationship of parameters of oxygen uptake kinetics, in particular the amplitude of the so-called 'slow component' of oxygen uptake, to ratings of pleasure–displeasure during exercise above CP. During constant-work exercise above CP, oxygen uptake cannot attain a steady state. The slow component of oxygen uptake represents an additional gradual increase, beyond the primary component (the rapid increase over the first ∼3 min), causing oxygen uptake to rise continuously toward its peak value. Therefore, the amplitude of the slow component is considered an important determinant of exercise performance (Burnley and Jones, 2007, 2018; Jones and Burnley, 2005; Jones et al., 2010). The slow component is presumed to reflect a composite of several factors, including muscle fiber recruitment, lactate accumulation, catecholamine levels and rises in core and muscle temperature (Barstow et al., 1996; Jones et al., 2011; Pringle et al., 2003). Regardless of whether glycogen depletion does (Carter et al., 2004) or does not (Bouckaert et al., 2004) alter the amplitude of the slow component of oxygen uptake, our third hypothesis was that individuals exhibiting a smaller amplitude would also report a less steep decline in pleasure–displeasure over time.

MATERIALS AND METHODS

Participants

Given the absence of a previous study investigating the effects of glycogen depletion on ratings of pleasure–displeasure during exercise above CP and until volitional termination, sample size calculations were based on a within-subjects comparison of declines in ratings of pleasure–displeasure between two 15 min high-intensity exercise conditions culminating in heart rates of ∼173 and ∼183 beats min^{-1} (Ekkekakis et al., 2008), which resulted in a large effect (d=0.81). Therefore, considering a large effect for a comparison between two dependent means (d=0.80), α=0.05 and 1−β=0.80, a sample size of 15 was required to yield sufficient statistical power.

Accordingly, the sample consisted of 15 volunteers (13 men, 2 women; age: 23.4±2.2 years; height: 177.5±8.4 cm; body mass: 77.6±12.4 kg; maximum oxygen uptake rate, $\dot{V}_{O_2,max}$: 46.0±8.0 ml kg^{-1} min^{-1}). Average self-reported physical activity was rated as 6±2 on a 15-point rating scale (Jamnick et al., 2016), indicating participation in vigorous activity, such as running, swimming or cycling, between 60 and 180 min per week. All participants completed a medical history questionnaire to ensure they did not suffer from cardiovascular, metabolic or renal disease, and had no signs or symptoms suggestive of such diseases (American College of Sports Medicine, 2018). The study was approved by the Institutional Review Board. Participants were informed of all experimental procedures and possible risks before providing written informed consent.

Measures and procedures

Overview

Participants completed three cycling exercise protocols on separates days, with at least 4 days between visits. Each exercise was performed on the same electronically braked cycle ergometer (Excalibur Sport, Lode, Groningen, The Netherlands) and expired gases were analyzed using the same metabolic cart (TrueOne 2400, Parvomedics, Logan, UT, USA), which was calibrated before each test in accordance with guidelines provided by the manufacturer. Participant diet data were obtained using a 3 day food diary. The validity of the food diary was evaluated with a 24 h recall interview (Penn et al., 2010). Dietary intake was analyzed for total caloric intake and macronutrient content using commercial software (The Food Processor Nutrition Analysis Software, ESHA Research, Salem, OR, USA). The two remaining laboratory visits were counterbalanced and consisted of an exercise bout at a power output 10% above CP until volitional termination in a GL or GD condition.

3 min all-out test (3MT)

During the first visit, participants completed a cycling 3MT with a verification bout for the determination of CP, work performed above CP (W') and maximal oxygen uptake ($\dot{V}_{O_2,max}$) (Clark et al., 2013; Dicks et al., 2016; Vanhatalo et al., 2007). The load for the 3MT was derived from a series of regression equations which included height, body mass and physical activity rating (Dicks et al., 2016; Jamnick et al., 2016). Following a 5 min warm-up at 50 W, participants were instructed to pedal at their maximal cadence and put forth an all-out effort for 3 min. No performance-related feedback was provided other than cadence (Halperin et al., 2015). Following the 3MT, participants completed a 3 min active-recovery stage at 50 W. During recovery, the raw power data from the cycle ergometer were exported and filtered through a preset, two-pass Butterworth filter with a 5 Hz cutoff (Johnson et al., 2011). The end power (last 30 s) of the 3MT was used to determine CP, and integrated power>CP during the initial 150 s was used to determine W' expressed in joules (Burnley et al., 2006; Vanhatalo et al., 2007). Following recovery, participants performed a verification bout at 10%>CP at their preferred cadence until volitional termination. $\dot{V}_{O_2,max}$ was defined as the highest 15 s average during the verification stage (Clark et al., 2013; Dicks et al., 2016; Midgley et al., 2007).

GL and GD conditions

Manipulation of glycogen levels was accomplished via a combination of diet and exercise. Glycogen loading was ensured by increasing carbohydrate intake by 50% for 3 days before testing without altering the total energy intake and the percentage of calories from protein (Sherman, 1991). Increasing carbohydrate intake has been found to significantly increase muscle glycogen stores with minimal impact on the heart rate and oxygen uptake response to vigorous exercise (Kavouras et al., 2004). Dietary fat

was decreased, to accommodate the increased intake of carbohydrates. Sports beverages were provided as the additional carbohydrate source. GD was ensured by performing a glycogen-depleting exercise protocol (see below; Miura et al., 2000) while maintaining normal macronutrient intake for the 3 days leading up to the GD condition. A second 3 day food diary was used to assess adherence to the GL and GD dietary requirements.

The GL condition consisted of an exercise bout at 10%>CP until volitional termination. Baseline capillary blood was acquired and analyzed for lactate (bLac; Accutrend Plus, Roche Diagnostics, Mannheim, Germany) 5 min before exercise and within 30 s post-exercise. Gas exchange data were collected using the same metabolic analyzer as in the first visit.

Ratings of pleasure–displeasure were acquired using the Feeling Scale (FS; Hardy and Rejeski, 1989) at rest (5 min before exercise) and every minute during exercise. The FS is an 11-point, single-item, bipolar rating scale commonly used for the assessment of affective valence (pleasure–displeasure) during exercise. The scale ranges from +5 to −5. Anchors are provided at zero ('neutral') and all odd integers, ranging from 'very good' (+5) to 'very bad' (−5).

Following baseline assessment, participants warmed-up on the cycle ergometer for 5 min at 50 W. Following the warm-up, the work rate instantly increased to 10%>CP. Participants were instructed to maintain their preferred cadence and to put forth their best effort until they could no longer continue.

The GD condition started with a glycogen-depletion exercise protocol (Miura et al., 2000), which consisted of 60 min of cycling at 85% of CP followed by 30 min of seated rest. Water was available *ad libitum*. Following the rest period, participants completed the exercise bout at 10%>CP until volitional termination, in identical fashion to the GL condition.

Data reduction

The $\dot{V}_{O_2}$ data from GD and GL exercise bouts were modeled to characterize the oxygen uptake kinetics following the methods described by Bell et al. (2001). Breath-by-breath $\dot{V}_{O_2}$ data were linearly interpolated to provide second-by-second values. Phase 1 data (i.e. the cardiodynamic component), from the first ∼20 s of exercise, were omitted from the kinetics analysis because phase 1 is not directly representative of active muscle oxygen utilization (Linnarsson, 1974; Whipp et al., 1982a,b). Using non-linear least-squares regression (gnuplot 5.0), the $\dot{V}_{O_2}$ responses were analyzed for the presence of phase 2, the 'primary component', using monoexponential modeling (see Eqn 1 below) and for the presence of phase 3, the 'slow component', using biexponential modeling (see Eqn 2 below). We first modeled the data as a monoexpoential response (primary component only) and identified the characteristics of the monoexponential region using the following initial estimates; primary time delay (TD_p), 20 s; time delay for the slow component (TD_s), 180 s; primary time constant (τ_p), 30 s. Next, we modeled the data as a biexponential response (primary and slow component) using the initial estimates of the primary component with the addition of the slow-component time constant (τ_s; 180 s). gnuplot identified the breakpoint between the two phases using the following criteria: a systematic increase in $\tau\dot{V}_{O_2}$ and $\Delta\dot{V}_{O_2}$ sum of squares, a decrease in variance, a systematic rise in the χ^2 for the fitted model, and a departure from the even distribution of residuals around zero:

$$\dot{V}_{O_2}(t) = a0 + a_p \times [1 - e^{-t/\tau_p}], \quad (1)$$

$$\dot{V}_{O_2}(t) = a0 + a_p \times [1 - e^{-t/\tau_p}] + a_s \times [1 - e^{-(t-TD_s)/\tau_s)}], \quad (2)$$

where $\dot{V}_{O_2}(t)$ represents the absolute $\dot{V}_{O_2}$ at a given time (t) and $a0$ is the virtual $\dot{V}_{O_2}$ at 20 s. The parameters a_p and a_s are the asymptotic amplitudes for the exponential terms fitting the primary and slow component, respectively (calculated relative to the starting point of 20 s); τ_p and τ_s are the respective time constants; and TD_p and TD_s are the respective time delays for the primary and slow component (see Fig. 1). The end-exercise $\dot{V}_{O_2}$ was defined as the mean $\dot{V}_{O_2}$ measured over the final 15 s of exercise.

Following the modeling of monoexponential and biexponential $\dot{V}_{O_2}$ responses, we determined which model better characterized the response of each participant. Best-fit parameters were chosen by the values that minimized the residual sum of squares and χ^2 statistic. A smaller χ^2 and mean squared error indicated a better fit. As a validity check, models were run with the slow component τ both underestimated (e.g. 15 s) and overestimated (e.g. 70 s), to ensure that the minimized residuals were not due to locally minimized least-squares residuals. A maximum of 100 iterations was allowed before the model was deemed non-converging, indicating a poor fit.

Statistical analyses

Manipulation checks were conducted to assess the equivalence of dietary conditions. Specifically, analyses of variance (ANOVA) with repeated measures were used to compare mean dietary intake for fat, protein, carbohydrates and total kcal for baseline, pre-GD and pre-GL conditions. To check the effects of the glycogen-depletion manipulation, a series of repeated-measures ANOVA compared the main effects of condition (GL versus GD) for $\dot{V}_{O_2,peak}$, end bLac, peak respiratory exchange ratio (RER_{peak}), peak ventilation ($\dot{V}_{E,peak}$), peak carbon dioxide production rate ($\dot{V}_{CO_2,peak}$), peak ventilatory equivalent for carbon dioxide ($\dot{V}_E/\dot{V}_{CO_2,peak}$) and the parameters of the oxygen uptake kinetics defining the monoexponential or biexponential fit.

Given that t_{LIM} varied among participants, changes in FS ratings over time were expressed as the individual slope over time (ΔFS min^{-1}). A repeated-measures ANOVA was used to examine differences between conditions for the FS slope (Hypothesis 1). Moreover, for both conditions, we examined Pearson correlations between the FS slope and t_{LIM} (Hypothesis 2) and between the FS slope and the amplitude of the slow component (Hypothesis 3).

RESULTS

Participant physiological characteristics

The CP, W' and $\dot{V}_{O_2,max}$ values derived from the 3MT were 196.6±50 W, 10.2±3.8 kJ and 46.0±7.8 ml kg^{-1} min^{-1}, respectively.

Manipulation checks

The glycogen-depletion manipulation was successful in producing two experimental conditions with distinct levels of homeostatic perturbation. Analysis of the 3 day dietary recall data indicated that participants consumed 50% more carbohydrates prior to the GL (304.9±95.7 g) than to the GD condition (203.5±108.4 g; $F_{1,14}$=11.314, P=0.005, d=0.99). The GD condition evoked lower values for $\dot{V}_{CO_2,peak}$, RER_{peak}, bLac and $\dot{V}_{O_2,peak}$ (see Table 1). More importantly, as expected, t_{LIM} was shorter for GD than for GL ($F_{1,14}$=6.834, P=0.021, d=0.42).

Hypothesis 1

No differences were found between conditions for baseline FS ($F_{1,14}$=0.208, P=0.655) or end-of-exercise FS ($F_{1,14}$=2.154, P=0.164; Table 1). However, as hypothesized, the comparison of the FS slopes during exercise indicated a significantly steeper

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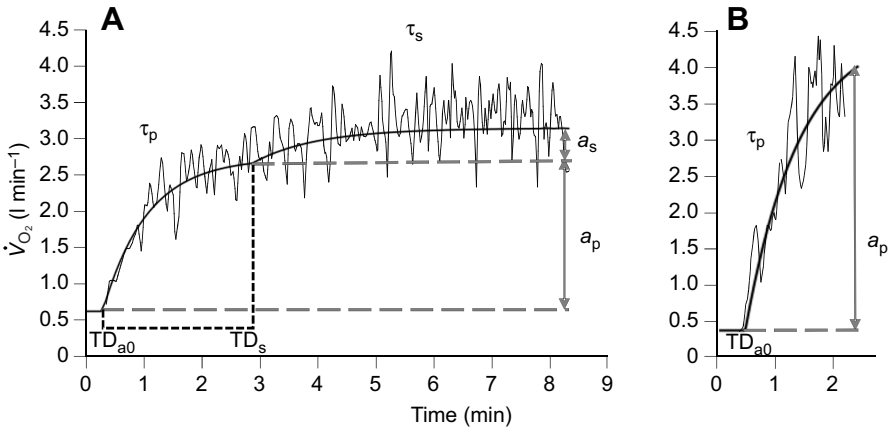

Fig. 1. Biexponential and monoexponential modeling of oxygen uptake kinetics for a typical participant during an on-transient square-wave exercise bout at 10%>critical power (CP) in the glycogen-loaded (GL) condition. (A) Biexponential modeling; (B) monoexponential modeling. The primary (a_p) and slow-component (a_s) amplitudes, respective time constants (τ_p, τ_s) and time delay of the slow component of oxygen uptake (TD_s) for each phase are labeled (refer to Materials and Methods for analysis description). TD_{a0} represents the time at the start of the model (i.e. at 20 s), truncating the cardiodynamic phase.

decline in FS ratings in the GD compared with the GL condition ($F_{1,14}$=9.061, P=0.009, d=0.70; see Fig. 2).

Hypothesis 2

For both conditions, the slope of FS ratings over time was significantly correlated with t_{LIM} (GL: r=0.85; GD: r=0.83; for both, P<0.001), indicating that participants with a steeper rate of decline in FS had a shorter t_{LIM} compared with those with a less steep decline (see Fig. 3).

Hypothesis 3

Overall, glycogen depletion did not alter $\dot{V}_{O_2}$ kinetics (see Table 1). In both the GD and GL conditions, monoexponential modeling of the oxygen uptake kinetics resulted in superior fit (verified by a χ^2 test) for eight participants, whereas biexponential modeling, indicating the presence of a slow component, resulted in a superior fit for seven participants. Examples of a monoexponential and a biexponential oxygen uptake response from two participants are displayed in Fig. 1. This outcome precluded the proper testing of Hypothesis 3. The correlations between the amplitude of the slow component (a_s) and the slope of FS ratings (GD: r=0.71; GL: r=0.66) indicated 44–50% of shared variance between the two variables but, given the small sample size (n=7), they did not reach statistical significance (P=0.07; P=0.11).

Examination of the data indicated that a likely reason for the inability to detect a clear slow component in some participants was that they had shorter tests (t_{LIM}). Specifically, in GD, those who exhibited a slow component averaged 470.7±105.9 s, whereas those who did not averaged 239.1±77.7 s ($F_{1,14}$=23.766, P<0.001, d=2.52). Likewise, in GL, those who exhibited a slow component averaged 506.3±61.0 s, whereas those who did not averaged 324.8 ±147.7 s ($F_{1,14}$=9.132, P=0.009, d=1.56). Importantly, participants who exhibited a slow component also had a less steep decline in FS ratings. Specifically, in GD, those who exhibited a slow component averaged −1.1±0.4 FS units min^{-1}, whereas those who did not averaged −2.5±1.1 FS units min^{-1} ($F_{1,14}$=10.086, P=0.007, d=1.64). Likewise, in GL, participants who exhibited a slow component averaged a decline of −0.7±0.2 FS units min^{-1}, whereas those who did not averaged −1.7±1.1 FS units min^{-1} ($F_{1,14}$=5.574, P=0.035, d=1.22).

Table 1. Affective responses, physiological variables and performance outcomes in glycogen-depleted (GD) and glycogen-loaded (GL) experimental conditions

	GD	GL	Effect sizes for mean differences: d=(mean$_{GL}$−mean$_{GD}$)/s.d.$_{pooled}$
t_{LIM} (s)	347.2±148.6	409.5±145.9*	0.42
FS ratings at baseline	2.7±1.9	2.9±1.6	0.11
FS ratings at end	−4.7±0.4	−4.4±0.6	0.60
FS slope (ΔFS min^{-1})	−1.9±1.1	−1.2±0.9**	0.70
$\dot{V}_{O_2,peak}$ (l min^{-1})	3.3±0.8	3.4±0.7*	0.13
$\dot{V}_{E,peak}$ (l min^{-1})	101.6±23.3	108.4±18.6	0.32
$\dot{V}_{CO_2,peak}$ (l min^{-1})	2.6±0.7	2.8±0.7*	0.29
$\dot{V}_E/\dot{V}_{CO_2,peak}$ (l min^{-1})	2.5±0.5	2.6±0.5	0.20
End bLac (mmol l^{-1})	9.2±2.5	12.4±4.2*	0.96
RER_{peak}	0.9±0.1	1.1±0.1**	2.00
$a0$ (l)	[0.9±0.4]	[0.7±0.4]	n/a
TD_p (s)	6.6±8.7	4.3±6.6	−0.30
a_p (l)	2.1±0.5	2.2±0.7	0.17
τ_p (s)	38.7±9.6	39.7±13.8	−0.09
TD_s (s)	172.3±35.1	166.6±36.4	−0.16
a_s (l)	0.6±0.3	0.5±0.2	−0.40
τ_s (s)	185.0±70.6	137.1±77.4	−0.65

GD and GL data are means±s.d. t_{LIM}, time to exhaustion; FS, Feeling Scale; $\dot{V}_{O_2,peak}$, peak oxygen consumption (highest 15 s average); $\dot{V}_{E,peak}$, peak ventilation rate (highest 15 s average); $\dot{V}_{CO_2,peak}$, peak carbon dioxide production (highest 15 s average); $\dot{V}_E/\dot{V}_{CO_2,peak}$, peak ventilatory equivalent of carbon dioxide (highest 15 s average); End bLac, post-exercise capillary blood lactate concentration; RER_{peak}, peak respiratory exchange ratio (highest 15 s average); $a0$, O_2 at 20 s used as the 'prior' steady state (i.e. a virtual a0); TD_p, primary component time delay; a_p, amplitude of the primary component of oxygen uptake kinetics; τ_p, time constant of the primary component of oxygen uptake kinetics; TD_s, time delay of the slow component of oxygen uptake kinetics; a_s, amplitude of the slow component of oxygen uptake kinetics; τ_s, time constant of the slow component of oxygen uptake kinetics. *P<0.05. **P<0.01.

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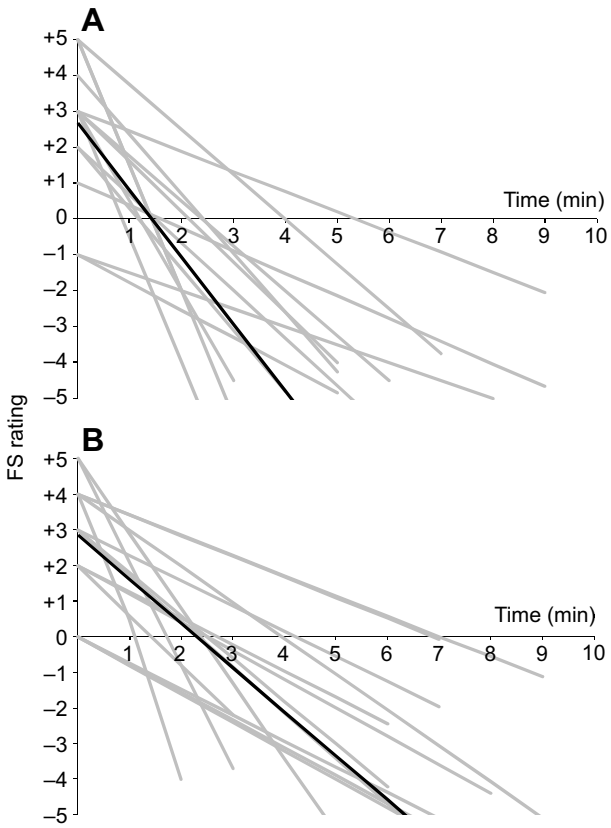

Fig. 2. Individual slopes of Feeling Scale (FS) ratings (gray lines) and group average FS slope (black lines) in the glycogen-depleted (GD) and GL conditions. (A) GD: b=–1.9; (B) GL: b=–1.2 [where b is the unstandardized slope of FS ratings over time (per minute)]. A one-way ANOVA revealed a significant difference in FS slope between the GD and GL conditions ($F_{1,14}$=9.061, P=0.009, d=0.70, n=15).

DISCUSSION

The purpose of the present study was to examine the utility of ratings of pleasure–displeasure as indicators of the severity of the homeostatic perturbation during exhaustive exercise. We experimentally manipulated the severity of homeostatic perturbation via glycogen depletion, compromised W', and observed that changes in ratings of pleasure–displeasure responded to the perturbation in the anticipated direction. Moreover, the individual rate of decline in ratings of pleasure–displeasure correlated closely with the amount of time participants persevered during exercise above CP until volitional termination. As the presumed mechanistic basis of W' (i.e. muscle bioenergetics) involves predictable and progressive metabolic perturbations intrinsically linked to exercise tolerance, the correlations between changes along the dimension of pleasure–displeasure and t_{LIM} suggest that these changes may serve as a conscious proxy of W' utilization (i.e. indicative of the severity of the perturbations).

To put the strength of the correlations between the slope of FS ratings and t_{LIM} into perspective (i.e. GL: r=0.85; GD: r=0.83), readers should keep in mind that, as a single-item rating scale, the FS is inherently susceptible to a certain degree of random measurement error and, therefore, FS-based measurements likely exhibit less-than-perfect reliability. Following classical test theory, as unreliability has an attenuating effect on estimates of correlation [$r'_{12}=r_{12}/(\sqrt{r_{11}}\cdot\sqrt{r_{22}})$], the slope of FS could be estimated to correlate with t_{LIM} perfectly or nearly perfectly (e.g. for GL, r'=1.00 assuming a reliability of 0.70 or r'=0.95 assuming a reliability of 0.80 for FS and error-free measurement for t_{LIM}). Therefore, it seems plausible that pleasure–displeasure is a crucial regulator of exercise performance near the limit of tolerance.

The broader aim of the present study was to serve as a cross-disciplinary bridge, connecting research investigating the factors that regulate and limit exercise performance to fields of inquiry that have already endorsed the idea that homeostatic perturbations enter consciousness mainly via declines in pleasure. For example, in affective psychology, affect is theorized to consist of 'continually changing feelings that are a property of consciousness resulting from the ongoing changes in homeostasis' (Feldman Barrett, 2015, p. 60). According to Feldman Barrett (2015, p. 60), 'any "perturbation" that influences homeostasis (changes in blood glucose levels, hormones, physical activity, etc.) or that the brain *predicts* will change homeostasis, could conceivably produce changes in affect'. In neurology, according to Damasio (2000, p. 20), affective feelings 'are always related to homeostatic regulation, always related to the processes of promoting the maintenance of life, and always poised to avoid the loss of integrity that is a harbinger of death or death itself'. In other words, interoceptive awareness is inherently valenced, manifesting itself in consciousness colored by gradations of pleasure or displeasure:

> The addition of a felt experiential component to the basic somatic mapping emerged and prevailed in evolution because of the benefits it conferred on life regulation. Given that body states are necessarily valenced – they are either good or bad from the point of view of homeostasis – feelings are powerful proxies of ongoing biological value and natural guides of adaptive behavior (Damasio and Carvalho, 2013, p. 145).

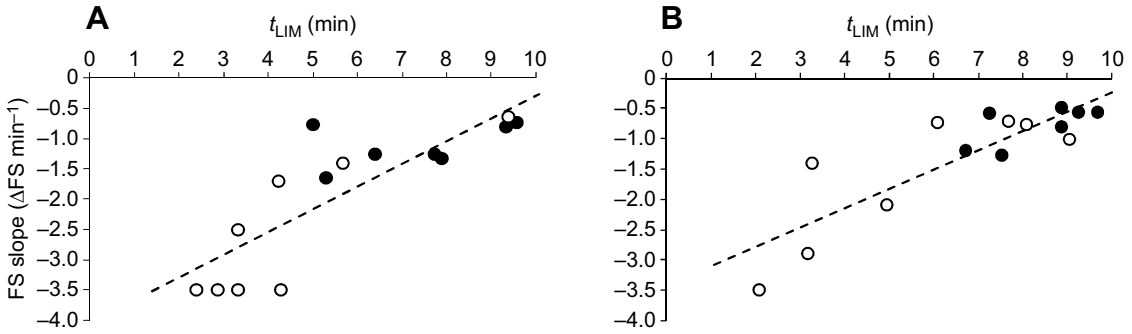

Fig. 3. Pearson correlation coefficients between the slopes of FS ratings and t_{LIM} in the GD and GL conditions. (A) GD: r=0.83, P<0.001, n=15; (B) GL: r=0.85, P<0.001, n=15. In both panels, participants eliciting a slow component are indicated with solid circles (n=7) and those without are indicated with open circles (n=8).

Similarly, in (human) clinical neuroscience, according to Leknes and Tracey (2010), 'hedonic feelings exist to encourage the constant optimization of our internal homeostatic balance' (Leknes and Tracey, 2010, p. 322) and 'the close relationship between homeostatic processes and hedonic feelings point to an evolutionary benefit for pleasure-seeking, pain-avoiding individuals' (Leknes and Tracey, 2010, p. 328). In (animal) basic neuroscience, according to Craig (2002, p. 657), pleasant and unpleasant 'feelings from the body are directly related to homeostatic needs and associated with behavioral motivations that are crucial for the maintenance of body integrity'.

The idea that exercise-induced homeostatic perturbations enter consciousness primarily via declines in pleasure is also accepted in exercise psychology. According to the dual-mode theory (DMT) of affective responses to exercise (Ekkekakis, 2003, 2009a), at exercise intensities exceeding the CP, all or nearly all individuals are expected to report declines in pleasure. For example, during a graded treadmill test, 90% of participants reported declining FS ratings from the stage after the gas exchange threshold until the point of volitional termination, while the remaining 10% reported negative but stable ratings (Ekkekakis et al., 2005). Consistent with the viewpoints from affective psychology, neurology and neuroscience, such declines in pleasure are theorized to represent an evolutionary adaptation, the function of which is to compel the termination of exercise and, therefore, the prevention of the impending metabolic crisis.

Within the research cluster investigating the regulation of exercise performance from an exercise–physiology disciplinary perspective, some authors have characterized 'fatigue' as 'an emotion' (Noakes, 2012), an 'emotional construct' (Baden et al., 2005, p. 745) or 'a pain' (Mauger, 2013), and have expressed the view that 'affect may be the primary psychological regulator of pacing strategy' (Renfree et al., 2012, p. 121) or 'core affect is a primary regulator of exercise performance' (Venhorst et al., 2018, p. 963). However, within the discipline of exercise physiology at large, the suggestion that a subjective construct, such as pleasure–displeasure, may be a crucial regulator of exercise performance will likely be deemed controversial. The idea that the brain plays an important role in the regulation of exercise performance remains a point of contention (e.g. Noakes, 2011; Weir et al., 2006) and subjective constructs are still viewed reluctantly (Jones and Killian, 2000).

If the sense of exertional physical fatigue represents a primordial affective response, this would imply that it should engage the same – extensively studied – brain mechanisms (e.g. Etkin et al., 2015; Lindquist et al., 2012; Pessoa, 2017). This suggestion could be a catalyst in unravelling mysteries that have long vexed exercise and fatigue researchers. For example, Chaudhuri and Behan (2004, p. 986) proposed that 'brain-derived central fatigue is related to circuits that connect basal ganglia, amygdala, thalamus, and frontal cortex'. However, the absence of a guiding conceptual framework precluded a specific proposal about how these brain areas may interact. Genova et al. (2011, p. 379) similarly speculated that the sense of fatigue emerges from a functional impairment of a cortical–subcortical circuitry that includes 'the basal ganglia, the frontal cortex, the thalamus, and the amygdala' but conceded that 'we know very little about its precise mechanism'. These brain areas have now been shown to be the main components of the network involved in the genesis and regulation of affect (Etkin et al., 2015; Lindquist et al., 2012; Pessoa, 2017). This recognition offers an intriguing suggestion for what the sense of exertional physical fatigue represents; namely, an affective response.

In the exercise sciences, researchers have also made some related discoveries but, not having a guiding conceptual framework, could not articulate their implications. For example, it is well established that the oxygenation of the dorsolateral prefrontal cortex declines, even to below-baseline levels, at exercise intensities above the CP (Ekkekakis, 2009b; Rooks et al., 2010). However, the lack of input from affective psychology and neuroscience has hindered the interpretation of the functional significance of this finding. Authors have speculated that the prefrontal cortex 'may be intimately involved in the capacity to tolerate high levels of physical exertion and possibly in the determination of exercise termination' (Robertson and Marino, 2016, p. 465) but it has not been possible to pinpoint a specific mechanism. Acknowledging affect as a regulator of exercise performance would enable researchers to draw insights from the knowledge base of affective neuroscience. A reduction of prefrontal activation is an extensively documented phenomenon in situations of high stress (Arnsten, 2009) and has been linked to a disinhibition of subcortical structures involved in the expression of affective responses, such as the amygdala (Etkin et al., 2015; Lindquist et al., 2012). In turn, loss of prefrontal inhibition of the amygdala is associated with a switch from prefrontally mediated, 'rational' behavioral options (e.g. perseverance through discomfort in order to demonstrate superior fitness during an exercise test or to win a race) to more 'inflexible' or 'instinctual' options (e.g. discontinuing the effort in the face of severe discomfort), likely mediated by the striatum (Phelps et al., 2014).

Recent neurobiological models of exercise regulation (Lutz, 2018) and fatigue (McMorris et al., 2018) acknowledge the importance of monitoring homeostatic balance, identify brain areas known to be involved in the genesis and regulation of affective states as relevant (i.e. amygdala, insula, prefrontal cortex, anterior cingulate) and incorporate the notion that exercise regulation and termination reflect a balance between symbolically represented 'costs' and 'rewards', but stop short of explicitly assigning a central role to affect. Neglecting the centrality of affect overlooks the intrinsic 'coupling between interoceptive and affective activity' (Strigo and Craig, 2016, p. 7), evidenced by dense interconnections between the interoceptive (i.e. nucleus of the solitary tract, thalamus, insula, anterior cingulate) and affective centers (i.e. amygdala). Moreover, recognizing that affect can serve as a 'common currency' (Berridge and Kringelbach, 2015; Cabanac, 1992) can help address problems stemming from the fact that the 'costs' and 'rewards' presumed to underlie behavioral choices (e.g. slowing down, stopping) are heterogeneous things (e.g. physical discomfort versus pride or money one expects to gain). In order to be compared, they must be converted on a common scale: pleasure versus displeasure. We propose that exercise is terminated when the uncontrollable displeasure inherent in the severe homeostatic perturbation that accompanies exercise above CP exceeds any pleasure that can be expected from persevering. We also propose that stopping is probably not a rational decision (e.g. believing that continuing may cause injury; see McMorris et al., 2018, p. 104) but rather is a reflection of the inherent association of displeasure with the urge to stop or avoid (Schulze, 1995).

We speculate that the long absence of pleasure–displeasure from models of exercise regulation and termination may be due to the fact that the construct of perceived exertion has become entrenched in the exercise-science literature as the only widely recognized subjective variable since the late 1960s. The idea that 'the increase in perception of effort occurring during prolonged exercise determines performance in time to exhaustion tasks' (de Morree and Marcora, 2015, p. 256) and 'is the cardinal exercise

stopper during high-intensity aerobic exercise' (Staiano et al., 2018, p. 175) has gained wide acceptance. The present study was not intended as a comparison of the relative importance of perceived exertion and affect as determinants of exercise performance. Indeed, we acknowledge that the slope of ratings of perceived exertion exhibits correlations with t_{LIM} of similar magnitude to those between the slope of FS and t_{LIM} in the present study (i.e. −0.77 to −0.84 in Pires et al., 2011 for intensities proximal to CP).

More than 50 years after the inception of the construct of perceived exertion, there is still ambivalence about its exact nature (e.g. Abbiss et al., 2015). Researchers remain divided on whether perceptions of exertion reflect afferent physiological cues or corollary discharges from efferent motor commands to working muscles (e.g. de Morree and Marcora, 2015). There is also disagreement as to whether a rating of perceived exertion represents 'a marker of "fatigue"' (Swart et al., 2009, p. 782) or whether 'perceived exertion scales should not be used to measure fatigue' (Micklewright et al., 2017, p. 2377).

Although everyone can offer a rating on a scale of perceived exertion when asked, this response does not result from a specialized sensory system (i.e. it is not analogous to a vision or hearing test). Rather, the response is constructed by synthesizing data from a heterogeneous range of sources. This follows Borg's (1982) original conceptualization of perceived exertion as an amalgam of various interoceptive (e.g. proprioceptive awareness, inspiratory resistance, muscle tension, thermal distress) and exteroceptive (e.g. stereoscopic vision, sensation of headwind) inputs, as well as the moderating influence of numerous trait and state variables (e.g. experience, competitiveness, fear).

Following our proposal that pleasure–displeasure is the main channel via which information about a homeostatic perturbation enters consciousness, we submit that, near the limit of exercise tolerance (i.e. when homeostasis is significantly perturbed), what has commonly been termed 'perceived exertion' is, in fact, displeasure. This idea is consistent with one of the earliest conceptual models of perceived exertion. According to Robertson (1982, p. 395), below the lactate threshold, ratings of perceived exertion, presumably due to the gating of interoceptive cues, are generally uncoupled from indices of metabolic strain, reflecting merely 'an awareness of movement' (i.e. proprioception: the ratings increase depending on how fast one perceives his or her movements to be). This view is supported by findings that the ratings of perceived exertion are mostly unrelated to indices of metabolic strain (e.g. heart rate, blood lactate, respiratory frequency) at low intensities (e.g. Borg et al., 1985).

Between the lactate threshold and respiratory compensation, intensified interoceptive cues enter consciousness, signaling the onset of a perturbation. Consequently, at this range of intensity, what is commonly termed 'perceived exertion' reflects mild discomfort (i.e. exercise is experienced as 'uncomfortable but tolerable'; see Robertson, 1982, p. 395). In support of this claim, when most individuals exceed the gas exchange threshold (typically coincident with the lactate threshold), they rate their exertion using the first number that is accompanied by a negatively valenced anchor, namely '13' or 'somewhat hard' (Ekkekakis et al., 2004).

Finally, from respiratory compensation to peak exercise capacity (delimited by the volitional termination of the effort), what is commonly termed 'perceived exertion' reflects intense displeasure (i.e. exercise is experienced as 'painful or unpleasant'; see Robertson, 1982, p. 395). Exercise is terminated when the displeasure becomes uncontrollable and thus intolerable. In support of this claim, while ratings of perceived exertion and ratings of pleasure–displeasure show little variance overlap at low exercise intensities, they become strongly inversely correlated at high intensities (e.g. Acevedo et al., 2003; Ekkekakis et al., 2004; Hardy and Rejeski, 1989). The strong inverse relationship has been interpreted as an indication that perceived exertion 'has an affective component' (Baden et al., 2005, p. 742) or is 'influenced by affect' (Baden et al., 2005, p. 746). Instead, we propose that, at high intensities, the two constructs morph into one: the decline in pleasure (or surge of displeasure) is the channel via which the severity of exertion (e.g. the degree of homeostatic perturbation or the proximity to a metabolic crisis) enters consciousness. This notion is consistent with Borg's (1998) own perspective, according to which strong interoceptive cues elicited by near-maximal exercise become inherently unpleasant, compelling the termination of effort: 'When we exercise very hard, we feel it throughout our entire body. Breathlessness becomes annoying, and we feel the fatigue in our muscles. If these feelings become unpleasant, we may want to stop exercising' (Borg, 1998, p. v).

Moreover, it should be emphasized that, according to Borg (1986, p. 5), 'the concept of fatigue should be distinguished from the concept of perceived exertion even though these two concepts have very much in common'. An important reason for this distinction is that, while ratings of perceived exertion scale linearly with exercise intensity, reports of fatigue only appear following an individually determined threshold intensity that presumably signifies the onset of a substantial homeostatic perturbation. This important observation dates to the earliest scholarly work on fatigue by Mosso (1904, p. 154), who wrote: 'With regard to the feeling of fatigue, the same thing takes place as happens in the case of every stimulus which acts upon our nerves; we begin to perceive it only when it has attained a certain intensity'. Mosso (1904) was referring to the fact that gating mechanisms, at multiple sites within the interoceptive processing network, keep the workings of the body outside conscious awareness until homeostasis is compromised. The same idea was later supported by Cannon (1932, p. 307), who noted that the function of bodily systems is ordinarily 'so well regulated by inherent automatisms that the phenomena of fatigue rarely appear'; phenomena of fatigue arise only when it becomes necessary to impose a 'check on excessive activity' (Cannon, 1932, p. 308). While ratings of perceived exertion increase in a linear fashion throughout the entire range of exercise intensity, ratings of pleasure–displeasure begin to decline proximally to the gas exchange ventilatory threshold and show an increasingly accelerating decline thereafter (Ekkekakis et al., 2004, 2011).

The present study has several strengths, including an effective perturbation of the muscle bioenergetic environment by reducing glycogen availability (with a validated glycogen-depletion protocol completed by all participants, with strict dietary control). The effectiveness of the manipulation was evidenced by differences in an array of physiological variables, as well as a significant impairment in exercise performance. However, in the present study, not all participants elicited a detectable slow component of oxygen uptake, and this precluded proper testing of the hypothesis that the amplitude of the slow component would correlate with the slope of ratings of pleasure–displeasure. While ratings of pleasure–displeasure were found to respond in the anticipated direction to homeostatic perturbations and to correlate closely with perseverance near the limit of exercise tolerance, this does not constitute evidence that pleasure–displeasure is a causal agent in exercise regulation or termination. Such a demonstration will require experimental manipulation of pleasure–displeasure in future studies. The primary value of the present study stems from its cross-

disciplinary conceptual approach: the study of exercise regulation, including the study of the sense of exertional physical fatigue, stands to gain both much-needed conceptual clarity and well-grounded neurobiological hypotheses by incorporating the construct of affective responses.

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Competing interests
The authors declare no competing or financial interests.

Author contributions
Conceptualization: M.E.H., P.E., N.D.D., R.W.P.; Methodology: M.E.H., P.E., N.D.D., R.W.P.; Formal analysis: M.E.H., P.E., R.W.P.; Investigation: M.E.H., P.E., N.D.D., R.W.P.; Resources: R.W.P.; Data curation: M.E.H.; Writing - original draft: M.E.H., P.E., N.D.D., R.W.P.; Writing - review & editing: M.E.H., P.E., N.D.D., R.W.P.; Supervision: P.E., N.D.D., R.W.P.; Project administration: M.E.H., R.W.P.

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