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TOPICAL REVIEW

Physiological basis of brief vigorous exercise to improve health

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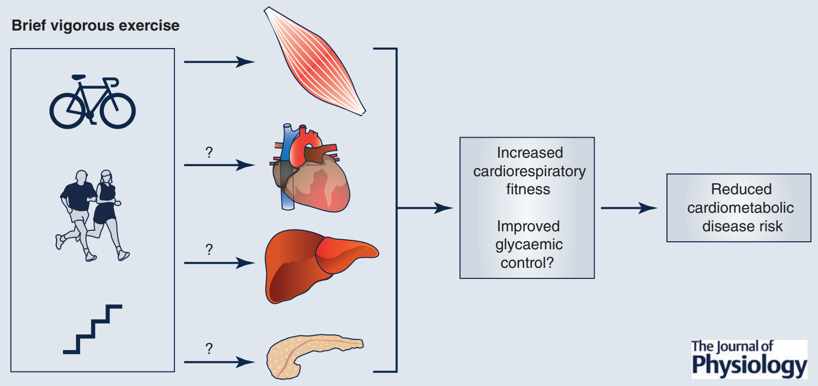

Abstract This review considers the physiological basis of brief vigorous exercise to improve health, with a focus on cardiorespiratory fitness (CRF) and glycaemic control, and the potential underlying mechanisms involved. We defined 'brief' as a protocol lasting ≤15 min including warm-up, cool-down and recovery, and involving a total of ≤5 min of 'vigorous' exercise, which was classified as meeting or exceeding the lower end of the range for this relative intensity as per the criteria from the American College of Sports Medicine. The physiological mechanisms responsible for the increase in CRF, as measured by maximal oxygen update ($\dot{V}_{O_2\,max}$), after brief vigorous exercise are unclear and likely depend on various factors including the specific nature of the intervention as well as the time course of the response. Limited available evidence suggests the potential for an increased oxygen extraction by active muscle (i.e. greater arterio-venous oxygen difference), since an increase in $\dot{V}_{O_2max}$ has been reported after several weeks of brief vigorous exercise despite no measurable change in cardiac output. Emerging evidence indicates that brief vigorous exercise can improve glycaemic control, suggesting that this type of exercise could potentially play a role in the prevention and management of type 2 diabetes. The acute

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response is not well characterized but several studies have shown that several weeks of vigorous exercise improves estimates of insulin sensitivity as determined by various methods including by hyperinsulinaemic–euglycaemic clamp. The physiological mechanisms underlying improved CRF and glycaemic control after brief vigorous exercise, and the broader impact on health, remain fruitful areas of investigation.

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Abstract figure legend Potential for brief vigorous exercise to reduce cardiometabolic disease risk

Introduction

Public health agencies including the World Health Organization generally recommend that adults do at least 150 min a week of moderate-intensity or 75 min a week of vigorous-intensity aerobic physical activity, or some equivalent combination, to promote health. A notable change to the recently updated Physical Activity Guidelines for Americans (Piercy *et al.* 2018) was elimination of the previous requirement that physical activity must be accumulated in bouts lasting at least 10 min. This stipulation was unsupported by empirical evidence (Stamatakis *et al.* 2019), and removal of the provision aligns with an increasing body of evidence that suggests regularly performing *brief vigorous exercise* is efficacious to improve health markers, including cardiorespiratory fitness (CRF) and glycaemic control. The present review considers the physiological basis of brief vigorous exercise to improve health, with an emphasis on CRF and glycaemic control, and the potential underlying mechanisms involved. A systematic review or meta-analysis approach was not specifically employed, but to assess the relevant literature, 'brief' was defined as a protocol in which the total period of vigorous exercise lasted ≤5 min. This could involve a single continuous bout that lasted up to 5 min, or, in the case of intermittent exercise (i.e. interval training, which involves repeated bouts of exercise interspersed with short recovery periods), the maximum duration of vigorous exercise for all bouts had to be ≤5 min (e.g. five 1 min intervals). The maximal session duration for any protocol had to be ≤15 min including warm-up, cool-down and recovery periods in the case of intermittent protocols. 'Vigorous' exercise was defined as meeting or exceeding the lower end of the range for this relative intensity, as defined by the American College of Sports Medicine (ACSM; Garber *et al.* 2011). It corresponded to exercise that elicited a percentage of maximal heart rate of at least 77%, a percentage of maximal oxygen uptake of at least 64%, and/or a rating of perceived exertion (RPE) of at least 14 based on the Borg 6–20 scale. For the purposes of this review, the definition of 'vigorous' therefore included exercise protocols classified as 'maximal' by the ACSM (Garber *et al.* 2011), since there was no upper range limited specified for intensity.

Distinguishing brief vigorous exercise from sprint interval training

Sprint interval training (SIT) refers to an extreme version of intermittent exercise, generally defined as bouts performed in an 'all out' manner or at an absolute intensity that exceeds the workload necessary to elicit maximal oxygen uptake ($\dot{V}_{O_2max}$; used interchangeably for the purposes of the present review with peak oxygen uptake, $\dot{V}_{O_2peak}$) (Weston *et al.* 2014). Many SIT studies are based on interventions that require particularly specialized equipment – the most common being repeated 30-s Wingate Test protocols that are performed on an ergometer against a fixed resistance, usually equivalent to 0.075 kg/kg body mass, which is applied either manually or via a computer interface, such that absolute workload is variable and corresponds to pedal cadence. This mode of exercise is not commonly available outside of a laboratory setting, and thus it is challenging for a fitness enthusiast to mimic this style of training using a standard cycle ergometer as typically available in a studio. In spite of the need for specialized ergometers, some have argued that brief vigorous exercise protocols based on this type of modality might be feasible to implement outside of a laboratory setting (Vollaard & Metcalfe, 2017) and new products aimed at the commercial fitness market are emerging in this regard. Nonetheless, the design of many Wingate-based training studies – which typically involve four to six bouts separated by 4–5 min of recovery – means the total time commitment is ≥20 min. Thus, except when included as part of other reviews cited here, or where otherwise noted, many 'classic' Wingate-based studies are not considered in the present review. Some studies that employed interventions characterized as 'SIT', including those that involved modified Wingate Test designs, are

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included if the objectively measured intensity and total time commitment met the definition above.

The effect of brief vigorous exercise on cardiorespiratory fitness

Brief vigorous exercise is effective to increase CRF, as suggested by the pioneering work of Tabata *et al.* (1996). The protocol in that study does not meet the explicit definition used here, but is referenced for historical perspective and given the widespread popularity of 'Tabata-style' interval training with fitness enthusiasts. The Tabata protocol involves alternating periods of 20 s intense effort and 10 s recovery, repeated 8 times, for a total of 4 min (the original study was performed using cycling at ∼170% $\dot{V}_{O_2max}$, and was preceded by a 10 min warm-up). Tabata *et al.* (1996) reported that 6 weeks of training using this protocol, when performed 4 times per week in addition to one 30 min bout of moderate-intensity continuous exercise, increased $\dot{V}_{O_2peak}$ by ∼7 ml/kg/min (∼15%) in young, active men. The increase in $\dot{V}_{O_2max}$ was similar to a group who trained solely using the moderate-intensity protocol, 5 days per week. A notable observation from this study was that, in spite of the intense nature of the intermittent exercise protocol, the 'session was not exhaustive'. This highlights the disconnect between absolute workload and perceived effort that can be observed during brief vigorous exercise. That is, individuals can perform exercise deemed 'near maximal', 'maximal', or 'supramaximal', but RPE values are lower than what is typically associated with (longer) continuous efforts at similar intensities. This phenomenon may be important as brief vigorous exercise protocols are translated to settings outside of a research laboratory. In addition, it is possible that traditional RPE measurements may need to be adapted or interpreted with caution when trying to estimate workload/effort during brief vigorous exercise, particularly when intermittent protocols are compared to continuous.

Recent studies have demonstrated the efficacy of brief vigorous exercise – consistent with the definition employed here, and involving a smaller total work than the protocol used by Tabata *et al.* (1996) – to improve $\dot{V}_{O_2max}$ (for review, see Vollaard & Metcalfe, 2017; Vollard *et al.* 2017). For example, Gillen *et al.* (2014, 2016) examined a 10 min protocol that involved 3 × 20 s 'all out' cycling efforts, performed using a modified Wingate Test in which the resistance was equivalent to 0.05 kg/kg body mass. The remainder of the protocol involved low-intensity cycling (50 W) for a 2 min warm-up, 2 min recovery periods between sprints, and 3 min cool-down. In sedentary but otherwise healthy adults, peak heart rate elicited during the sprints was ∼90–95% of maximum (Gillen *et al.* 2014) and the mean RPE was 16 ± 1 (Gillen *et al.* 2016). The protocol increased $\dot{V}_{O_2peak}$ by 12% when performed 3 days per week for 6 weeks (Gillen *et al.* 2014, 2016), and by 19% after 12 weeks (Gillen *et al.* 2016), which was the same mean increase as found in a comparison group who performed moderate-intensity continuous training for 50 min per session. Other authors have reported similar mean increases in $\dot{V}_{O_2max}$ (∼10–13% over 6 weeks) when participants performed protocols similar to that employed by Gillen and colleagues. In particular, Metcalfe, Vollaard and colleagues have conducted a series of studies focused on 'reduced exertion high-intensity training' (REHIT) (Metcalfe *et al.* 2012, 2016). The REHIT protocol involves a maximum of two 20 s 'all out' cycling bouts – typically eliciting an RPE of 13–14 – over a 10 min period that otherwise involves a low-intensity warm-up, cool-down and recovery periods between sprints.

Researchers have also demonstrated the efficacy of brief vigorous exercise protocols deemed more 'practical' (i.e. with greater potential for translation outside of a laboratory setting), including stair climbing and constant workload cycle ergometer protocols. Allison *et al.* (2017) reported that mean heart rate and RPE were similar when previously sedentary young women performed an acute session of either cycling or stair climbing, using a 10 min protocol that involves 3 × 20 s sprints. Similar to the results reported by Gillen *et al.* (2014, 2016) for cycling, 18 sessions of stair climbing over 6 weeks increased $\dot{V}_{O_2peak}$ by 12%, which corresponded to approximately 1 metabolic equivalent (MET) (Allison *et al.* 2017). Phillips *et al.* (2017) examined a cycling protocol that involved five 1 min efforts at an intensity of ∼100–125% $\dot{V}_{O_2max}$, performed over a ∼15 min period including warm-up, recovery periods and cool-down. When performed three times per week for 6 weeks, the protocol increased $\dot{V}_{O_2max}$ by an average of ∼10% in a relatively large (n = 136) group of previously sedentary overweight and obese adults at risk for type 2 diabetes (T2D). Reljic *et al.* (2018) also showed the efficacy of a constant-load cycling protocol that involved five 1 min bouts, interspersed with 1 min recovery periods, in addition to a 2 min warm-up and 3 min cool down, and performed at a target intensity of 85–95% of maximal heart rate (HR). When performed 2 days per week for 8 weeks, the protocol elicited increases in $\dot{V}_{O_2peak}$ of 27%, which was similar to another group who performed 38 min of continuous moderate-intensity exercise at 65–75% of maximal HR. Thus, brief vigorous exercise, consisting of either a few short hard sprints, or strenuous but submaximal efforts lasting as short as 1 min, and set within a total time commitment of ≤15 min per session and ≤30 min per week, can improve $\dot{V}_{O_2peak}$ after 6–12 weeks of training.

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How does brief vigorous exercise increase cardiorespiratory fitness?

The physiological mechanisms responsible for the increase in $\dot{V}_{O_2 peak}$ after brief vigorous exercise are unclear, and likely depend on various factors including the specific nature of the intervention as well as the time course of the response. Increases in $\dot{V}_{O_2 max}$ after exercise training of sufficient intensity and volume are believed to be largely facilitated by expansion of red blood cell volume and an associated improvement in stroke volume, which also adapts independent of changes in red blood cell volume (Lundby *et al.* 2017). To our knowledge, only two studies have assessed these cardiovascular responses to brief vigorous exercise as defined here. Raleigh *et al.* (2018) studied the effects of a Tabata-like protocol that involved a 5 min warm-up, followed by eight 20 s cycling intervals at an intensity equivalent to 170% of $\dot{V}_{O_2 max}$ power output, interspersed by 10 s of rest, for a total session duration of 9 min. Active men who performed 16 sessions of training over 4 weeks experienced a mean increase in $\dot{V}_{O_2 max}$ of ∼9%, but there was no change in maximal cardiac output as determined by an inert gas rebreathing method. Based on Fick's principle, it was reasoned that the change in $\dot{V}_{O_2 max}$ may have been due to an increased oxygen extraction by active muscle (i.e. greater arterio-venous oxygen difference), potentially related to an increased capillary density or mitochondrial content, both of which were demonstrated in the study (Raleigh *et al.* 2018). Some of the same authors (Bentley *et al.* 2019) conducted a similar study that employed the same protocol in a different group of active male participants, and reported similar findings: $\dot{V}_{O_2 max}$ increased after training by ∼10%, and while the submaximal cardiac output:$\dot{V}_{O_2}$ ratio was altered in some subjects, maximal cardiac output was unchanged. Additional studies are warranted to clarify the mechanisms responsible for the increased $\dot{V}_{O_2 max}$ observed after brief, vigorous exercise including the time course for responses.

The effect of brief vigorous exercise on glycaemic control

Emerging evidence indicates that brief vigorous exercise can improve glycaemic control, suggesting that this type of exercise may play a role in the prevention and management of T2D. A single session of exercise enhances insulin sensitivity, an effect largely attributed to skeletal muscle and that can last for up to ∼24 h post-exercise (Devlin *et al.* 1987; Kjaer *et al.* 1990; Newsom *et al.* 2013). Although much research has focused on the impacts of exercise training on skeletal muscle insulin sensitivity and glucose transport (reviewed in Henriksen, 2002; Sylow *et al.* 2017), structural and functional adaptations in liver, adipose, pancreas and blood vessels following a period of training are all likely involved in the whole body improvements in insulin sensitivity and glucose control. Thus, when exploring the impact of brief vigorous exercise on glycaemic regulation it is important to delineate whether effects are the result of acute exercise (or last session within a training programme), an adaptation to training, and/or a combination of the two.

Acute studies. To our knowledge, the impact of an acute bout of brief vigorous exercise as defined in this review on insulin sensitivity has not been well characterized. Metcalfe *et al.* (2016), using the aforementioned REHIT protocol, demonstrated no impact on estimates of insulin sensitivity and glucose tolerance from an oral glucose tolerance test (OGTT) performed 14–16 h after an acute session in young healthy participants. A recent pilot study by Godkin *et al.* (2018) also reported no impact of an acute bout of brief vigorous stair climbing on subsequent 24 h glucose control, assessed by continuous glucose monitoring (CGM), in participants with T2D. These findings are in contrast to previous interval training studies in which the exercise was of longer duration and higher volume (Gillen *et al.* 2012; Little *et al.* 2014), suggesting that a possible dose–response threshold may exist.

Acute exercise has the potential to immediately lower glucose levels via enhanced insulin-independent skeletal muscle glucose uptake, particularly if exercise is performed in the postprandial state (Erickson *et al.* 2017). With acute vigorous exercise, increased hepatic glucose production that is stimulated by counter-regulatory hormones will ultimately dictate the prevailing impact on blood glucose concentration. Classic studies in participants with normoglycaemia and T2D have shown that brief vigorous exercise (5 min at 100–110% $\dot{V}_{O_2 max}$) within a 12 min total exercise session performed in the fasted state results in an acute increase in blood glucose that may persist for up to 60 min post-exercise (Kjaer *et al.* 1990). This acute increase in blood glucose when vigorous exercise is performed in the fasted state is attributed to elevated hepatic glucose production that exceeds the increase in skeletal muscle glucose uptake (Kjaer *et al.* 1990). Thus, it may be important to consider how brief vigorous exercise affects counter-regulatory responses and acute glucose concentrations if this type of exercise is to be promoted for improving glycaemic control. It is currently unclear whether brief vigorous exercise of different durations and patterns elicits the same response when performed in the postprandial, as opposed to fasted, state but preliminary reports indicate that brief vigorous stair-climbing exercise performed in the post-prandial period can acutely lower glucose in participants with T2D (Godkin *et al.* 2018). The potential influence of brief vigorous exercise, and possible

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modifying factors, on acute glucose regulation is depicted in Fig. 1.

Training studies. Metcalfe and colleagues (2012) were one of the first to show that brief vigorous exercise could improve estimates of insulin sensitivity. A REHIT protocol involving two 10–20 s cycling sprints within a 10 min training session, performed 3 times per week for 6 weeks, improved OGTT-derived measures in six healthy but previously inactive males. Interestingly, estimates of OGTT-derived insulin sensitivity were not improved in eight overweight/obese females in this same study. A subsequent study by this group did not observe sex-based differences in the responses to this type of training, and also questioned the robustness of the previously reported improvement in insulin sensitivity (Metcalfe *et al.* 2016). Ruffino and colleagues (2017) also compared measures of glucose control after REHIT or standard care walking exercise using a randomized crossover trial involving 16 male participants with T2D who completed 8 weeks of training. In contrast to the study hypotheses, neither brief vigorous exercise nor moderate-intensity walking influenced OGTT-derived estimates of insulin sensitivity or glycaemic control assessed by CGM. Plasma fructosamine (which reflects average glucose over a 2–3 week period), however, was similarly reduced by ∼5% after both exercise treatments. Other authors have reported improvements in indices of glucose control after brief vigorous exercise. Gillen and colleagues (2016) examined the impact of a protocol that involved three 20 s 'all out' cycling sprints over 10 min on insulin sensitivity assessed by intravenous glucose tolerance test in overweight males. Insulin sensitivity was improved by ∼50% after 36 sessions of training over 12 weeks, and glucose area under the curve was significantly reduced. In agreement, studies by Søgaard *et al.* (2018) and Phillips *et al.* (2017) using hyperinsulinaemic–euglycaemic clamp and homeostasis model assessment of insulin resistance (HOMA-IR), respectively, have reported improved whole body insulin sensitivity following 6 weeks of training involving five 1 min vigorous intervals.

Using a more practical model that involves 60 s bouts of vigorously ascending and slowing descending a stairwell, Godkin and colleagues (2018) found no impact of 18 sessions of training over 6 weeks on CGM-derived markers of glucose control, fasting glucose, fasting insulin or fructosamine in a small ($n = 6$) group of T2D patients. Overall, a limited number of studies examining the impact of brief vigorous exercise on measures of glucose control and insulin sensitivity have produced mixed results. It appears that insulin sensitivity is improved but whether this translates into improved glycaemic control, particularly in people with T2D, is unclear. Differences in study design, exercise protocol, measurement techniques, and study population make comparisons and general conclusions inherently challenging.

How does brief vigorous exercise increase glycaemic control?

The acute effects of traditional moderate-intensity continuous exercise on insulin sensitivity appear related, at least in part, to muscle glycogen depletion and enhanced insulin-mediated GLUT4 translocation to the sarcolemma

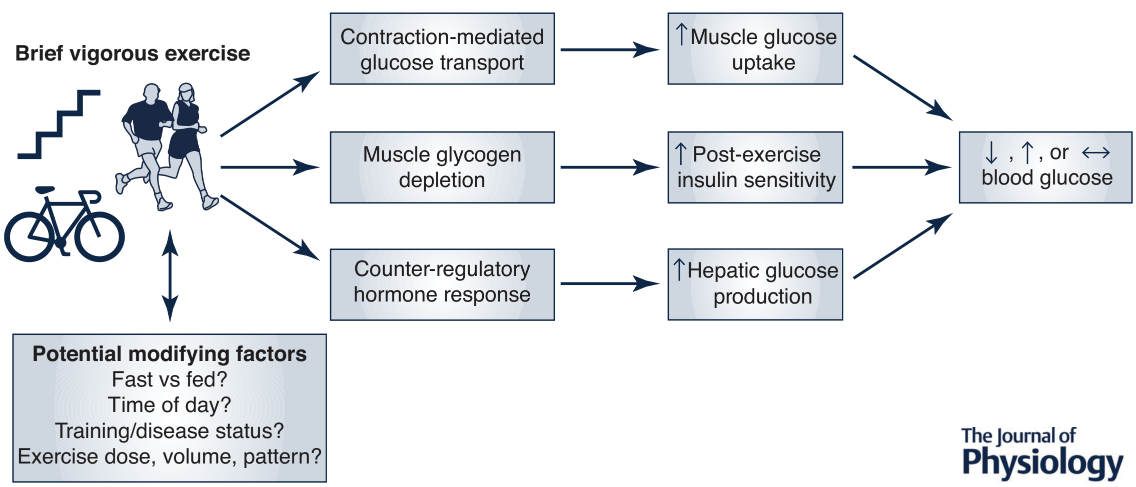

Figure 1. Potential factors influencing how brief vigorous exercise can impact blood glucose levels
The interactions between contraction-mediated glucose transport, muscle glycogen depletion, and counter-regulatory hormone responses influence muscle glucose uptake, post-exercise insulin sensitivity and hepatic glucose output to ultimately determine the impact of brief vigorous exercise on blood glucose levels acutely and in the post-exercise recovery period. It is likely that such acute responses are modified by factors such as whether exercise is performed in the fasted *vs*. fed state, the time of day, baseline training and disease status, and the exercise dose, volume or pattern.

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(reviewed in Holloszy, 2003). Presumably these same mechanisms could enhance muscle insulin sensitivity following brief vigorous exercise but direct measurements of these parameters are limited. It does appear that different brief vigorous exercise protocols do lead to significant muscle glycogen depletion and activation of skeletal muscle signalling pathways involved in improving insulin sensitivity (Cochran *et al.* 2014; Metcalfe *et al.* 2015), but linking these isolated responses in muscle biopsy samples to improved whole body insulin sensitivity and glycaemic control has not been accomplished. Brief vigorous exercise that can elicit substantial reductions (∼20–30%) in muscle glycogen would be hypothesized to have more potential to enhance insulin sensitivity and improve glycaemic control (Cartee *et al.* 1989; Jensen *et al.* 2011). In this regard, whole-body exercise that engages greater muscle mass may be optimal when prescribing brief vigorous exercise with the goal of improving glycaemic control. Including vigorous bouts that are long enough to substantially deplete muscle glycogen, along with performing more vigorous intervals throughout the brief session, might also be logical strategies in attempts to maximize the acute glucose-lowering effects of brief vigorous exercise sessions. Such a strategy would need to be balanced (at least at the start of a training programme) with the knowledge that unaccustomed vigorous exercise could lead to muscle damage, which can impair muscle insulin sensitivity (Kirwan *et al.* 1992).

To our knowledge, studies comparing different brief vigorous exercise protocols on muscle insulin sensitivity and associated mechanisms have not been reported and this area remains ripe for investigation. Improvements in basal insulin sensitivity and glucose tolerance following training in some studies (e.g. Metcalfe *et al.* 2012; Gillen *et al.* 2016; Søgaard *et al.*, 2018) are likely related to a complex interplay of structural and functional adaptations in a range of tissues including skeletal muscle, liver, adipose tissue, the vasculature, the pancreas and others. It is inherently difficult to tease out which of these tissues or mechanisms are responsible for training-induced changes in insulin sensitivity and glycaemic regulation but the increases in muscle mitochondrial, GLUT4 and resting glycogen content following brief vigorous exercise training are likely candidates (Gillen *et al.* 2014, 2016; Søgaard *et al.* 2018). Reductions in total or regional adiposity (Søgaard *et al.* 2018) may also be linked to improved whole body insulin sensitivity. More studies employing the hyperinsulinaemic–euglycaemic clamp technique would help identify if skeletal muscle insulin sensitivity is improved following brief vigorous exercise interventions. Research examining how brief vigorous exercise impacts liver insulin sensitivity and β-cell function is limited, with very few studies exploring how any form of brief vigorous exercise impacts these parameters. However, there is evidence that some markers of liver insulin resistance and β-cell dysfunction can be favourably affected by higher volume interval training protocols (Madsen *et al.* 2015; Nieuwoudt *et al.* 2017; Winding *et al.* 2018; Heiskanen *et al.* 2018). Future studies are clearly needed to elucidate the physiological mechanisms responsible for improvements in insulin sensitivity and glycaemic control following brief vigorous exercise; experiments involving clamps, dynamic measures of β-cell function, and glucose tracers would be informative in this regard.

Another hypothesized mechanism whereby vigorous exercise might influence insulin sensitivity over the longer term is through reductions in appetite as a limited number of brief vigorous exercise studies have been reported to acutely reduce appetite in the hours following a single session of training (Islam *et al.* 2017). Whether such a mechanism can influence energy balance, body composition, glucose control and insulin sensitivity over weeks or months remains to be determined. Improvements in food tracking technology and use of new methods such as ecological momentary assessment (Dunton, 2017) could allow further insight into such mechanisms influencing glycaemic control in response to brief vigorous exercise.

Conclusions and future directions

Brief vigorous exercise – defined here as protocols in which the total period of vigorous exercise lasted ≤5 min within a total session duration of ≤15 min – is efficacious for improving CRF. The impact of brief vigorous exercise on glycaemic control is less clear, but there is evidence that various brief intermittent-type protocols can improve markers of insulin sensitivity and glucose regulation. The physiological mechanisms underlying improved CRF and glycaemic control following brief vigorous exercise training warrant further investigation, but preliminary work suggest at least some responses are similar to that induced by more prolonged periods of higher-volume exercise performed at lower intensities. There has been intense scientific and public interest in brief vigorous exercise in recent years, largely stemming from work showing that SIT can elicit physiological remodelling traditionally associated with prolonged moderate-intensity exercise in a time-efficient manner (Gibala *et al.* 2012; MacInnis & Gibala, 2017). By exploring the mechanisms mediating physiological adaptations to this type of training, scientists will be able to determine whether brief vigorous exercise can substitute for more traditional forms of exercise and understand how it compares for improving performance and health. Incorporating traditional ‘cardio’ training with resistance training is one promising area where such a hybrid-style of brief vigorous exercise may be a time-efficient exercise model for improving fitness and metabolic health (Fealy

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et al. 2018), including in older individuals (Winett and Ogletree 2019). The concept of 'exercise snacks', whereby isolated, short bouts (~20 s) of vigorous exercise can be incorporated into the day with several hours of rest in between (Jenkins *et al.* 2019; Little *et al.* 2019) is another interesting idea for moving brief vigorous exercise from the laboratory to the real-world. Recent suggestions that 'high-intensity incidental physical activity' should be translated for health promotion (Stamatakis *et al.* 2019) hold promise to bring physiological research on brief vigorous exercise to the forefront of public health.

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Additional information

Competing interests

None declared.

Author contributions

M.J.G. conceived the initial outline for this review article, with input from J.P.L. Both authors contributed equally to the drafting of the manuscript. Both authors approved the final version of the manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All persons designated as authors qualify for authorship and only those who qualify for authorship are listed.

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