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REVIEW ARTICLE

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Effects of fasted vs fed-state exercise on performance and post-exercise metabolism: A systematic review and meta-analysis

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The effects of nutrition on exercise metabolism and performance remain an important topic among sports scientists, clinical, and athletic populations. Recently, fasted exercise has garnered interest as a beneficial stimulus which induces superior metabolic adaptations to fed exercise in key peripheral tissues. Conversely, pre-exercise feeding augments exercise performance compared with fasting conditions. Given these seemingly divergent effects on performance and metabolism, an appraisal of the literature is warranted. This review determined the effects of fasting vs pre-exercise feeding on continuous aerobic and anaerobic or intermittent exercise performance, and post-exercise metabolic adaptations. A search was performed using the MEDLINE and PubMed search engines. The literature search identified 46 studies meeting the relevant inclusion criteria. The Delphi list was used to assess study quality. A meta-analysis and meta-regression were performed where appropriate. Findings indicated that pre-exercise feeding enhanced prolonged ($P = .012$), but not shorter duration aerobic exercise performance ($P = .687$). Fasted exercise increased post-exercise circulating FFAs ($P = .023$) compared to fed exercise. It is evidenced that pre-exercise feeding blunted signaling in skeletal muscle and adipose tissue implicated in regulating components of metabolism, including mitochondrial adaptation and substrate utilization. This review's findings support the hypothesis that the fasted and fed conditions can divergently influence exercise metabolism and performance. Pre-exercise feeding bolsters prolonged aerobic performance, while seminal evidence highlights potential beneficial metabolic adaptations that fasted exercise may induce in peripheral tissues. However, further research is required to fully elucidate the acute and chronic physiological adaptations to fasted vs fed exercise.

KEYWORDS
exercise adaptation, performance nutrition, substrate metabolism

1 | INTRODUCTION

The relationship between exercise, nutrition, and metabolism is complex, and the molecular mechanisms by which they interact are not fully characterized. Investigating novel diet-exercise interactions holds relevance for the sports nutrition sphere, as optimizing metabolic and training adaptations to exercise is a critical determinant of athletic performance.[1,2] Moreover, current literature has assessed the efficacy of combining nutritional and exercise interventions to improve metabolic health biomarkers including insulin sensitivity, glucose, and lipid metabolism.[3,4]

Recently, fasting-based interventions such as intermittent fasting have garnered interest as alternatives to

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conventional dietary strategies for improving metabolic biomarkers in both healthy and clinical populations.[5,6] This is based on the hypothesis that such interventions act on similar biological pathways to conventional methods, while potentially being a more feasible long-term approach. Fasting is characterized by the absence of energy intake for sustained time periods, ranging from several hours to days.[7] Most individuals spend time fasting overnight while sleeping (~8-10 hours), but the duration of this period may vary depending on habitual eating patterns and time spent sleeping. As the fasted period continues past the first few hours, substrate utilization predominantly shifts from glycogenolysis to utilizing lipids for energy,[8] and expression of genes involved in lipolysis and fatty acid oxidation in various peripheral tissues are upregulated.[9]

Regular aerobic exercise improves metabolism in different peripheral tissues, including skeletal muscle, liver, and adipose tissue.[10-12] In skeletal muscle, exercising in the fasted state promotes utilization of fatty acids and intramuscular triglycerides as primary fuel sources while suppressing glucose metabolism compared with fed conditions, both after acute exercise and in response to a chronic training intervention.[13-15] This proposedly occurs via altered gene and protein expression of various downstream targets including pyruvate dehydrogenase kinase isozyme 4 (PDK4), AMP-activated protein kinase (AMPK), glucose transporter type 4 (GLUT4), uncoupling protein-3, and fatty acid translocase (CD36).[13,14,16] Moreover, long-term fasted exercise is evidenced to upregulate activity of mitochondrial enzymes such as citrate synthase (CS) and β-hydroxyacyl coenzyme A dehydrogenase (β-HAD) compared with the carbohydrate-fed state.[15] These findings support the rationale that training in a glucose-deprived state induces adaptations which improve fuel efficiency and utilization during exercise. However, regarding studies investigating potential divergent responses to exercise in fasted or fed conditions, changes in acute exercise studies may not necessarily be directly applicable to studies investigating chronic training adaptations and the responses to feeding vs fasting.

Interestingly, a recent fasted vs fed exercise trial found that pre-exercise feeding blunted the expression of several key genes involved in adipose tissue metabolism.[17] These findings again indicate that acute nutritional status can profoundly affect the magnitude of post-exercise physiological adaptations in important endocrine tissues. Given that these cellular adaptations are a critical determinant of exercise performance, understanding these mechanisms and the potential role of nutrition in optimizing these adaptations is imperative. Pre-exercise carbohydrate feeding benefits continuous aerobic exercise performance,[18] but research has recently focused on alternative nutritional strategies that can simultaneously enhance both metabolism and performance, such as training in a protein fed, but carbohydrate-depleted state.[19] Clearly, an appraisal of the current literature in the inter-related areas of fasting, metabolism, and exercise performance is warranted. The effects of fasted vs fed-state exercise on substrate utilization during exercise have been summarized elsewhere,[20] and are beyond the scope of this review. However, gaps in the literature remain regarding an appraisal of post-exercise metabolic and performance responses to exercise in fasted and fed conditions. This systematic review and meta-analysis summarized current findings regarding the effects of fasting vs fed pre-exercise conditions on post-exercise metabolic and performance adaptations to continuous aerobic, anaerobic, and intermittent exercise. For the purposes of this review, aerobic and anaerobic exercise are defined by the metabolic pathways which primarily contribute to energy provision during these types of exercise. Intermittent exercise is characterized as exercise comprising periods of high-intensity exercise interspersed with lower intensity exercise.

2 | METHODS

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[21]

2.1 | Study selection

This review evaluated randomized and non-randomized control trials (parallel and crossover designs, blinded, and non-blinded), Latin square designs, and case studies. Continuous aerobic, anaerobic and intermittent exercise were established as protocols of interest, with acute and chronic interventions being included. Studies had to compare the same exercise intervention in both fasted and fed conditions. To be included in final analyses, papers had to assess performance or post-exercise metabolism. Human adults (aged ≥18 years) were selected as the target population in this review. Healthy and clinical as well as trained and untrained study populations were included.

To specifically assess the effects of pre-exercise nutritional status on metabolism and exercise performance, studies where feeding occurred during exercise were excluded. The fasting condition was required to be that of an overnight fast (minimum 8 hours) or longer. Studies where ergogenic aids, such as caffeine, were consumed pre-exercise were excluded. Similarly, studies using intravenous infusions of nutrients or corresponding tracer infusions during exercise were also excluded from final analyses. Studies assessing only substrate metabolism changes during exercise in fasted and fed conditions were excluded as this has previously been comprehensively reviewed by Vieira et al.[20] Ramadan fasting may have potential confounding effects on exercise performance or metabolism such as sleep deprivation or reduced caloric intake,[22,23] thus studies comparing the effects of Ramadan fasting vs fed-state exercise were also excluded.

2.2 | Literature search

The electronic databases MEDLINE (via the EBSCO platform) and PubMed were searched from inception until April 2017, and updated on June 28th 2017. The specific search criteria used for this systematic review was as follows: (((((“exercise”[MeSH Terms]) OR “aerobic”) OR “intermittent”) OR “interval”)) AND (((“fasting”[MeSH Terms]) OR (“fast” OR “fasting” OR “time-restricted feeding” OR “fasted state” OR “energy restriction” OR “fed” OR “carbohydrate loading” OR “low carbohydrate” OR “glucose deprived” OR “glucose depleted” OR “diet restriction” OR “low glucose” OR “fasted”))). Articles were limited to human studies in adult populations. Additionally, hand searching of reference lists was also completed on studies included in this review and other relevant papers.

2.3 | Data extraction and quality assessment

A step by step overview of data extraction and study selection processes involved in this review are included below (Figure 1). Data extracted from selected papers included author, year of publication, journal publication, study design, population type, number of participants, sex, age, training status, fasting condition, feeding condition, intervention frequency and duration, exercise type, exercise duration and intensity, statistical tests used, performance measures, metabolic measures, and statistical outcomes of each study. The methodological quality of studies included for review was assessed using the Delphi list, a criteria list developed by Delphi consensus among international experts in the field of quality assessment of randomized clinical trials.[24]

2.4 | Data analysis

Effect size (Hedges g [g]) was calculated for each trial (fed vs fasted [k]) using a pooled standard deviation, and mean difference between the fasted and fed groups or conditions groups.[25] The obtained effect is interpreted according to Cohen[26] (0.2 = ‘small’; 0.5 = ‘medium’; 0.8 = ‘large’). Heterogeneity was assessed by Cochran’s Q (Q) and I^2. Heterogeneity was observed between study effect sizes (ES) (Performance [$Q = 61.1$, $P = .068$, $I^2 = 25\%$]; circulating glucose and free fatty acids [FFA] [$Q \leq K - 1$]), and as methodology differed between studies (eg performance measure, population [ie sex, training status], feed type, dose, and timing) a random effects model was used to calculate the pooled ES for exercise performance, and post-exercise circulating glucose and FFA, with a [lower:upper] 95% confidence interval[25,27] (R Studio 1.1.383). A meta-regression was used to determine moderator effects for fitness level (VO_2 max), feed type (carbohydrate or mixed meal, fat), feed proximity to exercise (outside of or within 60 minutes), and performance-type measure (long-duration exercise [>60 minutes] vs short-duration exercise [<60 minutes]) (SPSS 24). Four moderators were selected a priori based on theoretical relation, supporting empirical evidence, and k.[25,28,29]

3 | RESULTS

In total, 13 138 studies were identified from database searching in PubMed and Medline, which were screened by title and abstract after removal of duplicates. Of these, 99 were included for full-text review, with a further 75 papers excluded due to not meeting the relevant inclusion/exclusion criteria. The remaining 24 papers were included in final analyses. A further 22 studies were identified for inclusion through manually searching references lists of other relevant papers. Table 1 shows the summary characteristics of included studies which assessed the effects of fasted vs fed-state exercise on metabolic or performance adaptations.

3.1 | Quality assessment

The results for quality assessment using the Delphi list are summarized in Table 1. Studies were ranked based on a maximum possible score of 9 criteria which evaluate different indicators of study quality. Rankings were defined as excellent (≥8), very good (6-7), moderate (4-5), and low (≤3)-quality study design. There were certain issues with specific aspects of quality in several studies. No studies reported whether or not treatment allocation was used, while 18 studies did not implement intention-to-treat analyses. Blinding of participants was a challenge in some studies given the nature of their design, for example, if a study was investigating the effects of a pre-exercise meal vs fasting condition on exercise performance. Consequently, only 16 studies included a blinding measure for participants.

3.2 | Exercise performance

Collectively, 23 studies assessed performance during acute exercise. Of these, 20 evaluated responses to continuous aerobic exercise, while 3 determined performance changes in fasted vs fed conditions during anaerobic or intermittent exercise. One study investigated the effects of

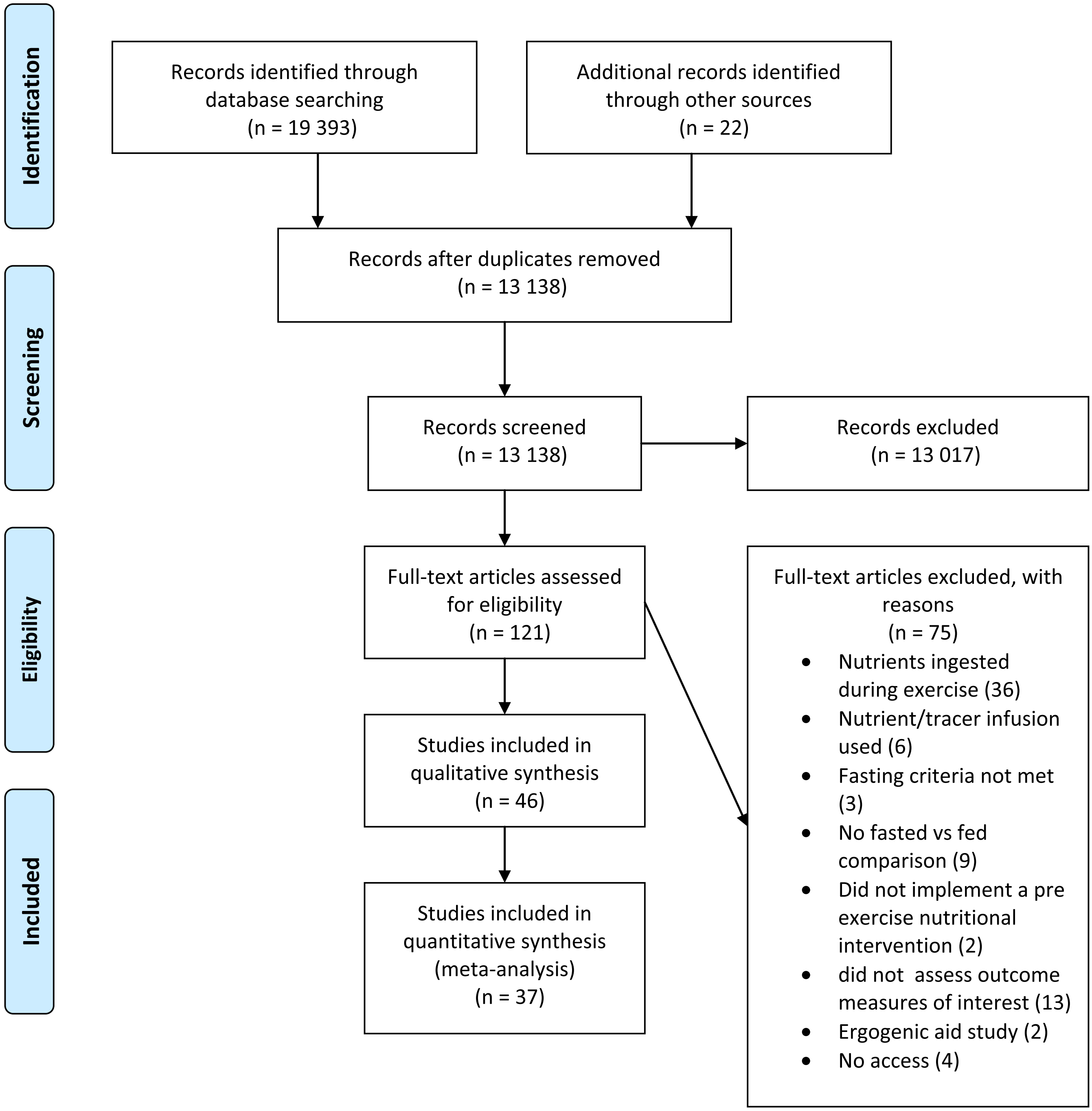

FIGURE 1 Study selection and flow diagram of articles included in systematic review and meta-analysis

a 6-week intervention on anaerobic exercise performance markers. Summary outcomes of these studies are presented in Table 2. A small feeding ES was observed for continuous aerobic exercise performance ($k = 47$; $g = 0.2$ [0:0.3]; $Z = 1.77$; $P = .076$). ES varied by exercise performance duration only ($\beta = 0.326$, $P = .011$). A difference in overall ES was observed for subgroup analysis between short- and long-duration exercise performance ($Z = 2.150$; $P = .032$). A small feeding ES was observed for long-duration exercise performance ($k = 25$; $g = 0.3$ [0.1:0.5]; $Z = 2.51$; $P = .012$), whereas no feeding effect was observed for short-duration exercise performance ($k = 22$; $g = 0$ [−0.3:0.2]; $Z = 0.40$; $P = .687$).

3.2.1 | Aerobic exercise

Most studies in this review evaluated the effects of fasted vs fed exercise on performance during continuous long-duration aerobic exercise (>60 minutes). Of these, 54% found that pre-exercise feeding improved performance,[31,47,54,55,61,67,72] while the remainder evidenced no difference between fasted and fed groups.[30,35,37,58,59,62] Regarding studies showing

TABLE 1 Summary characteristics of studies included in systematic review

Author	Quality score	N female	N male	Age range	Training status	Fasting condition	Feeding condition	Pre-exercise feed timing	Exercise Type	Performance measures	Post-exercise metabolic measures	Post-exercise measurement period
Alberici et al (1993)[30]	5	0	8	Not reported	Trained	Overnight fast (12 h)	One (440 kcal, 46 g CHO, 24 g FAT) or Two (880 kcal, 92 g CHO, 48 g FAT) large candy bars	30 min	Aerobic exercise	Cycling time to exhaustion	Glucose + FFA metabolism	0-20 min post
Anderson et al (1994)[31]	5	0	9	Not reported	Trained	Overnight fast (12 h)	70 g oatmeal or glucose	60 min	Aerobic exercise	Cycling time to exhaustion	-	-
Bennard & Doucet (2006)[32]	4	0	8	21-27	Trained	Overnight fast	Low GI (400 kcal, 80 g CHO, GI ~48) or high GI (400 kcal, 80 g CHO, GI ~103) meal	45 min	Aerobic exercise	-	Glucose metabolism	0-2 h post
Bergman & Brooks (1999)[33]	5	0	14	19-32	Trained & Untrained	Overnight fast	CHO-based meal (550 kcal, 87% CHO, 2% FAT, 11% PRO)	3 h	Aerobic exercise	-	-	0 h post
Boone et al (1995)[34]	5	0	20	Not reported	Not reported	36 h fast	3 pre-prepared meals per day	Not reported	Aerobic exercise	VO_2 max	-	-
Calles-Escandon et al (1991)[35]	4	0	8	Not reported	Not reported	Overnight fast	65 g fructose or isocaloric mixed snack meal (260 kcal, 43 g CHO, 9 g FAT, 3 g PRO)	30 min	Aerobic exercise	Cycling time to exhaustion	Glucose + FFA metabolism	0-60 min post
Cappon et al (1993)[36]	6	1	10	22-35	Trained	Overnight fast	Liquid high-fat (115 mL double cream) or glucose (136.8 g) drink	45 min	Anaerobic exercise	-	Glucose metabolism + metabolic hormone signalling	0-90 min post
Chen et al (2017)[17]	4	0	10	18-35	Untrained	Overnight fast (12 h)	CHO-based meal (648 kcal, 120.1 g CHO, 12.7 g FAT, 20.9 g PRO)	2 h	Aerobic exercise	-	Glucose + FFA metabolism + adipose tissue metabolism	0-60 min post
Chryssanthopoulus et al (1994)[37]	7	4	5	Not reported	Trained	Overnight fast	75 g glucose	30 min	Aerobic exercise	Running time to exhaustion	Glucose metabolism	0 h post
Coyle et al (1985)[38]	4	0	7	Not reported	Trained	Overnight fast (16 h)	CHO-based meal (2 g/kg CHO, 0.3 g/kg PRO)	4 h	Aerobic exercise	-	Glucose + FFA metabolism	0 h post
Crowe & Caulfield (2012)[39]	3	0	1	40	Trained	44 h fast	Non-fasting (not specified)	Not reported	Aerobic exercise	-	CHO oxidation	0-10 min post

(Continues)

TABLE 1 (Continued)

Author	Quality score	N female	N male	Age range	Training status	Fasting condition	Feeding condition	Pre-exercise feed timing	Exercise Type	Performance measures	Post-exercise metabolic measures	Post-exercise measurement period
Enevoldsen et al (2004)[40]	5	0	7	21-31	Not reported	Overnight fast (12 h)	Mixed meal (3.5 MJ, 60% CHO, 20% PRO, 20% FAT)	60 min	Aerobic exercise	-	Glucose + FFA metabolism + metabolic hormone signalling	0-3 h post
Erdmann et al (2010)[41]	4	12	8	Not reported	Not reported	Overnight fast (12 h)	CHO-based meal (290 kcal, 47 g CHO, 4.6 g PRO, 9 g FAT), or PRO-based meal (160 kcal, 0 g CHO, 33.3 g PRO, 3 g FAT)	30 min or 2 h	Aerobic exercise	-	Glucose metabolism + metabolic hormone signalling	0-60 min post
Ferland et al (2007)[42]	5	0	10	36-64	Untrained	Overnight fast (12 h)	Mixed meal (60% CHO, 17% PRO, 30% FAT)	2 h	Aerobic exercise	-	Glucose metabolism	0-30 min post
Ferland et al (2009)[43]	6	0	10	34-71	Untrained	Overnight fast	High GI (452 kcal, 67 g CHO, 16 g PRO, 14 g FAT, GI ~80) or low GI (453 kcal, 68 g CHO, 16 g PRO, 14 g FAT, GI ~49) meal, low calorie meal (358 kcal, 44 g CHO, 16 g PRO, 14 g FAT, GI ~65), high-fat low CHO meal (30 g CHO, 17 g PRO, 31 g FAT, GI ~65)	2 h 15 min	Aerobic exercise	-	Glucose + FFA metabolism + metabolic hormone signalling	0-30 min post
Fielding et al (1987)[44]	8	0	6	Not reported	Trained	Overnight fast (12 h)	75 g glucose or fructose	30 min	Aerobic exercise	-	Glucose metabolism	0 h post
Galloway et al (2014)[45]	8	0	17	Not reported	Trained	Overnight fast (≥10 h)	6.4% CHO drink (32 g CHO)	30 min or 2 h	Anaerobic exercise	Cycling time to exhaustion	Glucose metabolism	0-3 min post
Gillen et al (2013)[46]	4	16	0	Not reported	Untrained	Overnight fast (≥10 h)	CHO-based meal (74% CHO, 12% PRO, 14% FAT)	60 min	Intermittent exercise	Wingate exercise performance	Glucose + skeletal muscle metabolism	Baseline, 6 wk post

(Continues)

TABLE 1 (Continued)

Author	Quality score	N female	N male	Age range	Training status	Fasting condition	Feeding condition	Pre-exercise feed timing	Exercise Type	Performance measures	Post-exercise metabolic measures	Post-exercise measurement period
Gleeson et al (1986)[47]	8	0	6	Not reported	Not reported	Overnight fast	1 g/kg glucose or glycerol	45 min	Aerobic exercise	Cycling time to exhaustion	Glucose + FFA metabolism	0-15 min post
Gonzalez et al (2013)[48]	5	0	12	Not reported	Untrained	Overnight fast (10-14 h)	Porridge meal (60% CHO, 17% PRO, 23% FAT)	2 h	Aerobic exercise	-	Glucose + FFA metabolism	0-90 min post
Guerra et al (2011)[49]	4	0	15	Not reported	Not reported	Overnight fast	75 g glucose	63 min	Anaerobic exercise	-	Glucose + skeletal muscle metabolism	0-4 h post
Guerra et al (2010)[50]	4	0	15	Not reported	Not reported	Overnight fast	75 g glucose	63 min	Anaerobic exercise	-	Glucose + skeletal muscle metabolism	0-4 h post
Hargreaves et al (1985)[51]	7	0	8	Not reported	Not reported	Overnight fast	50 g glucose or fructose	45 min	Aerobic exercise	-	Glucose metabolism	0 h post
Isacco et al (2012)[52]	5	21	0	18-30	Trained	Overnight fast (≥14 h)	Mixed meal (50% CHO, 15% PRO, 35% FAT)	3 h	Aerobic exercise	-	Glucose + FFA metabolism + metabolic hormone signalling	0-90 min post
Jentjens et al (2003)[53]	5	0	9	Not reported	Trained	Overnight fast (10-12 h)	25 g, 75 g or 200 g glucose	45 min	Aerobic exercise	Fixed work time trial performance	Glucose metabolism	0 h post
Kirwan et al (1998)[54]	6	6	0	Not reported	Trained	Overnight fast	75 g rolled oats or oat flour	45 min	Aerobic exercise	Cycling time to exhaustion	Glucose + FFA metabolism + metabolic hormone signalling	0 h post
Kirwan et al (2001)[55]	6	0	6	Not reported	Trained	Overnight fast	75 g mod (rolled oats; GI ~61) or high GI (puffed rice; GI ~82) CHO	45 min	Aerobic exercise	Cycling time to exhaustion	Glucose + FFA metabolism + metabolic hormone signalling	0 h post

(Continues)

TABLE 1 (Continued)

Author	Quality score	N female	N male	Age range	Training status	Fasting condition	Feeding condition	Pre-exercise feed timing	Exercise Type	Performance measures	Post-exercise metabolic measures	Post-exercise measurement period
Koivisto et al (1981)[56]	8	0	9	Not reported	Trained	Overnight fast (10-12 h)	75 g glucose or fructose	45 min	Aerobic exercise	Cycling time to exhaustion	Glucose + FFA metabolism + metabolic hormone signalling	0-30 min post
Little et al (2010)[57]	6	0	16	Not reported	Trained	Overnight fast (min 10 h)	1.5 g/kg BM low (lentils; GI 26) or high GI meal (potato and egg white; GI 76);	2 h	Intermittent exercise	Total distance completed during intermittent exercise test	Glucose + FFA metabolism + metabolic hormone signalling	0 h post
McMurray et al (1983)[58]	7	6	0	Not reported	Trained	Overnight fast	100 g glucose or fructose	45 min	Aerobic exercise	-	Glucose + FFA metabolism	0 h post
Miller et al (1983)[59]	7	1	9	Not reported	Trained	Overnight fast	1 g/kg BM glycerol	30 min	Aerobic exercise	Fixed work time trial performance	Glucose + FFA metabolism	0-30 min post
Neufer et al (1987)[60]	5	0	10	Not reported	Trained	Overnight fast	Liquid CHO (45 g glucose/fructose) or confectionary bar (45 g CHO, 9 g FAT, 3 g PRO) or meal + confectionary bar (200 g CHO + confectionary bar)	5 min or 4 h	Aerobic exercise	Fixed work time trial performance	Glucose metabolism	0 h post
Nieman et al (1987)[61]	4	0	9	Not reported	Trained	27 h fast	7 kcal/kg BM liquid mixed meal (52.8% CHO, 15.2% PRO, 32% FAT)	3 h	Aerobic exercise	Running time to exhaustion	Glucose + FFA metabolism + metabolic hormone signalling	0 h post
Nieman et al (2015)[62]	6	8	16	24-55	Trained	Overnight fast (≥9 h)	7 kcal/kg BM chia seed oil	30 min	Aerobic exercise	Running time to exhaustion	Glucose metabolism + metabolic hormone signalling	0-4 h post

(Continues)

TABLE 1 (Continued)

Author	Quality score	N female	N male	Age range	Training status	Fasting condition	Feeding condition	Pre-exercise feed timing	Exercise Type	Performance measures	Post-exercise metabolic measures	Post-exercise measurement period
Paul et al (1996a)[63]	6	6	6	Not reported	Trained	Overnight fast	Wheat, corn or oat-based cereal (368 kcal for male, 281 kcal for women; with 4 g sucrose and skimmed milk; 95 mL for women & 125 mL for men)	90 min	Aerobic exercise	Fixed distance time trial performance	Glucose + FFA metabolism	0-60 min post
Paul et al (1996b)[64]	6	6	6	Not reported	Trained	Overnight fast	Wheat, corn or oat-based cereal (368 kcal for male, 281 kcal for women; with 4 g sucrose and skimmed milk; 95 mL for women and 125 mL for men)	90 min	Aerobic exercise	Fixed distance time trial performance	Glucose + FFA metabolism	0-60 min post
Poirier et al (2001)[65]	5	0	10	43-60	Untrained	Overnight fast	Mixed meal (495 kcal, 49% CHO, 34% FAT, 17% PRO)	2 h	Aerobic exercise	-	Glucose + FFA metabo-lism + metabolic hormone signalling	0-30 min post
Pritchett et al (2008)[66]	4	0	10	Not reported	Trained	Overnight fast (≥8 h)	Low GI nutritional bar (160 kcal, 20 g CHO, 4 g FAT, 11 g PRO)	15 or 60 min	Intermittent exercise	Wingate exercise performance	Glucose metabolism	0 h post
Schabort et al (1999)[67]	4	0	7	Not reported	Trained	Overnight fast	CHO-based meal (468 kcal, 98 g CHO, 17.2 g PRO, 0.87 g FAT)	3 h	Aerobic exercise	Cycling time to exhaustion	Glucose + FFA metabo-lism + metabolic hormone signalling	0 h post
Scott et al (2012)[68]	3	0	10	Not reported	Trained	Overnight fast	Mixed meal (2.3 MJ, 60% CHO, 8% PRO, 32% FAT)	2 h 15 min	Aerobic exercise	-	Glucose metabo-lism + metabolic hormone signalling	0-3 h post

(Continues)

TABLE 1 (Continued)

Author	Quality score	N female	N male	Age range	Training status	Fasting condition	Feeding condition	Pre-exercise feed timing	Exercise Type	Performance measures	Post-exercise metabolic measures	Post-exercise measurement period
Sherman et al (1989)[69]	8	1	9	Not reported	Trained	Overnight fast (10 h)	Low (733 kcal, 45 g CHO), medium (733 kcal, 156 g CHO) or high-CHO (1248 kcal, 312 g CHO) liquid meals	4 h	Intermittent + aerobic exercise	Fixed work time trial performance	Glucose + FFA metabolism	0 h post
Sherman et al (1991)[70]	8	0	9	Not reported	Trained	Overnight fast (10 h)	1.1 g/kg BM or 2.2 g/kg BM CHO drink	60 min	Aerobic exercise	Fixed work time trial performance	Glucose + FFA metabolism	0 h post
Terada et al (2016)[71]	4	2	8	47-69	Untrained	Overnight fast (12 h)	Mixed meal (600 kcal, 50% CHO, 30% FAT, 20% PRO)	60 min	Intermittent exercise	-	Glucose metabolism	0-24 h post
Thomas et al (1991)[72]	4	0	8	20-40	Trained	Overnight fast (12 h)	1 g/kg BM CHO (Lentils; GI 29, baked potato; GI 98, or glucose; GI 100)	60 min	Aerobic exercise	Cycling time to exhaustion	Glucose + FFA metabolism	0 h post
Ziogas et al (1998)[73]	5	0	7	Not reported	Trained	Overnight fast	Mixed meal (756 kcal, 59% CHO, 29% FAT, 12% PRO)	3 h	Aerobic exercise	-	Glucose metabolism	0-5 min post
Zoladz et al (2005)[74]	5	0	8	Not reported	Not reported	Overnight fast	Mixed meal (870 kcal, 120 g CHO, 30 g PRO, 30 g FAT)	2 h	Aerobic exercise	-	Glucose metabolism + metabolic hormone signalling	0 h post

a beneficial effect of acute pre-exercise feeding on aerobic exercise performance, 1 provided a mixed meal,[61] 1 implemented a high-carbohydrate meal,[67] and 5 provided predominantly carbohydrate as an energy source.[31,47,54,55,72] A further 7 studies evaluated markers of shorter duration (<60 minutes) aerobic performance.[53,56,60,63,64,69,70] Of these, 57% found no differences in performance between fasted and fed conditions.[53,56,63,64] The remaining studies determined that pre-exercise feeding bolstered time trial performance.[60,69,70] Of these, 2 provided carbohydrates,[69,70] while the other provided carbohydrate-based meals[60] as pre-exercise feeding condition.

3.2.2 | Anaerobic and intermittent exercise

Four studies in this review assessed anaerobic and intermittent exercise performance. Galloway et al[45] found that pre-exercise carbohydrate ingestion improved time to exhaustion during anaerobic exercise compared with fasted conditions. Regarding intermittent exercise, 3 studies found that performing high-intensity interval training (HIIT) in fasted or fed conditions did not affect performance measures over a single exercise bout or following a chronic intervention.[46,57,66]

3.3 | Metabolism

Forty-five studies in this review assessed post-exercise changes in metabolic biomarkers between fasted and fed conditions. Fuel metabolism responses were evaluated in 42 studies, while 14 papers determined changes in endocrine signaling in fasted and fed exercise states. Additionally, 4 trials assessed metabolic signaling in peripheral tissues between fasted and fed conditions. Summary outcomes for these studies are presented in Table 2.

TABLE 2 Exercise performance and post-exercise metabolic outcomes of studies included in systematic review

Author	Performance results	Performance outcomes	Post-exercise metabolic outcomes
Alberici et al (1993)[30]	No difference between groups	↔	↑ glucose in fed vs fasted
Anderson et al (1994)[31]	Oats (84) vs fasted (66) min	↑	-
Bennard & Doucet (2006)[32]	-	-	No difference between groups
Bergman & Brooks (1999)[33]	-	-	No difference between groups
Boone et al (1995)[34]	No difference between groups	↔	-
Calles-Escandon et al (1991)[35]	No difference between groups	↔	No difference between groups
Cappon et al (1993)[36]	-	-	↓ growth hormone in high-fat feeding vs fasted ↑ somatostatin in high-fat feeding vs fasted
Chen et al (2017)[17]	-	-	↑ glucose/insulin in fed vs fasted ↓ FFAs in fed vs fasted ↓ PDK4, ATGL, HSL, CD36, GLUT4, IRS mRNA expression in fed vs fasted ↓ IRS2 protein expression in fed vs fasted
Chryssanthopoulus et al (1994)[37]	No difference between groups	↔	No difference between groups
Coyle et al (1985)[38]	-	-	No difference between groups
Crowe & Caulfield (2012)[39]	-	-	↑ carbohydrate oxidation in fed vs fasted
Enevoldsen et al (2004)[40]	-	-	↓ FFAs in fed vs fasted ↑ glucose in fed vs fasted ↑ insulin in fed vs fasted ↓ adrenaline in fed vs fasted
Erdmann et al (2010)[41]	-	-	↑ insulin in CHO-fed vs fasted ↑ insulin in PRO-fed vs fasted
Ferland et al (2007)[42]	-	-	No difference between groups
Ferland et al (2009)[43]	-	-	↑ adrenaline in fed vs fasted

(Continues)

TABLE 2 (Continued)

Author	Performance results	Performance outcomes	Post-exercise metabolic outcomes
Fielding et al (1987)[44]	-	-	No difference between groups
Galloway et al (2014)[45]	CHO30 vs all other groups	↑	↓ glucose in fed vs fasted
Gillen et al (2013)[46]	No difference between groups	↔	No difference between groups
Gleeson et al (1986)[47]	Glucose (108.6) vs fasted (95.9) min	↑	↓FFAs in fed vs fasted ↑ glucose in glycerol-fed vs fasted
Gonzalez et al (2013)[48]	-	-	No difference between groups
Guerra et al (2011)[49]	-	-	↑ insulin in fed vs fasted ↓ glucose in fed vs fasted ↓ ERK1/2, STAT3 & SOCS3 expression in fed vs fasted
Guerra et al (2010)[50]	-	-	↑ insulin in fed vs fasted ↓ glucose in fed vs fasted ↓ Thr172-AMPKα in fed vs fasted ↑ Ser485-AMPK 1/Ser491-AMPK 2 in fed vs fasted ↑ Ser473-Akt in fed vs fasted ↓ SIRT1 protein in fed vs fasted
Hargreaves et al (1985)[51]	-	-	No difference between groups
Isacco et al (2012)[52]	-	-	↓ insulin in fed vs fasted
Jentjens et al (2003)[53]	No difference between groups	↔	No difference between groups
Kirwan et al (1998)[54]	Rolled oats (266) vs fasted (225) min	↑	No difference between groups
Kirwan et al (2001)[55]	Mod GI (165) vs fasted (141) min	↑	No difference between groups
Koivisto et al (1981)[56]	No difference between groups	↔	No difference between groups
Little et al (2010)[57]	No difference between groups	↔	↑ insulin in fed vs fasted ↓ FFAs in fed vs fasted ↑ catecholamines in high-GI fed vs fasted
McMurray et al (1983)[58]	No difference between groups	↔	No difference between groups
Miller et al (1983)[59]	No difference between groups	↔	No difference between groups
Neufer et al (1987)[60]	Meal + CHO, glucose + fructose, snack bar vs fasted Meal + CHO vs all other trials	↑	No difference between groups
Nieman et al (1987)[61]	CHO-fed performance 44.7% greater than vs fasted	↑	↓ noradrenaline in fed vs fasted
Nieman et al (2015)[62]	No difference between groups	↔	No difference between groups
Paul et al (1996a)[63]	No difference between groups	↔	↓ FFAs in wheat meal vs fasted
Paul et al (1996b)[64]	No difference between groups	↔	↓ FFAs in wheat meal vs fasted
Poirier et al (2001)[65]	-	-	No difference between groups
Pritchett et al (2008)[66]	No difference between groups	↔	No difference between groups
Schabort et al (1999)[67]	CHO (135.7) vs fasted (109) min	↑	No difference between groups
Scott et al (2012)[68]	-	-	↓ glucose in fed vs fasted
Sherman et al (1989)[69]	High-CHO (47.9) vs fasted (56.2) min	↑	No difference between groups
Sherman et al (1991)[70]	Both fed conditions 12.5% improved vs fasted	↑	↑ glucose in high-CHO vs fasted ↑ insulin in high-CHO vs fasted ↓ FFAs in high-CHO vs fasted
Terada et al (2016)[71]	-	-	No difference between groups

(Continues)

TABLE 2 (Continued)

Author	Performance results	Performance outcomes	Post-exercise metabolic outcomes
Thomas et al (1991)[72]	Lentils vs all other trials	↑	↑ glucose in low/high GI vs fasted ↓ FFAs in fed vs fasted
Ziogas et al (1998)[73]	-	-	No difference between groups
Zoladz et al (2005)[74]	-	-	No difference between groups

↔ indicates values remain unchanged in fed vs fasted conditions; ↑ indicates values increase in fed vs fasted conditions; ↓ indicates values decrease in fed vs. fasted conditions.

3.3.1 | Glucose

Forty-two studies assessed changes in circulating glucose and/or insulin in response to exercise in fasted or fed conditions, with 10 identifying significant changes in post-exercise glucose levels between fasted and fed conditions. Six trials determined that glucose was increased in fed conditions following submaximal[17,40] or prolonged aerobic exercise.[30,47,70,72] The remaining studies indicated glucose was greater in fasted conditions following acute anaerobic[45,49,50] or submaximal exercise.[68] Feeding conditions eliciting increases in glucose following exercise compared with fasted conditions included a mixed meal,[30,40] a glycerol bolus,[47] a carbohydrate-based meal,[17] an oral carbohydrate solution, [70] and low/high glycaemic index (GI) carbohydrates.[72] Conversely, feeding interventions which resulted in lower blood glucose compared with fasting included an oral carbohydrate solution,[45] a glucose bolus,[49,50] and a mixed meal.[68] Gillen et al[46] observed no differences in oral glucose tolerance responses to 6 weeks of fasted vs fed-state HIIT. No overall pooled effect was observed post-exercise for circulating glucose ($k = 35$; $g = 0.1$ [−0.2:0.4]; $Z = 0.83$; $P = .406$). No moderator effects were observed for any variable within the meta-regression ($P \geq 470$).

Eight studies demonstrated significant changes in post-exercise insulin concentrations between acute nutritional conditions. Of these, 88% indicated increased insulin in fed conditions,[17,40,41,49,50,57,70] while another study indicated insulin was raised post-exercise in fasted conditions.[52] However, while a statistically significant post-exercise increase in insulin was observed by Isacco et al[52] in fasted compared with fed conditions, a difference of ~6 pmol/L may be quite small in biological terms. Feeding conditions in these studies included a mixed meal,[40] a carbohydrate-based meal,[17,41,57] a glucose bolus,[49,50] and an oral carbohydrate solution.[70] Two studies assessed metabolic responses to anaerobic exercise[49,50] while a third evaluated responses to acute intermittent exercise.[57] Gillen et al[46] found no differences in insulin sensitivity between groups following 6 weeks of fasted or fed-state HIIT.

3.3.2 | Free fatty acids

FFA concentrations were elevated in 38% of studies where it was measured in the fasted vs fed condition.[17,40,47,57,63,64,70,72] A large fasting effect was observed for post-exercise circulating FFA ($k = 36$; $g = 0.7$ [0.1:1.2]; $Z = 2.27$; $P = .023$). No moderator effects were observed for any variable ($P \geq .351$).

3.3.3 | Metabolic hormone signaling

Fourteen studies included in analyses evaluated changes in metabolic hormone signaling in fasted and fed exercise conditions, with 35% finding significant differences between groups.[36,40,43,57,61] Cappon et al[36] evidenced that performing anaerobic exercise after high-fat diet feeding reduces growth hormone secretion while elevating somatostatin levels, compared with fasted conditions. Another 3 studies identified altered endocrine signaling between fasted and fed conditions during continuous aerobic exercise.[40,43,61] Two studies found that exercising after consuming a mixed meal induced lower adrenaline levels in healthy subjects[40] and diabetic patients.[43] A third study demonstrated that fasted exercise raised noradrenaline levels compared with fed conditions following consumption of a mixed meal.[61] Finally, an acute HIIT study found post-exercise catecholamine concentrations were elevated following a high GI meal compared with exercise in the fasted state.[57]

3.3.4 | Skeletal muscle metabolism

Metabolic signaling changes in skeletal muscle were assessed in response to both anaerobic[49,50] and intermittent exercise[46]; however, no studies meeting our inclusion criteria evaluated such changes in response to continuous aerobic exercise. Gillen et al[46] implemented a chronic HIIT intervention where untrained overweight/obese women exercised in fasted conditions or after consuming a carbohydrate-based meal. Although HIIT exerted significant effects on various skeletal muscle biomarkers, no differences were observed between fasted and fed conditions in mitochondrial markers of enzymatic activity such as CS or β-HAD. Conversely, 2 studies assessing responses to acute anaerobic exercise following glucose feeding vs fasting demonstrated differences between these conditions in a number of signaling markers. Guerra et al[50] found that glucose ingestion significantly blunted the phosphorylation of signal transducer and activator of transcription 3 (STAT3), extracellular signal-regulated kinase (ERK1/2), and suppressor of cytokine signaling 3 (SOCS3) when compared with fasting conditions during recovery. A similar investigation[49] determined that glucose ingestion prior to anaerobic sprint exercise blunted the elevation of Thr172-AMPKα phosphorylation seen in the fasting group while the relative change in Ser485-AMPKα1/Ser491-AMPKα2 activation was significantly raised by glucose ingestion. Ser473-Akt phosphorylation was also increased immediately post-exercise in the glucose group compared with fasting conditions. Moreover, protein expression of sirtuin 1 (SIRT1) was elevated 120 minutes after fasted exercise, but glucose feeding blunted this response.

3.3.5 | Adipose tissue metabolism

Little evidence exists on the effects of exercising in fasted and fed conditions on metabolic signaling in adipose tissue. A recent seminal paper determined the effects of exercising in fasted vs fed conditions on adipose tissue messenger RNA (mRNA) and protein expression of key enzymes involved in lipid metabolism.[17] This study demonstrated that ingestion of a carbohydrate-based meal before prolonged aerobic exercise blunted the mRNA expression of PDK4, adipose triglyceride lipase (ATGL), hormone-sensitive lipase (HSL), CD36, GLUT4, and insulin receptor substrate 2 (IRS2). Furthermore, IRS2 protein expression was elevated under fasting conditions compared with pre-exercise feeding.

4 | DISCUSSION

4.1 | Exercise performance

For continuous aerobic exercise, several studies found no changes between fasted and fed conditions, although pre-exercise feeding bolstered prolonged (>60 minutes) aerobic capacity compared with fasted conditions. The similar performance responses between fasted and fed conditions in individual studies may be attributed to different factors. These may include using an alternative fuel source to carbohydrates or a carbohydrate-based meal,[59,62] a reduced magnitude of performance responses in trained vs untrained study populations,[30,37,58] or a large study population heterogeneity in terms of aerobic capacity.[35] Findings on shorter duration exercise (<60 minutes) demonstrated no overall performance effect for either fasted or fed exercise. The effects of pre-exercise feeding on anaerobic and intermittent exercise performance also indicate no differences between short- or long-term fasted vs fed-state HIIT,[46,57,66] while one study evidenced improved anaerobic performance after pre-exercise feeding.[45] These equivocal findings may reflect the fact that each study used different exercise protocols, or that pre-exercise feeding simply does not bolster intermittent exercise performance. While differences were observed between short- and long-duration exercise performance, given the small amount of studies evaluating performance responses to anaerobic and intermittent exercise, it remains difficult to make definitive inferences from results pertaining to this specific mode of exercise.

Overall results indicated that performance was not affected by pre-exercise feed timing. Interestingly, in the 4 studies where feeding occurred 3-4 hours pre-exercise, performance was categorically improved.[60,61,67,69] This could reflect increases in muscle/liver glycogen stores which are not attained when feeding is timed in the 60 minutes before exercise,[75] thus enhancing performance. Only 2 studies in this review assessed the effects of nutrient ingestion at multiple time points.[45,66] Pritchett et al[66] found no differences in intermittent exercise performance when feeding occurred 15 or 60 minutes pre-exercise. Conversely, Galloway et al[45] demonstrated that carbohydrate ingestion 30 minutes before anaerobic exercise bolstered performance compared with fasted conditions. Given the lack of available evidence, further research is required to determine whether pre-exercise feed timing influences anaerobic or intermittent exercise performance.

Meal composition and GI remain topics of debate in sports nutrition,[76] and its effects on performance were compared in 4 studies.[31,55,57,72] Of these studies, 75% determined that ingesting low/moderate GI carbohydrates pre-exercise improved prolonged aerobic capacity compared with fasting conditions, while high GI carbohydrates did not enhance performance. Endurance performance may improve as a result of enhanced fat oxidation and slower glucose release observed following low GI carbohydrate ingestion,[76] thus preserving glycogen stores for higher intensity exercise. Thomas et al[72] had similar findings, with low GI food consumption inducing lower carbohydrate oxidation rates during prolonged exercise compared with high GI ingestion. While not all studies report performance enhancements from low GI compared with high GI carbohydrate ingestion, no studies report performance decrements in response to low GI food consumption.[18] While of interest, these limited findings make it difficult to ascertain if GI truly influences exercise performance.

4.2 | Metabolism

Several acute studies evidenced post-exercise circulating glucose increases in fed vs fasted conditions following continuous aerobic exercise. This may reflect increased glucose availability for fuel utilization, or potential increases in glycogenolysis observed during prolonged exercise.[77] Conversely, glucose increased, while insulin was decreased during acute fasted vs fed anaerobic exercise in 3 studies.[45,49,50] Similar findings are observed elsewhere[78] and potentially indicate greater demands for glucose utilization during high-intensity exercise. The comparable results observed in some studies in terms of post-exercise circulating substrates may potentially be explained by the sample population characteristics. Metabolic flexibility is a key determinant of the ability to shift from glucose to fat oxidation during different physiological conditions, such as the fasted vs fed state.[79] Moreover, metabolic flexibility is purportedly influenced by environmental factors, including training status and fat mass.[80] Interestingly, of the 8 studies using sedentary and/or overweight/obese sample populations, 75% evidenced no changes in post-exercise glucose, insulin or FFAs between fasted and fed conditions. This may potentially explain the lack of change in these measures observed in these trials.

The effect of fasted vs fed-state exercise on skeletal muscle metabolic signaling was also evaluated.[46,49,50] Regarding long-term fasted vs fed-state exercise responses, Gillen et al[46] suggested that adaptations to intermittent exercise are similar irrespective of pre-exercise nutritional condition. However, other evidence has not investigated if chronic adaptations to intermittent exercise differ between fasted and fed conditions. Conversely, differences in metabolic signaling were detected between acute fasted and fed conditions following sprint exercise.[49,50] Fasted Wingate exercise increased SIRT1 expression and phosphorylated AMPK,[49] whereas pre-exercise glucose ingestion abated these effects. AMPK has myriad downstream effects on gene expression and is implicated in regulating mitochondrial biogenesis, substrate utilization, and autophagy.[81] SIRT1 is purportedly implicated in regulating metabolic processes primarily concerning mitochondrial adaptation,[10,82] and its increased nuclear abundance has been previously observed following HIIT.[83] Moreover, evidence indicates anaerobic exercise acts as a leptin signaling mimetic.[50] Similar to SIRT1 and AMPK, pre-exercise glucose ingestion partially or wholly blunted leptin signaling responses, similarly suggesting that fasted conditions may optimize metabolic signaling adaptations. AMPK is a critical regulator of peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α), the so-called "master regulator" of mitochondrial biogenesis, and its activation upon energy depletion in muscle phosphorylates PGC-1α, resulting in increased mitochondrial gene expression.[84] SIRT1 also proposedly plays a role in mediating PGC-1α in peripheral tissues.[85] While no differences in PGC-1α expression were observed between acute nutritional conditions here, fasted sprint exercise may induce superior molecular signaling responses to fed conditions over a prolonged time frame, potentially translating to improved chronic adaptations. However, these hypotheses have not been conclusively answered in the literature.

Circulating FFA concentrations were greater following fasted vs fed exercise. These findings were evidenced during prolonged exercise, suggesting that triglyceride mobilization from adipose tissue is increased, in turn elevating circulating FFA concentrations for potential use as fuel.[7] Interestingly, Chen et al[17] presented seminal evidence concerning the mechanisms by which lipid mobilization from adipose tissue occurs in response to fasted exercise. Specifically, mRNA expression of key lipolytic enzymes such as ATGL and HSL[86] was upregulated during fasted, but not fed exercise. Moreover, studies which evidenced endocrine signaling changes during fasted exercise bolstered these findings. Circulating levels of adrenaline,[40,43] noradrenaline,[61] and growth hormone[36] were increased in fasting conditions. Catecholamines are critical in the activation of fasting-induced lipolysis,[87] while growth hormone also stimulates this process.[88] Collectively, these findings outline potential mechanisms by which fasted exercise promotes lipid utilization compared with fed conditions.

4.3 | Perspectives

The review's findings indicate that fasted vs fed exercise conditions differentially affect performance and post-exercise metabolism. Pre-exercise feeding enhances performance during prolonged (>60 minutes) aerobic exercise, whereas performance did not differ during shorter duration aerobic exercise between fasted and fed conditions. Several individual studies suggest nutrient timing and meal composition influence exercise performance, and these factors should be tailored based on exercise type. Additionally, consuming lower GI compared with high-GI carbohydrates may augment prolonged aerobic performance. Regarding metabolism, fasted exercise mobilizes and promotes FFA utilization, with seminal evidence outlining potential mechanisms by which this occurs in adipose tissue. Fasted training activates signaling pathways which beneficially regulate metabolic adaptations in skeletal muscle, whereas pre-exercise feeding abrogates such effects. However, significant literature gaps remain regarding this topic. Further research is imperative to elucidate the effects of fasted vs fed exercise on skeletal muscle and adipose tissue metabolism, particularly following a chronic intervention. Similarly, unconventional feeding conditions such as the low-carbohydrate or protein-fed state have not been thoroughly investigated regarding their effects on metabolism and performance. Future studies are required to establish nutritional strategies which optimize metabolic and performance adaptations to exercise.

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CONFLICT OF INTEREST

None declared.

AUTHORS' CONTRIBUTIONS

T.P. Aird and B.P. Carson were responsible for review conceptualization and systematic searching. T.P. Aird, R.W. Davies and B.P. Carson completed the meta-analysis writing and final revisions of this manuscript.

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