

# **Oral Presence of Carbohydrate and Caffeine: Independent and Combined Effects on Endurance Performance**

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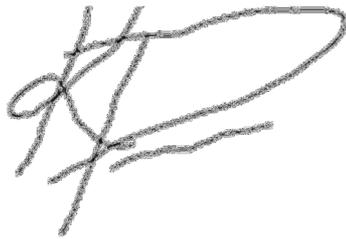
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**Attestation of Authorship**

I hereby declare that this submission is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person (except where explicitly defined in the acknowledgements), nor material which to a substantial extent has been submitted for the award of any other degree or diploma of a university or other institution of higher learning.

Signed:

A handwritten signature in black ink, consisting of several overlapping loops and lines, positioned to the right of the word "Signed:".

Date: 1 January, 2014.

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## **Ethical Approval**

Ethical approval for this thesis research was granted by the Auckland University of Technology Ethics Committee (AUTEC) on 25-August-2012, with AUTEC Reference number 12/187

## **Thesis overview**

This thesis adheres to pathway one, as classified by Auckland University post-graduate thesis structure guidelines (AUT Post Graduate handbook 2013). The layout of this thesis follows the conventional pathway whereby the document is wholly written. It consists of five chapters with references for each chapter presented at the end of the thesis. Chapter One provides an overview of the thesis. Chapter Two (Literature Review) introduces the reader to the concept of fatigue and central governance during exercise followed by outlining how these aspects of exercise performance may be ergogenic aids. Carbohydrate supplements and proposed physiological mechanisms are discussed before the concept of carbohydrate mouth-rinsing is introduced and discussed in terms of its proposed physiological mechanism of action and implications for endurance exercise performance. Caffeine is then discussed in terms of its physiological mechanisms, impact on exercise performance, and finally the effects of sublingual delivery and exercise performance are discussed. Chapter Three is the methods and includes the adopted experimental design and procedures. Chapter Four presents the results. Chapter Five is the discussion and provides an evaluation of the study findings including limitations, applications of findings and areas of potential future research in this area.

## Abstract

**Background:** Carbohydrate ingestion and mouth-rinsing has been shown to improve exercise performance during high-intensity, short duration endurance exercise. The precise mechanisms underlying the ergogenic effects remains unidentified, but have been partially attributed to central effects being mediated via the detection of carbohydrate in the mouth by oral 'energy-receptors'. Similarly, caffeine ingestion and delivery via the buccal cavity has been shown to improve endurance exercise performance, with ergogenic effects attributed to centrally mediated effects on adenosine receptor sites. However, no study has investigated whether providing carbohydrate and/or caffeine late in exercise can improve performance when under realistic conditions of exercise-induced fatigue. **Aim:** To determine the independent and combined effects of carbohydrate and caffeine chewing gum on self-paced cycling time-trial performance under the influence of exercise-induced fatigue. Further, the study aimed to examine the possibility of the chewing gums' contents mediating central mechanistic effects on subconscious motor output (pacing) during time-trial performance. **Method:** Using a double-blind, repeated measures, cross over design, eleven male competitive cyclists (Mean  $\pm$  SD: age:  $32.2 \pm 7.5$  yr, body mass:  $74.3 \pm 6.8$  kg;  $\dot{V}O_{2peak}$ :  $60.2 \pm 4.0$  ml·kg<sup>-1</sup>·min<sup>-1</sup>) performed 90-min constant-load cycle at 80% of their second ventilatory threshold ( $207 \pm 30$  W) followed by a 20-km time-trial under each condition. At the beginning and at every 25% of the total distance (5, 10, 15 km) during the time-trial, participants were given one piece of chewing gum to chew for 3 km (~5 min) containing either: placebo (PLA: artificial sweeteners), carbohydrate (CHO: ~1.8 g sucrose per piece + artificial sweeteners), caffeine (CAF: 50 mg per piece + artificial sweeteners), and carbohydrate and caffeine (CHO+CAF: ~1.8 g sucrose + 50 mg caffeine per piece + artificial sweeteners). Power output and heart rate were recorded continuously throughout the trial. Blood glucose and lactate samples were obtained before and after the time-trial, whilst perceptual measures on completion only. Data were analysed using an MS Excel spreadsheet designed for statistical analysis. The uncertainty in the effect was expressed as 90% confidence limits and a smallest worthwhile effect of 1.0% for power output was assumed. **Results:** No substantial alterations in time-trial performance were observed with CHO (Mean  $\pm$  SD:  $271 \pm 35$  W), CAF ( $273 \pm 40$  W), or CHO+CAF ( $270 \pm 37$  W) compared with PLA ( $270 \pm 37$  W). However, mean power output had a tendency to be improved in the first two quarters of the 20-km time-trial with CHO (Mean  $\pm$ 90%CL:  $1.6 \pm 3.1$  and  $0.8 \pm 2.0$ %);

whilst in CAF and CHO+CAF trials, mean power output was substantially enhanced in the final quarter ( $4.2 \pm 3.0$  and  $2.0 \pm 1.8\%$ ). No differences in heart rate (ES <0.2) were observed between trials. Blood lactate concentrations on completion of the time-trials were substantially higher for CAF (ES  $\pm 90\%$ CL:  $0.90 \pm 1.09$  and  $0.85 \pm 0.55$ , respectively), and CHO+CAF ( $0.78 \pm 1.14$  and  $0.72 \pm 0.62$ , respectively) than PLA and CHO trials. Differences in changes in blood glucose between experimental trials were small ( $+1.1$ - $1.7$  mmol/L<sup>-1</sup>) and appeared unrelated to performance. **Conclusion:** Endurance performance, under conditions of fatigue and reduced glycogen, was not altered by the oral presence of carbohydrate and caffeine in chewing gum, either independently or combined. However, results support the theories of central activation and manipulation of the anticipatory regulation strategy in response to oral carbohydrate and/or caffeine by demonstrating subconsciously altered motor output during the time-trial. Specifically, carbohydrate appeared to facilitate an immediate increase in power output, whilst caffeine exhibited ergogenic effects later in exercise. Practically, the results suggest that 1) utilising an oral carbohydrate gum, in combination with prior ingestion of small amounts of carbohydrate early in exercise (<90min), or 2) the delivery of caffeine, via a chewing gum, in absence or presence of supplemental carbohydrate, may facilitate improvements in endurance performance by increasing central drive and thus, re-setting the internal pacing strategy to allow a higher power output at one's self-selected 'maximal' work rate.

## **Chapter One: Introduction**

At the 2012 London Olympic Games the winning margins in the men's road cycling time-trial, triathlon, and marathon were 1.38, 0.17, and 0.34%, respectively. Because small improvements in endurance performance at the elite level can be the difference between success and failure (Hopkins, 2001; Paton, & Hopkins., 2006), sports scientists are continually looking for ways to optimise training adaptations and competition performance through the use of ergogenic aids and nutritional supplements (Burke, 2008; Burke, Hawley, Wong, & Jeukendrup, 2011).

Endurance performance is dependent on an athlete's ability to produce and sustain high levels of speed or power during competition, with small deteriorations in performance within an event being termed 'fatigue' (Allen, Lamb, & Westerblad, 2008). The development of fatigue during exercise is a complex, multidimensional process that encompasses numerous sites and underlying factors, and for in depth reviews the reader is referred to the following sources (Abbiss & Laursen, 2005; Amann, 2011; Ament & Verkerke, 2009; Lambert, St Clair Gibson, & Noakes, 2005; Noakes, 2012; Noakes & St Clair Gibson, 2004; Noakes, St Clair Gibson, & Lambert, 2005). The onset of fatigue and its effect on performance has traditionally been focused on 'peripheral' factors (Merton, 1954); however it is now widely acknowledged that 'central' factors (Noakes, 2012; Nybo & Secher, 2004) play a key role in exercise regulation via their effect on neurophysiological and/or psychological aspects (Gandevia, 2001; Lambert et al., 2005; Noakes, 2012).

During high-intensity, short duration exercise less than 60 min, large homeostatic shifts occur within the peripheral biochemical and neurophysiological environments (i.e., blood, extracellular fluid and muscle cells), which coincide with fatigue originating primarily peripherally at the site of the working skeletal muscle. Conversely, during prolonged endurance exercise exceeding 2-3 hours, fatigue is more complex and the extent to which it originates peripherally or centrally, within the working muscle or more a global effect of the overall physiological system, depends on the relative intensity of the exercise and the amount of endogenous fuel available (Gandevia, 2001; Gandevia, Enoka, McComas, Stuart, & Thomas, 1995). However, of importance is that regardless of the location of fatigue and its contributing factors, the magnitude of allowable fatigue during exercise, and hence the anticipatory strategy for performance,

is determined by the brain, the central ‘governor’, in response to its interpretation of biological and perceptual aspects of fatigue (Amann, 2011; Ament & Verkerke, 2009; Noakes, 2012; Noakes & St Clair Gibson, 2004; Noakes et al., 2005). That performance is controlled within the brain is therefore of critical importance when seeking ways to enhance exercise performance.

The benefit of carbohydrate supplementation to endurance exercise greater than 1 h duration and of moderate intensity ( $\sim 65\text{-}70\% \dot{V}O_{2\max}$ ) has been well established (Coyle, 1992; Jeukendrup, 2004). Traditionally, improvements have been attributed to a reduction in peripheral-limiting performance factors such as: 1) sparing of endogenous muscle glycogen stores (Couture, Massicotte, Lavoie, Hillaire-Marcel, & Peronnet, 2002; Stellingwerff et al., 2007; Tsintzas & Williams, 1998); 2) prevention of liver glycogen depletion and subsequent development of hypoglycaemia and/or 3) allowing increased CHO oxidation rates (Coyle, Coggan, Hemmert, & Ivy, 1986; Jeukendrup et al., 1999). However more recent investigations of carbohydrate supplementation in shorter duration ( $<60\text{min}$ ), higher intensity ( $>75\% \dot{V}O_{2\max}$ ) exercise have also shown performance enhancements (Anantaraman, Carmine, Gaesser, & Weltman, 1995; Below, Mora-Rodriguez, Gonzalez-Alonso, & Coyle, 1995; el-Sayed, Balmer, & Rattu, 1997) despite limited carbohydrate absorption time and subsequent availability to active muscle as well as the fact that endogenous carbohydrate stores would not be considered restrictive to optimal performance (Jeukendrup, Brouns, Wagenmakers, & Saris, 1997; Jeukendrup, Hopkins, Aragon-Vargas, & Hulston, 2008; McConell, Canny, Daddo, Nance, & Snow, 2000).

In light of these observations, it has since been suggested that carbohydrate may mediate a central effect on exercise performance prior to changes in peripheral availability (Carter, Jeukendrup, Mann, & Jones, 2004). Carter and colleagues (2004) provided support for this theory by demonstrating a 2.9% improvement performance time in a 1 h cycle time-trial with carbohydrate mouth-rinsing compared with placebo ( $59.9 \pm 1.5$  vs.  $61.4 \pm 1.6$  min, respectively;  $p < 0.05$ ); which occurred primarily through significantly higher power outputs yet no associated increase in rating of perceived exertion ( $p < 0.05$ ). As such, these findings provided the first scientific support for carbohydrate’s mechanism of action being somewhat central in nature, and involving the brain and its role as the central governor in exercise. Since then, numerous carbohydrate mouth-rinse studies have reported improvements of 1.5-1.7% in running

and 1.8-6.3% in cycling time-trials (Carter, Jeukendrup, & Jones, 2004; Chambers, Bridge, & Jones, 2009; Gam, Guelfi, & Fournier, 2013; Lane, Bird, Burke, & Hawley, 2013; Pottier, Bouckaert, Gilis, Roels, & Derave, 2010; Rollo, Cole, Miller, & Williams, 2010; Rollo, Williams, Gant, & Nute, 2008; Sinclair et al., 2013), as well as improvements of 3.4-7.0% in a cycling time-to-exhaustion test (Fares & Kayser, 2011).

Similarly, caffeine (1, 3, 7-trimethylxanthine) has well-known benefits for exercise performance (Astorino & Roberson, 2010; Goldstein et al., 2010; Stuart, Hopkins, Cook, & Cairns, 2005) with demonstrated improvements in prolonged endurance exercise (>60 min) (Cox et al., 2002; Desbrow et al., 2012b; Kovacs, Stegen, & Brouns, 1998) and high-intensity and short duration aerobic events (>80%  $\dot{V}O_{2max}$  and <60 min) (Anderson et al., 2000; Bruce et al., 2000; O'Rourke, O'Brien, Knez, & Paton, 2008). Multiple mechanisms have been proposed to underlie these ergogenic effects such as: increased free fatty acid oxidation and sparing of endogenous glycogen, as well as increased mobilization of intracellular calcium (Costill, Dalsky, & Fink, 1978; Spriet et al., 1992). However, the most probable mechanism for caffeine's ergogenic action is as an agonist to adenosine at its receptor sites (Davis et al., 2003; Fredholm, Battig, Holmen, Nehlig, & Zwartau, 1999; Kalmar & Cafarelli, 2004; Spriet, 1995; Spriet & Gibala, 2004; Spriet et al., 1992) and its effect on central aspects of fatigue that improve exercise performance by lowering perception of skeletal muscle pain, perceived effort and force sensation (Graham, 2001b; Tarnopolsky, 2008).

As with carbohydrate, the most common method of caffeine supplementation for training and competition is through ingestion (Desbrow & Leveritt, 2006, 2007b). However, it has been shown that the oral presence of caffeine also facilitates an increase in central activation (Haase, Cerf-Ducastel, & Murphy, 2009), stimulating brain regions associated with motor control, pain perception, and emotional responses (Apkarian, Bushnell, Treede, & Zubieta, 2005; Vogt, 2005). Consequently, Beaven et al. (2013) investigated this phenomenon on exercise performance using a caffeine mouth-rinse. Administration of the 1.2% caffeine rinse immediately prior to performance of an all-out sprint substantially improved peak power output by  $27 \pm 27$  W (ES: 0.71) compared to placebo. Furthermore, Doering et al. (2013) also found improvements in performance time for a 1 h cycle time-trial in 70% of participants (N=10) with caffeine mouth-rinsing (35 mg) compared with placebo. Consequently, these findings suggest that there

is a possibility that caffeine exposure at the buccal cavity level could facilitate changes in central activation, prior to any observable change in caffeine plasma levels, and hence, enable a more rapid onset of caffeine's performance enhancing effects during exercise.

Alternatively, the rapid onset of ergogenic effects during exercise may relate to the rate at which caffeine is absorbed and hence, appears at adenosine receptor sites in the brain. Delivery via the oral mucosa allows for direct absorption of active ingredients into the bloodstream, by bypassing hepatic metabolic pathways, allowing for more rapid and effective onset of action, compared with ingestive methods (Rassing, 1994; Chaudhary & Shahiwala, 2010; Kamimori, Karyekar, Ottstetter et al., 2002). Thus, caffeine delivery via a chewing gum has been suggested as a novel method offering athletes a more rapid, effective ergogenic effect. Using this method, Paton et al., (2010) provided 300mg caffeine in gum halfway through 50 min of repeated high-intensity sprint cycling. Performance was improved 5.4% (90%CL  $\pm$ 3.6%; ES: 0.25) with caffeine compared to placebo, highlighting the potential for caffeine chewing gum to attenuate exercise-fatigue by exhibiting a rapid ergogenic onset. Furthermore, two newer studies have shown positive ergogenic effects when using caffeinated chewing gum prior to endurance exercise (Lane, Areta, Bird et al., 2013; Ryan, Kim, Fickes et al., 2013). Performance time improved by 2.0% during the ~40 min cycle time-trial in the study by Ryan et al., (2013) when caffeine was given 5 min prior to the start; and similarly Lane et al., (2013) showed an enhancement in power output of 4.0% for a simulated London Olympic Games time-trial (~60 min) when caffeine provided 40 and 10 min prior.

Collectively, the independent findings of carbohydrate mouth-rinsing and caffeine chewing gums highlight the efficacy of these supplements to improve endurance performance of events equal to or less than 1 hour. However, it remains unknown whether their delivery would be of ergogenic benefit to exercise longer than 1 hour, without prior administration, in order to attenuate fatigue and enhance performance. Additionally, it has been suggested that combining caffeine with existing carbohydrate fluid and fuel-replacement strategies may provide a synergistic effect for performance compared to that seen independently with carbohydrate or caffeine alone (Acker-Hewitt, Shafer, Saunders, Goh, & Luden, 2012; Cox et al., 2002). However, whether synergistic effects could be mediated through central stimulation within the oral cavity, without peripheral alterations in energy availability that occur with traditional combined

supplementation, remains unexplored in endurance exercise. Additionally, given the huge importance of a strong ‘finishing-burst’ in the last quarter of endurance events, determining whether providing combined carbohydrate and caffeine late in exercise can produce an additive ergogenic effect is a worthwhile avenue of exploration for the performance of elite athletes.

### ***1.1. Aim of the Thesis***

The aim of this thesis therefore is to address these gaps by investigating the use of oral delivery of carbohydrate and/or caffeine, via a chewing gum and without ingestion, on exercise performance.

### ***1.2. Study Aims***

1. The primary aim of this study is to examine the independent and combined effects of carbohydrate and caffeine chewing gum on self-paced cycling time-trial performance under the influence of exercise-induced fatigue.
2. A secondary aim is to examine the effects of the chewing gums’ contents on subconscious motor output (pacing) during performance of the time-trial.

### ***1.3. Hypothesis***

1. It is hypothesised that independently, carbohydrate and caffeine will enhance exercise performance compared to placebo; and that the combination of carbohydrate and caffeine will increase mean power output to a greater extent than when administered alone.
2. Carbohydrate and/or caffeine gum trials will alter the subconscious motor output (power) during the time-trial despite adopting identical pacing strategies in all trials.

### ***1.4. Significance of the Study***

Small performance changes, even of only 1%, are considered meaningful and worthwhile in highly-trained athletes as they can be the difference between success and failure. The potential for reducing fatigue and improving performance in training and competition via chewing gum containing either carbohydrate and/or caffeine may be

particularly advantageous during times when (1) the consumption of large volumes of carbohydrate is impractical or likely to result in gastrointestinal upset, (2) when carrying or consuming fluids/food is impractical or could be detrimental to performance and (3) in training where athletes want to remain in a glycogen depleted state ('train-low' concept).

## Chapter Two: Literature Review

### Oral Presence of Carbohydrate and Caffeine: Independent and Combined Effects on Endurance Performance

#### 2.1. Introduction

Successful endurance performance in most sporting events is determined by an athlete's ability to both produce and sustain high levels of power or speed. Nowhere is this more apparent than at the elite level, where the difference between winning and losing is less than 1-2% (Hopkins & Hewson, 2001; Paton & Hopkins., 2006; Pyne, Trewin, & Hopkins, 2004).

During high-intensity or prolonged exercise, the force generating capacity of working skeletal muscles tends to progressively decline, and the observation of this deterioration in motor output is typically termed 'fatigue' (Allen et al., 2008). Fatigue has generally been attributed to dysfunction of a 'peripheral' contractile process (Merton, 1954); however, it is now widely acknowledged that impairments occur within the 'central' system – i.e. brain and spinal cord (Noakes, 2012; Nybo & Secher, 2004). Conceptually, fatigue processes relate to one's physiological 'ability' to transfer chemical energy into mechanical work (Edwards, 1983; Vollestad & Sejersted, 1988), or one's central (neurophysiological and psychological) 'will' or ability to transmit nervous information to motor output (Gandevia, 2001; Lambert et al., 2005; Noakes, 2012). In an effort to limit fatigue factors and enhance performance, athletes frequently report ingesting carbohydrate and caffeine supplements during training and competition (Desbrow & Leveritt, 2007a; Jeukendrup, 2004; Philp, Burke, & Baar, 2011).

The benefit of carbohydrate supplementation to prolonged (>60min), moderate intensity (~65-70%  $\dot{V}O_{2max}$ ) endurance exercise is well established (Coyle, 1992; Jeukendrup, 2004) and has traditionally been attributed to improvements in peripheral fatigue-limiting factors, such as improved endogenous energy availability or maintenance of blood glucose levels (Couture et al., 2002; Coyle et al., 1986a; Jeukendrup et al., 1999; Stellingwerff et al., 2007; Tsintzas & Williams, 1998). However, ergogenic performance effects during shorter duration (<60 min), high-intensity (>75%  $\dot{V}O_{2max}$ ) exercise have also been shown with ingestion of carbohydrate supplements

(Anantaraman et al., 1995; Below et al., 1995; el-Sayed et al., 1997) and mouth-rinse solutions (Beaven et al., 2013; Carter et al 2004; Chambers et al., 2009; Gam et al., 2013; Gant, Stinear, & Byblow, 2010a; Lane, Bird, et al., 2013; Pottier et al., 2010; Rollo et al., 2010; Rollo et al., 2008; Sinclair et al., 2013) despite peripheral factors not being performance-limiting. Thus, the performance enhancing effects of carbohydrate ingestion may be centrally mediated, involving energy receptors in the mouth and subsequent stimulation of the brain's reward and motor control centres (Chambers et al., 2009; Frank et al., 2008).

Similarly, the benefits of caffeine on endurance exercise performance are well established (Goldstein et al., 2010; Spriet, 1995). Traditionally, benefits have been attributed to improvements in metabolic performance factors such as: increased free fatty acid oxidation, sparing of endogenous glycogen, and increased mobilization of intracellular calcium (Costill et al., 1978; Spriet et al., 1992). However, it is now widely acknowledged that caffeine's ergogenic mechanism of action involves its antagonistic effect on adenosine receptors in the brain, (Davis et al., 2003; Kalmar & Cafarelli, 2004; Romain Meeusen, Roelands, & Spriet, 2013; Spriet, 1995), which improves exercise performance by lowering perceived effort and enhancing neural drive for motor output (Graham, 2001b; Tarnopolsky, 2008). Traditionally caffeine's central effects have been mediated through absorption of ingested capsules and fluids, however the oral presence of caffeine and sublingual delivery has been suggested as a novel alternative for delivery of a more rapid ergogenic effect (Lane et al., 2013; Paton, Lowe, & Irvine, 2010; Ryan et al., 2013).

### *2.1.1. Aims of the review*

The aim of this review is to examine the concept of fatigue during exercise performance and how it might be influenced by two key ergogenic aids – carbohydrate and caffeine. Specifically, the review will examine carbohydrate and caffeine ingestion and exercise performance, the underlying mechanisms of action, as well as studies that have investigated the effects of carbohydrate mouth-rinsing and exercise performance and sublingual delivery of caffeine and exercise performance. Finally, the combined effects of carbohydrate and caffeine will be explored with reference to the non-ingestion but oral presence of these substances.

## ***2.2. Fatigue and Exercise***

Fatigue has been defined as a decrease in force production (Gandevia et al., 1995; Hagberg, 1981; Hawley & Reilly, 1997), or an inability to reproduce the original force (Bigland-Ritchie, 1981), with an increased perception of effort (Enoka & Stuart, 1992). The causes of fatigue are categorised as either peripheral - relating to one's 'ability' to transfer chemical energy into mechanical work (Edwards, 1983; Vollestad & Sejersted, 1988), or central in origin – relating to the 'will' or ability to voluntarily transmit nervous information to motor output (Gandevia, 2001; Lambert et al., 2005; Noakes, 2012).

Peripheral fatigue, or 'muscular' fatigue, occurs distal to the point of nerve stimulation and refers to processes originating within the muscle and its cells (Gandevia, 2001; Gandevia et al., 1995). Peripheral fatigue is defined as a reduction in the force generating capacity of skeletal muscle, in the presence of unaltered or increased neural drive, due to action potential failure, impairments in the excitation-contraction coupling and/or actin-myosin cross-bridge cycling (Hakkinen & Komi, 1983). Peripheral fatigue with exercise has been attributed to underlying factors that include reduced Krebs cycle intermediates (i.e. adenosine triphosphate, inorganic phosphate, phosphocreatine, lactate) (Allen et al., 2008; Fitts, 1994; Westerblad & Allen, 2003), decreased endogenous substrates (i.e. glucose or glycogen) (Chin & Allen, 1997; Enoka & Stuart, 1992), ionic alterations (e.g.  $K^+$ ,  $Na^+$ ,  $Ca^{2+}$ ) (Allen et al., 2008; Cairns & Lindinger, 2008; Fitts, 1994), acidosis (Allen et al., 2008; Cairns, 2006; Fitts, 1994), hypoxia (Amann et al., 2006; Enoka & Stuart, 1992), and/or damage to cell ultra-structures (Allen et al., 2008; Byrne, Twist, & Eston, 2004).

In contrast, 'central', or 'supraspinal' fatigue, occurs within the cerebral cortex of the brain and/or within the spinal cord (Taylor & Gandevia, 2008; Taylor, Todd, & Gandevia, 2006). Central fatigue is defined as a reduction in descending neural drive and/or impaired alpha motor neuron firing or recruitment rates for working skeletal muscle, resulting in a decline of skeletal muscle force production or tension development, independent of changes in contractility (Enoka & Stuart, 1992), and lowered motivation for maximal voluntary muscle force generation (Davis & Bailey, 1997). The physiological effects of central fatigue during exercise (see *Table 2-2*) may develop in response to one or more of the following underlying mechanisms: brain

hyperthermia (e.g. excessive brain temperature) (Baracos, 2001; Tucker, Rauch, Harley, & Noakes, 2004), reduced cerebral energy turnover in response to hypoglycaemia and reduced cerebral glucose uptake (Nybo & Secher, 2004), and altered neurotransmitter activity, such as increased serotonin (5-hydroxytryptamine, 5-HT) (Bailey, Davis, & Ahlborn, 1993b; Newsholme, 1987) and reduced dopamine (Bailey, Davis, & Ahlborn, 1993a; Davis & Bailey, 1997; Roelands & Meeusen, 2010).

Collectively, fatigue is a complex psycho-physiological process that encompasses numerous underlying factors, at multiple sites within the peripheral and/or central systems. Of importance however is how these various physiological effects influence and contribute to the development of exercise-associated fatigue and thus, affect one's ability to perform maximally during endurance exercise.

### *2.2.1. Fatigue and implications for exercise performance*

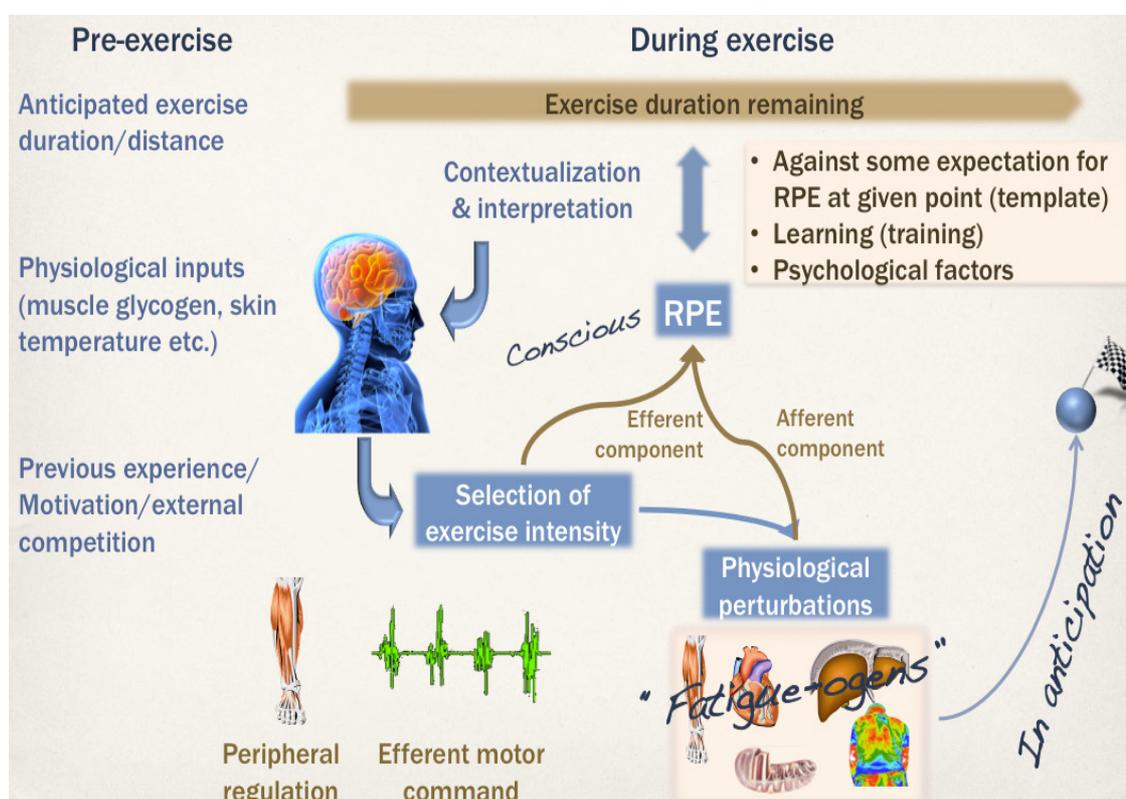
The effect of fatigue and the subsequent implications for exercise performance have been extensively investigated (For in-depth reviews see: Abbiss & Laursen, 2005; Amann, 2011; Ament & Verkerke, 2009; Lambert et al., 2005; Noakes, 2012; Noakes & St Clair Gibson, 2004; Noakes et al., 2005). In brief, it is generally agreed that during high-intensity, short duration exercise, that results in large homeostatic shifts in the peripheral biochemical and neurophysiological environments (i.e. blood, extracellular fluid and muscle cells), fatigue originates peripherally, primarily at the site of the muscle. However, the magnitude to which fatigue is 'allowed' to develop is controlled centrally within the central nervous system (Amann, 2011; Ament & Verkerke, 2009). In prolonged endurance exercise exceeding 2-3 hours duration, fatigue is more complex and the extent to which it originates peripherally or centrally depends on 1) the relative intensity of the exercise and 2) the amount of endogenous fuel available (Coggan & Coyle, 1991). Additionally, the extent to which fatigue originates peripherally or centrally during exercise depends on an individual's training status and physiology, the duration, intensity, and type of exercise, as well as the environmental conditions (Amann, 2011; Lepers, Hausswirth, Maffiuletti, Brisswalter, & van Hoecke, 2000; Lepers, Maffiuletti, Rochette, Brugniaux, & Millet, 2002; Meeusen, Watson, Hasegawa, Roelands, & Piacentini, 2006; Nybo & Nielsen, 2001; Sidhu, Cresswell, & Carroll, 2013; St Clair Gibson et al., 2006; Taylor, Butler, & Gandevia, 2000; Tucker et al.,

2004). However, of primary importance is that the underlying fatigue processes, which ultimately impact performance, reside centrally within the brain.

The central governor model is a theory used to explain the control and regulation of physiological fatigue during exercise by the subconscious brain or ‘governor’ (Noakes et al., 2005). The ‘central governor’ is not a structure or a single area, but a collection of many different processes, pathways, and brain regions, that serves as a self-preservation mechanism for maintenance of cellular integrity, physiological function, and organism survival (Kayser, 2003). During exercise these areas subconsciously regulate motor output (pacing strategy) by adjusting central drive and motor unit recruitment in order to preserve organism homeostasis and prevent catastrophic physiological failure (Noakes, 2012; Noakes & St Clair Gibson, 2004; Noakes et al., 2005). For example, it has been demonstrated that even at the point of volitional exhaustion and termination of exercise, endogenous fuel stores (i.e. plasma glucose, liver and muscle glycogen, ATP stores) are never fully exploited; an occurrence which likely protects muscle from rigour and/or the development of cerebral hypoglycemic coma (Fitts, 1994; Noakes et al., 2004). Similarly, during a maximal contraction, the maximal volitional force produced is less than the true performance capacity of muscle - and that seen with an additional tetanic stimulus - due to supraspinal drive being ‘governed’ centrally to prevent full activation of motor neurons to reduce the risk of damage to cell ultrastructures (Gandevia, 2001; Herbert & Gandevia, 1999; Reid, 1927). Thus, the resulting motor output during exercise may be confined to a subconscious physiological ‘safety’ threshold (Lambert et al., 2005; Noakes & St Clair Gibson, 2004; Noakes et al., 2005).

The brain’s main purpose during exercise is to function as a ‘governor’ of performance intensity by altering motor output to ensure physiological integrity is maintained and the exercise task successfully completed. This is often termed the anticipatory regulation strategy of exercise performance (Larkin, 2005). This concept is presented in *Figure 2-1* and is more commonly referred to as the anticipatory model of exercise performance and fatigue, which encompasses feedforward (outputs) and feedback (inputs) components to control and regulate motor performance prior to and during exercise (Larkin, 2005). Within this framework, the brain subconsciously uses inputs such as: 1) the expected duration of exercise, 2) previous experience, and 3) initial physiological status, to generate a pre-exercise pacing ‘template’ based on an ‘allowable’ development of fatigue (i.e. perceived exertion) and assurance of task completion

without physiological failure (Larkin, 2005). Once exercise has commenced, the brain continually monitors physiological outputs, including muscular force (Åstrand & Rodahl, 1977), heart rate, ventilation, respiratory rate, oxygen uptake, and blood-metabolite concentrations (Rodriguez, Di Marco, & Langley, 2009), to establish a conscious perceived effort for anticipation of task completion by altering central output to active muscles through changes in feed-forward mechanisms, relative to the subconscious pre-determined template, and thus, influencing performance by mediating changes in motor output. As such, it appears that the primary limiter for exercise performance is the brain, its interpretation of biological and perceptual aspects of fatigue, and the subsequent implications these have for regulation of exercise intensity and pacing.



**Figure 2-1.** Anticipatory model for regulation of exercise performance during self-paced endurance exercise (Source: Tucker, 2009; O'Brien et al., 2011).

More specifically, it has been suggested that the selection of motor output, resulting pacing strategy, and impairment to performance, is primarily governed by the central control motor cortex of the brain (Kayser, 2003; Lambert et al., 2005; Noakes & St Clair Gibson, 2004; Noakes et al., 2005). This area 'subconsciously' controls motor output by decreasing central motor drive and skeletal muscle activation, in response to

an anticipation circuit that interprets and monitors changes in the physiological milieu during exercise, combined with the influence of prior experience and knowledge of the duration of exercise remaining. Overall, these physiological feedback and feed-forward mechanisms ensure physiological integrity is maintained by regulating performance by altering work output through the setting of appropriate pacing, which ultimately influence the onset of fatigue (Craig, 2009; Jeukendrup & Chambers, 2010; Kayser, 2003; Noakes & St Clair Gibson, 2004; Okano et al., 2013).

This subjective rating of exercise fatigue and its biological link has important implications for overall performance outcomes by causing subconscious adjustments in power output and pacing. For example, during self-paced exercise, such as endurance time trials, the rate of increase in conscious perceived effort/fatigue remains fairly constant, with performance fluctuations seen through subconscious changes in work rate and power output. This variation occurs as a result of the pre-set physiological limits for motor output (i.e. the anticipatory pacing strategy) and the brain's subsequent interpretation of afferent feedback derived from physiological systems in response to changes in body temperature, oxygen availability, and energy substrate levels (Baracos, 2001; Lukaski, 2001; "Proceedings of the 1st International Meeting of the Congress on Nutrition and Athletic Performance. Edmonton, Alberta, Canada. August 8-11, 2001," 2001). Thus, during endurance exercise, there is a clear link between physiological aspects of fatigue and the sensation of effort aspects, which are influenced by conscious and subconscious regulation.

Consequently, that fatigue, and hence performance, is regulated by an anticipatory strategy involving the central governor (i.e. brain) and its interpretation of biological and perceptual aspects of fatigue, is of critical importance when seeking ways to enhance exercise performance. Thus, when attempting to influence performance outcomes during endurance exercise one should consider how the link between physiological aspects of fatigue and the sensation of perceived effort can be exploited to alter the brain's anticipation strategy for fatigue. Carbohydrate and caffeine are two readily available, legal ergogenic aids, which are frequently ingested during training and competition to limit fatigue and enhance performance (Desbrow & Leveritt, 2007a; Jeukendrup, 2004; Philp et al., 2011). These substances take advantage of the link between the 'governor' and motor output, by exhibiting a positive effect on the 'inputs' to the brain, such as the perception of fatigue, in order to facilitate a centrally-mediated

response on performance (Kalmar & Cafarelli, 2004; Nybo, 2003; Tarnopolsky, 2008). These two substances will be the focus of the proceeding sections of this review.

### **2.3. PART I: CARBOHYDRATE**

The ergogenic effects of ingesting carbohydrate during exercise have been well established since the 1980's. More recently, the benefits of ingesting carbohydrate supplements prior to and during endurance performance has been demonstrated in both fasted and fed states (Colombani, Mannhart, & Mettler, 2013; Vandenbergaeerde & Hopkins, 2011). Meta-analysis of 88 randomised control studies, assessing both fed and fasted athletes, demonstrated mean improvement in endurance performance and capacity (as assessed through time trials and time-to-exhaustion tests) of  $2.7 \pm 3.1$  and  $1.7 \pm 1.8\%$  in mean power output, respectively (Vandenbergaeerde & Hopkins, 2011).

It is well accepted that carbohydrate ingestion delays fatigue and improves performance during prolonged (>90min), moderate-intensity ( $60-75\% \dot{V}O_{2max}$ ) endurance exercise (Coyle et al., 1983; Coyle, Coggan, Hemmert, & Ivy., 1986; Howlett, Angus, Proietto, & Hargreaves., 1998; Jeukendrup et al., 1999; Stellingwerf et al., 2007; Tsintzas & Williams, 1998; van Loon et al., 1999), as well as during short (<60min), high-intensity ( $>75\% \dot{V}O_{2max}$ ) endurance exercise (Anantaraman et al., 1995; Ball, Headley, Vanderburgh, & Smith, 1995; Below et al., 1995; el-Sayed et al., 1997; Jeukendrup et al., 1997; Pottier et al., 2010). However, more recently, improvement in fatigue and performance have been found during short duration (<60min), high-intensity ( $>75\% \dot{V}O_{2max}$ ) endurance exercise, when using a carbohydrate mouth-rinse (without ingestion) (Carter, Jeukendrup, & Jones, 2004; Chambers et al., 2009; Fares & Kayser, 2011; Gam et al., 2013; Lane, Bird, et al., 2013; Painelli et al., 2011; Pottier et al., 2010; Rollo et al., 2010; Rollo et al., 2008) suggesting that ergogenic effects of carbohydrate may be centrally-mediated, involving energy receptors in the mouth and subsequent stimulation of the brain's reward and motor control centres (Chambers et al., 2009; Frank et al., 2008)

This part of the review will focus on current literature investigating carbohydrate ingestion and endurance exercise performance, proposed mechanisms of action, and the development of carbohydrate mouth-rinsing and its proposed physiological mechanisms. More specifically, a critical analysis of the research investigating

carbohydrate mouth-rinsing and its physiological mechanism related to performance enhancement will be carried out.

### ***2.3.1. Carbohydrate ingestion: physiological mechanisms of action and performance findings.***

Carbohydrate supplementation during prolonged endurance exercise enhances performance by delaying the onset of exercise-induced fatigue and cessation of exercise (Coggan & Coyle, 1991). The underlying physiological mechanisms are not completely understood, but have been attributed to improvements in peripherally-limiting fatigue factors such as: 1) sparing of endogenous muscle glycogen stores (Couture et al., 2002; Stellingwerff et al., 2007), 2) prevention of liver glycogen depletion and subsequent development of hypoglycaemia and/or 3) allowing increased carbohydrate oxidation rates (Coyle et al., 1986a; Jeukendrup et al., 1999).

Additionally, carbohydrate supplementation has been shown to improve performance during endurance exercise of high-intensity ( $>75\% \dot{V}O_{2\max}$ ) short duration ( $<60\text{min}$ ) (Anantaraman et al., 1995; Ball et al., 1995; Below et al., 1995; el-Sayed et al., 1997; Jeukendrup et al., 1997; Pottier et al., 2010), where peripheral factors, such as endogenous glycogen and blood glucose levels, would not be considered to be performance-limiting (Jeukendrup et al., 1997; Jeukendrup et al., 2008; McConell et al., 2000). For example, el-Sayed et al. (1997) investigated the effects of pre-exercise carbohydrate feeding on 1 h cycle time-trial performance in eight well-trained cyclists ( $\dot{V}O_{2\text{peak}} 66.5 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ). Participants ingested either an 8% carbohydrate or placebo solution 25 min prior to the time trial. Performance time was improved by 1.25% with carbohydrate compared with the placebo, which was associated with a 3.6% increase in mean power output ( $277 \pm 3$  and  $269 \pm 3$  W,  $p < 0.05$ , respectively). Similarly, Jeukendrup et al. (1997) used a protocol to examine the effects of pre- and during-exercise feedings on 1 h cycle time-trial performance in 19 well-trained cyclists ( $\dot{V}O_{2\max}$  for 17 males:  $72.9 \pm 1.4$  and 2 females:  $64.2 \pm 0.3 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ). Participants ingested either a 7.6 % carbohydrate solution or placebo immediately prior and every 25 % of the 1 h cycle time-trial. Performance time was significantly improved by 2.3 % with carbohydrate compared with the placebo condition ( $58.7 \pm 0.5$  min vs.  $60.1 \pm 0.6$  min,  $p < 0.05$ ). Endogenous carbohydrate stores would have been unlikely to have been performance-limiting in either study, since muscle glycogen levels of around

200 mmol.kg<sup>-1</sup>. dry muscle remain after 1 hour of intense ( $83 \pm 1\% \dot{V}O_{2\text{Peak}}$ ) cycle exercise (McConnell et al., 2000), suggesting that it is implausible for carbohydrate supplementation to have acted through a peripheral mechanism, such as by improving carbohydrate availability and oxidation. Indeed, only ~5–20 g of exogenous carbohydrate is metabolised in the first hour of exercise (Jeukendrup et al., 1997; Palmer et al., 1998).

In an effort to explain the findings of improved performance with carbohydrate supplementation over shorter duration, high-intensity endurance exercise, Carter, Jeukendrup, and Jones, (2004) performed an intravenous glucose infusion study where six trained cyclists ( $\dot{V}O_{2\text{max}} 61.7 \pm 2.0 \text{ ml.kg}^{-1}.\text{min}^{-1}$ ) received either 20% glucose or 0.9% saline at a rate of 1 g.min<sup>-1</sup> during a 1h cycling time-trial, thereby removing the rate-limiting step for glucose availability. With glucose there was a significant increase in plasma glucose availability ( $12.4 \pm 1.1$  vs.  $5.9 \pm 0.3 \text{ mmol/L}$ ,  $p < 0.001$ ) and an increased rate of glucose disappearance from plasma to tissues ( $88 \pm 7$  vs.  $49 \pm 5 \mu\text{mol.kg}^{-1}.\text{min}^{-1}$ ;  $p < 0.05$ ) compared to saline placebo. However, despite improved carbohydrate availability and oxidation, time-trial performance remained unchanged ( $59.9 \pm 1.5$  vs.  $60.0 \pm 1.5 \text{ min}$ , respectively;  $p > 0.05$ ). This led the authors to suggest that carbohydrate may mediate its effect centrally via a mechanism originating somewhere in the oral cavity.

### ***2.3.2. Carbohydrate mouth-rinsing: physiological effects***

The evidence demonstrating that carbohydrate ingestion can improve performance during short duration, high-intensity endurance exercise, despite failing to influence exogenous glucose uptake and overall carbohydrate oxidation has led to the suggestion that carbohydrate may mediate its ergogenic effects centrally.

The presence of carbohydrate in the oral cavity produces afferent activity in the facial, glossopharyngeal, and vagus nerves, resulting in activation of brain areas that include the nucleus in the medulla and pons (Bailey, Hermes, Andresen, & Aicher, 2006) insula/frontal operculum, orbitofrontal cortex, and striatum (Chambers et al., 2009; Frank et al., 2008; Haase et al., 2009). These areas have been shown to be associated with the control and regulation of arousal and emotion (Medford & Critchley, 2010),

pain perception (Wager & Feldman Barrett, 2004), and motor output (Gant, Ali, & Foskett, 2010; Gant, Stinear, & Byblow, 2010b), and as such, may influence exercise performance through its effects on central motor drive via increasing the excitability of descending cortico-motor pathways and the modulation of spinal motor neuron pools (Gant, Stinear, et al., 2010b; Yates & Stocker, 1998).

For example, Gant et al., (2010a) provided support for this theory when they examined the influence of carbohydrate presence in the oral cavity on cortico-motor pathway excitability, motor evoked potentials, and subsequent motor output capability during a maximal voluntary contraction of the elbow flexor muscles. Results confirmed an instantaneous increase in excitability of the cortico-motor pathway and enhanced motor evoked potentials in response to the presence of carbohydrate in both fresh and fatigued muscle states (9 and 30%, respectively), which in turn resulted in a 2% increase in motor output during the maximal voluntary isometric contraction. Interestingly, their results also demonstrated that improvements were 1) independent to the extent of muscular fatigue and perception of voluntary force, and 2) were not affected by peripheral factors, such as plasma glucose concentrations, as carbohydrate availability remained unchanged. Collectively these findings suggest that receptors in the oral cavity may also play an important role in transducing energy density for generation of afferent outputs that are capable of altering motor output and thus, influencing exercise performance.

As such, carbohydrate mouth-rinsing may be able to modify motor output during endurance exercise by altering afferent feedback within the brain, and to fatigued and fresh muscle, under the premise that 'energy' is being taken in. Support for this theory was first shown by Carter et al., (2004) who examined the effect of an oral mouth-rinse containing carbohydrate on endurance performance. Nine well-trained cyclists ( $\dot{V}O_{2\max}$   $63.2 \pm 8.0 \text{ml.kg}^{-1}.\text{min}^{-1}$ ) rinsed with 25 ml of a maltodextrin carbohydrate or water placebo during a 1 h cycling time-trial under double-blind conditions. Carbohydrate mouth-rinse significantly improved performance time by 2.9% compared with placebo ( $59.9 \pm 1.5$  vs.  $61.4 \pm 1.6$  min, respectively;  $p = 0.011$ ), suggesting that carbohydrate ingestion during exercise likely mediates its short-term ergogenic effect through receptors originating in the mouth. In addition, the authors noted significantly higher power outputs across the first three-quarters of the carbohydrate rinse trial, with no

associated increase in rating of perceived exertion ( $p < 0.05$ ), therefore providing further support for the central origin of the effect.

In an attempt to delve deeper into the mechanistic aspects of these observed ergogenic effects from carbohydrate presence in the oral cavity, Chambers et al. (2009) examined the link between carbohydrates and brain activation via functional magnetic resonance imaging (*fMRI*). In this study, a glucose mouth-rinse activated the insula/frontal operculum, orbitofrontal cortex and striatum areas in the brain, but these areas were unresponsive to the artificially-sweetened non-caloric placebo (saccharin and water). Furthermore, they also compared a non-sweet, maltodextrin carbohydrate mouth-rinse to the glucose and saccharin activation patterns using the *fMRI*. Results demonstrated that only carbohydrates in the oral cavity activated the insula/frontal operculum, orbitofrontal cortex and striatum areas in the brain, whilst artificial sweeteners did not. These findings provide support for the neurological central pathway of action proposed by Gant et al. (2010a) and the possibility that oral 'energy' receptors within the mouth are the primary mechanism of action, as changes in central activation were only seen with the presence of a 'caloric' carbohydrate and not in response to 'non-caloric' sweetener.

Furthermore, the second part of the Chambers et al. (2009) study aimed to establish whether observed increases in carbohydrate-induced changes in brain activation were associated with an improvement in endurance performance. Eight endurance-trained cyclists ( $\dot{V}O_{2\max}$ :  $60.8 \pm 4.1 \text{ ml.kg}^{-1}.\text{min}^{-1}$ ) rinsed with 25 ml of a 6.4 % glucose solution or taste-matched artificial-sweetened placebo (saccharin and water) during a 1 h cycle time-trial. Regardless of the type of carbohydrate, cycling time-trial performance was significantly ( $p < 0.05$ ) improved in both compared with placebo ( $62.6 \pm 4.7$  and  $60.4 \pm 3.7$  min, respectively). This finding was repeated in a second group of eight endurance-trained cyclists ( $\dot{V}O_{2\max}$ :  $57.8 \pm 3.2 \text{ ml.kg}^{-1}.\text{min}^{-1}$ ) who rinsed with either an artificially-sweetened maltodextrin carbohydrate mouth-rinse or taste-matched artificial sweetened placebo mouth-rinse (saccharin and water) (Performance time:  $64.6 \pm 4.9$  min and  $61.6 \pm 3.8$  min, respectively). Overall, these findings support the ability of carbohydrate's presence in the mouth to facilitate an increase in motor output as shown in the study of Gant et al. (2010a), and also confirmed the performance enhancements shown in the original study of Carter et al (2004).

In addition, support for the efficacy of carbohydrate's performance-enhancing effects being centrally mediated within the oral cavity is provided by the study of Pottier, Bouckaert, Gilis, et al., (2010), who aimed to determine whether the ergogenic effects of carbohydrates were mediated via oral presence or through swallowing and subsequently absorbing the carbohydrate during non-peripherally limiting exercise. Twelve endurance-trained cyclists ( $\dot{V}O_{2max}$ :  $61.7 \pm 3.1 \text{ ml.kg}^{-1}.\text{min}^{-1}$ ) performed four 1 h cycle time-trial performance tests under the following conditions: carbohydrate mouth-rinse, carbohydrate ingestion, placebo mouth-rinse, and placebo ingestion. Time to complete the time-trial test was 3.7% faster in the carbohydrate versus placebo mouth-rinse condition ( $61.7 \pm 5.1$  vs.  $64.1 \pm 6.5$  min,  $p=0.02$ ). However, of greatest importance was that performance time was fastest with carbohydrate mouth-rinse compared to carbohydrate ingestion ( $61.7 \pm 5.1$  vs.  $62.5 \pm 6.9$  min, respectively). These differences were attributed to the longer presence of carbohydrate in the oral cavity (5 s in carbohydrate mouth-rinsing vs. immediately swallowing in carbohydrate ingestion) when rinsing compared to swallowing, and possibly a greater density of energy receptors within the oral cavity; hence a likely greater degree of central stimulation.

In summary, although the physiological mechanisms of carbohydrate mouth-rinsing are yet to be fully understood and identified, the findings of improved brain activation concomitant with improved central motor drive, effort perception, and motor output, support the research investigating the possibility of these changes improving performance during endurance exercise.

### ***2.3.3. Effects of carbohydrate mouth rinse on performance measures***

Whilst physiological and metabolic responses to carbohydrate mouth-rinsing protocols are important for physiologists to understand underlying mechanisms of actions, the most important outcome for athletes and coaches is how such an intervention might improve performance. This part of the review is therefore dedicated to examining the research that has assessed performance with carbohydrate presence in the oral cavity.

The literature critiqued in this part of the review was retrieved using online search databases (i.e. PubMed, EBSCOhost, and SportDiscus). Extensive searching was carried out using independent and combined use of key search terms, including 'carbohydrate', 'mouth rinse', 'chewing gum', 'endurance', 'performance', 'oral', 'central' and

'exercise (running and cycling)'. From the database search, a total of 17 peer-reviewed studies were found to exist in relation to carbohydrate mouth-rinse and exercise performance, however there are no known studies that have investigated the effects of a carbohydrate chewing gum. Within the carbohydrate mouth-rinse studies, four examined its effects on sprint performance, one assessed its effects on resistance exercise, and the remaining twelve investigated the effects on endurance exercise performance in cycling and running. The findings of those investigating endurance performance are presented in *Table 2-1*.

**Table 2-1. Effect of carbohydrate mouth-rinse on endurance performance.**

Study (y)	Sample Size	Training status $\dot{V}O_{2Max}$ ( $ml.kg^{-1}.min^{-1}$ )	Test	Post Prandial status	Rinse Composition	Rinse Protocol: Frequency x Duration	Interval between rinses	Performance Measure (Mean $\pm$ SD)	Effect (%)
<b>Cycling Studies</b>									
Carter et al, (2004)	7M, 2F	ET 63.2 $\pm$ 8.0	Fixed Work 0.75 Wmax x 3600 (~1 h TT)	4 h	CHO: 6.4% MAL PLA: Water	8 x 5 s	7.5 min	Time (min): CHO: 59.6 $\pm$ 1.5*; PLA: 61.4 $\pm$ 1.6  Power (W): CHO: 259 $\pm$ 16*; PLA: 252 $\pm$ 16	CHO $\uparrow$ time 2.9%.
Beelen et al, (2009)	14M	ET	Fixed Work 0.75 Wmax x 3600 (~1 h TT)	2 h	CHO: 6.4% MAL PLA: Water.	8 x 5 s	7.5 min	Time (min): CHO: 68.1 $\pm$ 1.1; PLA: 67.5 $\pm$ 1.0  Power (W) CHO 265 $\pm$ 5; PLA: 266 $\pm$ 5	NS
Chambers et al, (2009) (study A)	8M	RT 60.8 $\pm$ 4.1	Fixed Work 0.75 Wmax x 3600 (~1 h TT)	6 h	CHO: 6.4% GLU + AS. PLA: Water+AS	8 x 10 s	7.5 min	Time (min) CHO: 60.4 $\pm$ 3.7*; PLA: 61.6 $\pm$ 3.8	CHO $\uparrow$ time 2.0%
Chambers et al, (2009) (study B)	6M, 2F	RT 57.8 $\pm$ 3.2	Fixed Work 0.75 Wmax x 3600 (~1 h TT)	6 h	CHO: 6.4% MAL + AS. PLA: Water + AS.	8 x 10 s	7.5 min	Time (min) CHO: 62.6 $\pm$ 4.7*; PLA: 64.6 $\pm$ 4.9	CHO $\uparrow$ time 3.1%
Pottier, Bouckaert, Gilis, Roels, & Derave, (2010)	12M	ET 61.7 $\pm$ 3.1	Fixed Work 0.75 Wmax x 3600 (~1 h TT)	3h	CHO: 6.0% SUC / GLU (5.4 g / 0.46 g per 100ml) + AS. PLA: Water + AS.	8 x 5 s	7.5 min	Time (min) CHO: 61.7 $\pm$ 5.1*; PLA: 64.1 $\pm$ 6.5  Power (W) CHO 265 $\pm$ 31*; PLA: 257 $\pm$ 34	CHO $\uparrow$ time 3.7%

Fares & Kayser, (2011)	13M	Active	TTE at 60% $W_{max}$	Fed: 3h Fst: O/N	CHO: 6.4% MAL + AS. PLA: water + AS	5-10 s /	5.0 min	Time (min) CHO <sub>Fed</sub> : 56.6 ± 12.2; PLA <sub>Fed</sub> : 54.7 ± 11.3 CHO <sub>Fst</sub> : 53.9 ± 12.8; PLA <sub>Fst</sub> : 58.3 ± 15.3	CHO ↑ time 3.4% in Fed & 7.0% in Fst CHO ↑ time 5.4%
Gam, Guelfi, & Fournier., (2013)	13M	RT	1 h TT 53.85 ± 5.40	4h	CHO: 6.4% MAL PLA: water	8 x 5 s	7.5 min	Time (min) CHO: 65.7 ± 11.07*; PLA: 69.4 ± 13.81	CHO ↑ time 5.4%
Lane et al, (2013)	12M	ET	1 h TT 64.0 ± 3.7	Fed: 2 h Fst: O/N	CHO: 6.4% MAL + AS PLA: water + AS	8 x 10 s /	7.5 min	Power (W) CHO <sub>Fed</sub> : 286 ± 6*; PLA <sub>Fed</sub> : 282 ± 6 CHO <sub>Fst</sub> : 281 ± 5*; PLA <sub>Fst</sub> : 273 ± 6	CHO ↑ PO 1.8 & 3.4% in Fed & Fst
Sinclair et al., (2013)	11M	RT	30 min TT	4 h	CHO: 6.4% MAL PLA: water	CHO <sub>5</sub> : 6 x 5 s CHO <sub>10</sub> : 6 x 10 s	6.0 min	Power (W) CHO <sub>5</sub> 152 ± 17 CHO <sub>10</sub> 156 ± 17* PLA: 146 ± 14	CHO <sub>5</sub> ↑ PO 3.4%; CHO <sub>10</sub> ↑ PO 6.8%.
<b>Running Studies</b>									
Whitham & McKinney (2007)	7M	RT	45 min TT 57.8 ± 3.7	4 h	CHO: 6.0% MAL + 3% non-sweet LJ PLA: Water + 3% non- sweet LJ	8 x 5 s	6.0 min	Distance (m) CHO: 9,333 ± 988 PLA: 9,309 ± 993	NS
Rollo et al., (2008)	10M	ET	30min TT 62.0 ± 3.0	O/N	CHO: 6.0% GLU + AS. PLA: water + AS.	6 x 5s	5.0 min	Distance (m) CHO: 6,584 ± 520* PLA: 6,469 ± 515	1.7%*
Rollo et al., (2010)	10M	ET	1 h TT 63.9 ± 34.3	O/N	CHO: 6.4% GLU + AS. PLA: Water + AS.	4 x 5 s	15.0 min	Distance (m) CHO: 14,298 ± 685* PLA: 14,086 ± 732	1.5%*

AS – artificially sweetened; GLU – glucose; MAL – maltodextrin; SUC – sucrose; Fst – fasted; O/N – overnight (>10 h); LJ – Lemon Juice.  
 CHO – carbohydrate; PLA - placebo  
 ET – endurance trained; RT – recreationally trained;  
 Active – not endurance trained; F – female; M – male;  
 $W_{max}$  – maximum power output from maximal capacity test.  
 TT – time-trial; TTE – time-to-exhaustion; ↑ - improved  
 \* - significant at  $p < 0.05$ ; NS – not statistically significant ( $p > 0.05$ );

Endurance performance can be assessed using one of two methodological testing procedures. The first is an open-loop, constant-load test whereby exercise intensity is externally fixed and participants are required to exercise until exhaustion, whilst the second is a closed-loop, time trial test that requires participants to perform a set amount distance, or work, as fast as they can (Doyle & Martinez, 1998), or to complete as much work as possible in a set time (Doherty, Balmer, Davison, Robinson, & Smith, 2003).

#### *2.3.3.1. Time-trials*

Time trial assessments for endurance performance are considered to be reliable and valid methods of assessing 'real-life' performance, since the exercise intensity is self-regulated (Sporer & McKenzie, 2007). To date, performance times with carbohydrate mouth-rinsing have been shown to improve performance by 1.8-6.3% in a ~1 h cycle time-trial in all (Carter et al. 2004; Chambers et al., 2009; Gam et al., 2013; Lane, Bird, Burke., et al., 2013; Pottier et al., 2010; Sinclair et al., 2013), but one study (Beelen et al., 2009); and similarly, performance during a 30-min and 1 h running time-trial improved by 1.5-1.7% in all (Rollo, Cole, Miller, et al., 2010; Rollo, Williams, Gant, et al., 2008) but one study (Whitham & McKinney, 2007). Collectively, the performance gains observed in current time-trial studies are in excess of the smallest worthwhile effect for both cycling (performance time and power output: 0.3-0.6% and 1.0-1.2%, respectively) (Paton & Hopkins, 2006; Paton & Hopkins, 2001), and running (0.5-1.0%) (Hopkins & Hewson, 2001) and therefore highlight the efficacy of such a practice to improve exercise performance in endurance events equal to or less than 1 hour duration.

In cycling mouth-rinse studies, there has been a high consistency of findings with six out of seven of those studies reporting ergogenic performance benefits with carbohydrate mouth-rinses versus placebo. The repeatability of the ergogenic effects are likely the result of researchers using well-trained endurance cyclists capable of reliably reproducing their performance (Zavorsky et al., 2007a) and that the test replicated the ~1 h time-trial (equivalent to fixed work of 0.75 Maximal aerobic power x 3600) used in the original mouth rinse study of Carter et al., (2004) and thus, imposed the same physiological stimulus.

In contrast to cycling investigations, running performance studies have had greater variation in their methodological testing procedures relating to equipment and test duration. For example, in Whitham and McKinney (2007) recreationally active participants ( $\dot{V}O_{2\max}$   $57.8 \pm 3.7$  ml.kg<sup>-1</sup>.min<sup>-1</sup>) complete a 45min time trial on a manual treadmill that required pace to be self-adjusted, whilst both Rollo et al. (2008) and Rollo et al. (2010) had endurance trained runners ( $\dot{V}O_{2\max}$   $62.0 \pm 3.0$  and  $63.9 \pm 4.3$  ml.kg<sup>-1</sup>.min<sup>-1</sup>, respectively) perform 30 min and 60 min trials on automated treadmills that allowed running pace to be freely adjusted. In order for running performance tests to be able to detect the smallest worthwhile change in performance, a coefficient of variation (CV) of less than 1.5% is required (Hopkins & Hewson, 2001). The automated treadmill used in the studies by Rollo et al. (2008, 2010) has high reliability with a CV of 1.4% (Schabert, Hopkins, & Hawley, 1998), whilst the traditional treadmill used by Whitham and McKinney (2007) had a CV of 2.7%. Additionally, if we accept that during exercise, the central governor may continuously regulate and adjust exercise intensity and pacing in response to the fatigue and physiological feedback (Noakes, 2007; Rauch, St Clair Gibson, Lambert & Noakes, 2005), the external validity of the latter study may be questionable since manual adjustment of running pace requires conscious effort and would therefore impair the ability to monitor the subconscious effect of the carbohydrate mouth-rinse on pacing and performance.

Collectively, these findings highlight the efficacy of using a carbohydrate mouth-rinse to improve endurance exercise performance during events equal to or less than 1-hour. However, it remains unknown whether such a practice could be an effective method of enhancing performance in events with durations greater than one hour.

### *2.3.3.2. Time-to-exhaustion tests*

Time to exhaustion tests are considered less transferable to actual competition performance than time-trial assessments (Sporer & McKenzie, 2007), however they do provide valuable insight into the mechanism(s) underlying the ergogenic nature of a supplement due to exhibition of a greater signal-to-noise ratio (Laursen, Francis, Abbiss, Newton, & Nosaka, 2007). To date, only the study of Fares and Kayser (2011) has examined the effects of a carbohydrate mouth rinse on endurance performance capacity during a cycle time-to-exhaustion test. In this study, 13 non-endurance trained participants cycled to volitional exhaustion at 60% maximal power output ( $W_{\max}$ )

whilst rinsing with a non-sweetened 25 mL carbohydrate mouth-rinse solution (6.4% maltodextrin) or placebo (water) for 5–10 s every 5 min under fasted (>12h post-prandial) and fed (3-h post-prandial) conditions. Endurance capacity improved by 3.4 and 7.0% when rinsing with carbohydrate compared with placebo under fed ( $56.6 \pm 12.2$  vs.  $54.7 \pm 11.3$  min, respectively) and fasted conditions ( $53.9 \pm 12.8$  vs.  $48.3 \pm 15.3$  min, respectively), and these improvements were also associated with a 6% reduction in the perceived level of exertion. Although physiological mechanisms were not explored, the results support the efficacy of achieving carbohydrate presence in the mouth to exert a centrally mediated endurance performance enhancement by positively influencing sensory feedback to the brain and thus allowing alterations in effort perception and motor output.

#### *2.3.3.3. Pre-loading time trials*

Another important measure for coaches to consider is the ‘actual’ performance after prior exercise and its resulting fatigue. This type of testing is sometimes referred to as ‘pre-loading’, as it incorporates a combination of constant load exercise for a set time period, followed by a time trial. Assessments of this type are suggested to provide greater reliability and insight into the effectiveness of a performance intervention (Doherty, Balmer, Davidson, et al., 2003; Doyle & Martinez, 1998), since the exercise task more closely represents the ‘exercise-induced’ dependency for muscle glycogen storage, hydration status, and fatigue, that would be experienced during a real competition event (Sewell & McGregor, 2008; van Loon, Oosterlaar, Hartgens, et al., 2003). This testing method has not been used in the mouth-rinsing studies to date, and as such it remains unknown whether the oral presence of carbohydrate could reduce the perception of existing fatigue and improve performance late in exercise.

#### *2.3.4. Confounding factors amongst current mouth-rinse studies*

In addition to the aforementioned differences in methodological assessment procedures, discrepancies in the magnitude and direction of existing performance findings, and/or the lack thereof with carbohydrate mouth-rinsing, may be due to the variance in factors influencing the sensitivity and activation of oral-receptors such as post prandial status, and the frequency and duration of mouth-rinses. Thus, these aspects have been highlighted in the proceeding section.

#### 2.3.4.1. Post-prandial status

Another important factor that may influence the effectiveness of a carbohydrate mouth-rinse is post-prandial status. Following prolonged periods of fasting, there is an increase in the degree of brain activation (i.e. Haase, Cerf-Ducastel, & Murphy., (2009) demonstrated greater brain activation within the insula, thalamus, and substantia nigra, during periods of fasting, and reduced activation of the parahippocampus, hippocampus, amygdala, and anterior cingulate during a post-prandial state) that occurs in response to detection of carbohydrate in the oral cavity, which affects one's subsequent glucose sensitivity and central activation to the presence of glucose (Haase et al., 2009). Thus, post prandial duration may influence the magnitude of the central effect of the carbohydrate mouth-rinsing procedure.

To date, it remains unclear whether oral 'energy' receptors become less responsive when the subject is in a fed versus a fasted state. Among earlier mouth-rinsing studies there was a general trend for ergogenic effects to be greater following a semi-fasted (4-6 h) (Beelen et al., 2009; Carter et al., 2004; Chambers et al., 2009; Pottier et al., 2010; Sinclair et al., 2013; Whitham & McKinney, 2007) or fasted state (overnight 12-13-h) (Rollo et al., 2010; Rollo et al., 2008) compared with a post-absorptive state (2-3-h) (Beelen et al., 2009). More recently, both Fares and Kayser (2011) and Lane et al., (2013) examined the effectiveness of a carbohydrate mouth-rinse following a period of overnight fasting or after consumption of a high carbohydrate meal to determine whether performance effects could be observed in post-absorptive representative of everyday athletic practices for competition and training. Fares & Kayser (2011) showed cycling time-to-exhaustion at a power output equivalent to 60%  $\dot{W}_{max}$  was improved by 7 and 3% with a carbohydrate mouth-rinse compared with placebo mouth-rinse in both the fasted and fed conditions, respectively. Similarly, Lane et al. (2013) demonstrated that regardless of post-prandial state, carbohydrate mouth-rinse significantly improved performance during a 1-h cycling time-trial compared with placebo; however the magnitude of the effect was significantly greater when completing trials in the fasted (12h) vs. fed (2-h) state, with changes in mean power equating to 3.4% vs. 1.8%, respectively. Interestingly, they demonstrated that 1) optimal performance was achieved with carbohydrate mouth rinsing in a fed state compared with a fed-placebo and fasted-carbohydrate ( $286 \pm 6$  W vs.  $281 \pm 5$  W and  $282 \pm 6$  W;  $p < 0.05$ ); and 2) fasted-carbohydrate resulted in similar performance to that achieved with fed-placebo ( $282 \pm 6$  W vs.  $281 \pm 5$  W;  $p = 0.05$ ). Together these findings support

the efficacy of using oral carbohydrate stimulation to enhance performance during both fed and fasted post-prandial states.

The aforementioned findings suggest that the presence of carbohydrate in the mouth may be able to facilitate performance improvements when endogenous energy stores are lowered by prior exercise, as would be the case during an endurance event. However, studies are yet to investigate the efficacy of a carbohydrate mouth-rinse to enhance performance during the later stages of exercise performance. Therefore, investigation into the area is warranted to determine whether such a practice may be advantageous in longer events where consuming carbohydrates can be difficult (i.e. triathlon, marathon, cycling road race, etc) and additionally, may provide further insight into the ergogenic effects of carbohydrate.

#### *2.3.4.2. Mouth-rinsing procedure: frequency and duration of rinses*

Another factor that may influence the ergogenic efficacy of a carbohydrate mouth-rinse is the temporal factors associated with oral carbohydrate presence and subsequent activation of energy receptors. These factors can be broken down to 1) the duration of rinsing, 2) the frequency of rinsing, and 3) the time between rinses.

The duration of carbohydrate presence in the oral cavity seems to be an important factor related to performance enhancement during short duration, high-intensity exercise; however, the optimal duration of 'energy' receptor stimulation remains unknown. Pottier et al. (2008) demonstrated the importance of time in the oral cavity when their study examined ergogenic differences between carbohydrate or placebo ingestion and mouth-rinsing, respectively. Performance time was fastest for carbohydrate mouth-rinsing versus carbohydrate ingestion, placebo ingestion, and placebo mouth-rinse, respectively ( $62.5 \pm 6.9$ ,  $63.2 \pm 6.9$ , and  $64.1 \pm 6.5$  min), which was attributed to the longer duration carbohydrate spent in the oral cavity when rinsing (5 s) compared with swallowing (immediate ingestion). Thus, central ergogenic effects of carbohydrate appear to be mediated through the oral presence of carbohydrate, rather than swallowing and subsequently absorbing the carbohydrate.

Additionally, it can be seen that most studies have adopted the original rinsing duration of Carter et al. (2004a), whereby carbohydrate was rinsed for 5 s, however whether this is most efficacious remains unknown. Recently, Sinclair et al. (2013) examined the

effect of a longer oral-exposure to carbohydrate could mediate a greater ergogenic effect. Eleven recreationally trained cyclists performed three 30 min time-trials under the following conditions: 5 s mouth-rinse with placebo or 6.4% carbohydrate mouth-rinse for either 5 and 10 s. Power output for the 30 min time-trial was significantly greater in the 10 s mouth-rinse trial compared to the PLA trial ( $156 \pm 17$  vs.  $146 \pm 14$  W;  $p < 0.01$ ). Additionally although there was no significant difference between the 5 and 10 s carbohydrate trial ( $152 \pm 17$  vs.  $156 \pm 17$  W, respectively) eight of the eleven participants had improved performance with the longer rinse of 10-s, which suggests that a longer exposure time for carbohydrate in the mouth may allow for greater oral receptor stimulation and central activation. However, further investigations are needed to determine the efficacy of more prolonged exposures on endurance performance gains.

### ***2.3.5. Summary of carbohydrate benefits for exercise performance***

It appears that there are potential ergogenic benefits with carbohydrate mouth-rinsing during endurance exercise performance of less than or equal to one hour duration. The current physiological rationale for this performance enhancement is that the presence of carbohydrate in the mouth activates ‘unidentified’ energy receptors within the mouth, that subsequently stimulate brain regions associated with pleasure, arousal, motivation and motor control; which consequently improves performance by reducing feelings of fatigue and improving motor function. Currently no studies have examined the effects of a carbohydrate chewing gum on exercise performance, but given the recent findings of carbohydrate mouth-rinse studies, it is likely that a gum would result in similar or potentially even greater stimulation of oral receptors, and subsequent central nervous system activation, since delivery via a gum would result in carbohydrate remaining in the mouth for a longer period.

In addition, the majority of existing mouth rinse studies have employed methodological procedures suited to laboratory testing, however these fail to assess the efficacy when using practical ‘real’ strategies of athletes such as being in a post-absorptive prandial state, and ensuring optimal provision of carbohydrate in the day and hours prior to exercise. Furthermore, it has yet to be investigated whether mouth-rinsing with carbohydrates late in exercise, when exercise-induced fatigue is present, could improve motor output and performance by enhancing central stimulation and overriding fatigue signals associated with the body’s anticipatory pacing (i.e. energy conservation)

strategy, allowing the ‘investment’ of more energy into motor output and consequently enhancing performance.

#### **2.4. PART II: CAFFEINE**

Caffeine (1, 3, 7-trimethylxanthine) is the one of the most widely used ergogenic aids for enhancing exercise training and competition performance (Burke, 2008). Scientific evidence has shown that caffeine improves endurance exercise performance by 1-3% across a range of different endurance exercise protocols including short duration, maximal exercise (~5-8 min; 95-100%  $\dot{V}O_{2\max}$ ) (Kovacs & Szucs, 1983; Mehes, Szekeres, Kovacsics, & Varga, 1954), short duration, high-intensity exercise (20-60 min; 80-95%  $\dot{V}O_{2\max}$ ) (Bruce, Anderson, Fraser, et al., 2000; Csernoch, Kovacs, Nilius, & Szucs, 1990; O'Rourke et al., 2008), and prolonged, moderate-intensity exercise (>90 min continuous exercise; 65-80%  $\dot{V}O_{2\max}$ ) (Cox, Desbrow, Montgomery, et al., 2002; Desbrow, Barrett, Minahan, et al., 2009, Desbrow, Biddulph, Devlin, et al., 2012; Kovacs et al., 1998; McNaughton, Lovell, Siegler, et al., 2008). Additionally, caffeine has been shown to enhance both short-duration, high-intensity cycling (<5 min) (Silva-Cavalcante, Correia-Oliveira, Santos, et al., 2013)

Possible physiological mechanisms that have been speculated to underlie caffeine's ergogenic actions on endurance performance include: 1) increased mobilization and oxidation of fat allowing possible sparing of muscle glycogen (Erickson, Schwarzkopf, & McKenzie, 1987; Graham & Spriet, 1991; Ivy, Costill, Fink, & Lower, 1979); 2) central nervous system effects that increase vigilance and motivation, increase motor unit recruitment and activation, and lower perceptions of effort, pain, and fatigue (Doherty & Smith, 2005; Nehlig, Daval, & Debry, 1992); and 3) may have direct effects on skeletal muscle cells to increase force production, endurance, and reduce fatigue (Tarnopolsky, 2008b). However, the effects within and on the central nervous system are accepted as the most important for enhancing performance (Davis, Zhao, Stock, et al., 2003; Kalmar & Cafarelli, 2004; Spriet, 1995).

This section of the review will focus on current literature investigating caffeine ingestion and endurance exercise performance, proposed physiological mechanisms of action, and the development of buccal delivery methods. More specifically, a critical analysis of the research investigating oral-mucosal delivery methods – caffeine mouth-

rinsing and/or chewing gum – and their effects on exercise performance will be carried out.

**2.4.1. Caffeine ingestion: physiological mechanisms of action** Caffeine's physiological mechanism of action was originally attributed to increased fat oxidation (Ivy et al., 1979) and the sparing of limited endogenous glycogen stores (Erickson et al., 1987; Graham & Spriet, 1991; Ivy et al., 1979). However, these effects have fallen out of favour in the past twenty years as researchers fail to substantiate claims for caffeine's ergogenic effect being peripheral and/or metabolic (Graham, 2001a; Jacobson, Febbraio, Arkininstall, & Hawley, 2001; Laurent et al., 2000; Roy, Bosman, & Tarnopolsky, 2001; Spriet, 1995; Van Soeren, Sathasivam, Spriet & Graham, 1993). For example, Graham and Spriet (2001a) examined the effect of ingesting 6mg.kg BM<sup>-1</sup> caffeine on substrate metabolism during a 1 h steady-state cycling trial (70%  $\dot{V}O_{2max}$ ). However, despite observing a significant increase in plasma epinephrine following caffeine ingestion, there was no difference in metabolic activity measured via respiratory exchange ratio, skeletal muscle glucose and free fatty acid uptake, net muscle glycogenolysis, glucose 6-phosphate concentration, or muscle acetyl CoA concentration when compared to the placebo condition (no caffeine). Similarly, an in-depth analysis performed by Graham and colleagues (1993) examined muscle biopsy results of similar caffeine and endurance exercise studies. The results confirmed that caffeine had no effect on peripheral metabolism by examining levels of muscle glycogen, citrate, acetyl-CoA, and glucose-6-phosphate, at rest and following completion of 10-15 min of moderate intensity (70-85%  $\dot{V}O_{2max}$ ) exercise. Thus, from a number of perspectives, it has been established that there is minimal evidence to support ergogenic aspects of caffeine being the result of shifts in carbohydrate and/or fat metabolism.

It is now acknowledged that caffeine's primary ergogenic effect is centrally oriented, involving its antagonist action on adenosine receptors within the brain and the central nervous system (Davis et al., 2003; Hogervorst, Riedel, Kovacs, Brouns, & Jolles, 1999; Jones, 2008; Kalmar & Cafarelli, 2004; Spriet, 1995). Caffeine easily crosses the blood-brain barrier to reduce the inhibitory effects of adenosine by 1) binding to the A1 adenosine-receptor on presynaptic membranes to increase the release of neurotransmitters; and 2) by blocking the A2a receptor on postsynaptic membranes

promoting dopamine transmission, which results in an enhancement in central neuro-motor pathway function, neuro- hormone and transmitter release (i.e. dopamine, ephinephrine), and improvements in ‘downstream’ neuromuscular factors (i.e. intracellular calcium mobilization, cortico-motor excitability, synaptic transmission, and motor-neuron activation (Fletcher, Smith, Tarnopolsky, & Wolfe, 2005; Graham, 2001b; Okada, Kiryu, Kawata, et al., 1997; Tarnopolsky, 2008). Consequently, these antagonistic physiological bonds, facilitate increases in exercise performance and motor performance by inducing effects on both the central and peripheral nervous system (Tarnopolsky, 2008b), to reduce feelings of pain and effort perception (Doherty & Smith, 2005), improve motor recruitment (Tarnopolsky, 2008) and excitation-contraction coupling (Mohr, Nielsen, & Bangsbo, 2011).

#### ***2.4.2. Caffeine ingestion and endurance exercise performance***

Caffeine is recognised as one of the most frequently used ergogenic aid by athletes for enhancing performance in training and competition (Burke, 2008). Indeed, Sokmen et al. (2008) published a scientific review of caffeine use in sports and provided athletes with advice and practical recommendations involving the medium of caffeine, timing of ingestion, and dosages required to enhance athletic performance.

There is extensive (and growing) scientific evidence to support claims that caffeine can enhance performance when ingestion prior to and throughout a variety of endurance exercise protocols, of various intensities and duration, across a variety of exercise modes (For comprehensive reviews see: Astorino & Roberson, 2010; Doherty & Smith, 2004; Ganio, Klau, Casa, Armstrong, & Maresh, 2009). Doherty and Smith (2004) used meta-analysis to quantify the effect of caffeine on endurance performance during time-to-exhaustion tests, whilst Ganio et al., (2009) performed a systematic review on the effect of caffeine on performance during endurance time-trial tests. Collectively, their findings demonstrated that caffeine enhanced both endurance capacity and performance ability by 12.3 and 3.2%, respectively.

Additionally, previous research has focused on the use of caffeine prior to exercise, when athletes are in a physiologically optimum state. More often than not however athletes perform sessions or finish races with reduced endogenous energy stores and under the presence of exercise-induced fatigue. Despite this, there is a paucity of

research examining the effects of caffeine under lowered energy availability and exercise-induced fatigue, and to date, it appears only two studies have investigated the ergogenic effect of caffeine under an exercise-induced glycogen reduced state (Lane et al., 2013; Silva-Cavalcante et al., 2013). In the first of these studies, Silva-Cavalcante et al. (2013) investigated the effects of caffeine on high-intensity endurance performance following completion of a validated glycogen depletion exercise protocol twelve hours prior. Seven well-trained cyclists ( $\dot{V}O_{2\text{peak}}$   $58.1 \pm 6.3 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ) ingested either caffeine ( $5 \text{ mg}\cdot\text{kg BM}^{-1}$ ) or placebo 1 h prior to performing a 4-km cycle time-trial. Results demonstrated that caffeine improved performance time by 4.1% (ES = 0.94, 95% CI = 0.10 – 1.78,  $P = 0.029$ ) compared to placebo. In the latter study, Lane et al., (2013) had twelve well-trained cyclists ( $61.5 \pm 4.0 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ) complete a 100-min steady state ride (power equivalent to 63% peak power output) to lower endogenous glycogen stores, before commencing a high-intensity interval cycling test (consisting of 8 x 5 min at maximal self-selected pace with 1 min recovery), with ingestion of either caffeine ( $3 \text{ mg}\cdot\text{kg BM}^{-1}$ ) or placebo 1 h prior. Results showed that caffeine improved mean power output by 3.5% ( $P=0.05$ ) for the maximal efforts compared to placebo. Together, these findings highlight the possibility of obtaining an ergogenic effect from caffeine when exposed to exercise-induced fatigue, and hence there is a need for further research to examine whether caffeine administration during prolonged exercise can enhance performance.

#### ***2.4.3. Caffeine administration practices***

Performance benefits with caffeine have been clearly shown when traditional practices, involving ingestion of a  $6 \text{ mg}\cdot\text{kg BM}^{-1}$  caffeine dose, 1 h prior to exercise, have been used (Doherty & Smith, 2004; Graham, 2001a, 2001b; Green, Wickwire, McLester, et al., 2007; Jones, 2008; Keisler & Armsey, 2006). However, reports of insomnia, headaches, anxiety, and gastrointestinal distress have also coincided with caffeine ingestion at these doses (Burke, 2008; Evans & Griffiths, 1992), which could adversely affect exercise performance. Consequently, the optimal dose and timing of administration necessary to illicit maximal performance benefits, in the absence of adverse reactions, is of great interest to athletes, coaches, and sports scientists alike.

### 2.4.3.1. Dosage

The importance of the caffeine dose on the ergogenic effects of caffeine has received much interest. Comparative studies have investigated the effects of different caffeine doses to determine whether a dose-response relationship exists. For example, Graham and Spriet (1995) investigated the effects of a 0, 3, 6, and 9 mg.kg BM<sup>-1</sup> caffeine dose on run time-to-exhaustion at 85%  $\dot{V}O_{2max}$  in well-trained runners ( $\dot{V}O_{2max}$  65.0-76.4 ml.kg<sup>-1</sup>.min<sup>-1</sup>). It was found that caffeine doses of 3 and 6 mg.kg BM<sup>-1</sup> improved run performance time significantly compared with placebo (22 ± 9 and 22 ± 7%, respectively; both  $P < 0.05$ ); however there was no performance difference for the 9 mg.kg BM<sup>-1</sup> caffeine trial compared with placebo despite the larger dose resulting in a higher plasma caffeine concentration and an amplified metabolic and hormonal response in circulating plasma epinephrine, glycerol, and free fatty acids. Likewise, Pasma, van Baak, and Jeukendrup (1995) investigated the effect of 0, 5, 9, and 13 mg.kg BM<sup>-1</sup> caffeine doses on cycle time-to-exhaustion at 80% maximal power output in well-trained cyclists ( $\dot{V}O_{2max}$  65.1 ± 2.6 ml.kg<sup>-1</sup>.min<sup>-1</sup>). Performance time was improved significantly in all caffeine conditions versus placebo (47 + 13, 58 ± 11, 59 ± 12 and 58 ± 12 min for 0, 5, 9 and 13 mg.kg BM<sup>-1</sup>, respectively), though of note was that there was no further performance improvements with 9 or 13 mg.kg BM<sup>-1</sup>.

Using a similar dose-response comparison, Desbrow et al. (2012a) examined these effects using a more competition-specific time-trial test. Trained cyclists ( $\dot{V}O_{2Peak}$  60.4 ± 4.1 ml.kg<sup>-1</sup>.min<sup>-1</sup>) ingested capsules of 0, 3, or 6 mg.kg BM<sup>-1</sup> caffeine prior to a 1 h cycle time-trial equivalent to 75% of peak power output. Caffeine significantly improved performance by 4.2 and 2.9%, respectively ( $p < 0.05$ ) in both caffeine treatments compared with placebo (62.3 ± 4.77, 63.18 ± 4.68, vs. 65.03 ± 5.67 min, respectively). Collectively, these findings suggest that a saturation effect for caffeine arises at higher doses, and discounts a direct dose-response relationship. Indeed, the response tends to plateau at around 3 mg.kg BM<sup>-1</sup>, although this may be somewhat individual.

In light of these findings, researchers have sought to identify the minimal dose required for maximal ergogenic effect. Kovacs, Stegan, and Brouns (1998) examined the efficacy of ingesting low-to-moderate caffeine doses on endurance cycling performance. In this study, trained cyclists ingested sport-drink containing placebo, 150, 225, or 320 mg caffeine during the warm up and at the one-third and two-third time points of a 1 h time-

trial. Caffeine significantly improved performance in all trials compared with control and placebo ( $60.4 \pm 1.0$ ,  $58.9 \pm 1.0$ ,  $58.9 \pm 1.2$ , and  $62.5 \pm 1.3$  min for 150, 225, 320 mg caffeine, and placebo, respectively). The results also showed no further performance benefit with ingestion of  $320 \text{ mg.kg BM}^{-1}$  versus  $225 \text{ mg.kg BM}^{-1}$ . Similarly, Cox et al. (2002) investigated the effect of a commercially available caffeinated cola ( $1.5 \text{ mg.kg BM}^{-1}$ ) or placebo (no caffeine) on endurance performance during a  $7 \text{ kJ/kgBM}^{-1}$  cycle time-trial after a 2 h constant-load cycling phase at power output equivalent to  $70\% \dot{V}O_{2\text{peak}}$ . Performance time was improved by 3.1% (95%CL -0.2-6.2) with cola compared with placebo. Making inferences on the effectiveness of lower caffeine doses in these two studies however is problematic, as participants were fed carbohydrate drinks throughout exercise, which is known to independently improve endurance performance (Burke, 2008; Jeukendrup, 2004).

Despite trained athletes frequently consuming less than the recommended 30-60 g per hour of carbohydrate (Jeukendrup, 2011) during 1) competition - which may be the result of the exercise intensity, gastrointestinal intolerance, and/or the implications of the event itself (i.e. movement constraints, limited ability to carry fuel, etc) (Burke, Wood, Pyne, Telford, & Saunders, 2005; Cox, Snow, & Burke, 2010) and 2) in training – which may be deliberate practice carried out for improved physiological adaptations (Hulston et al., 2010; Yeo et al., 2010), there is limited research investigating the independent effects of low caffeine doses (Desbrow, Barrett, Minahan, Grant, & Leveritt, 2009; Jenkins, Trilk, Singhal, O'Connor, & Cureton, 2008). Jenkins et al., (2008), examined the effects of ingesting placebo, 1, 2, or 3  $\text{mg.kg BM}^{-1}$  caffeine, on endurance performance using a preloaded time-trial. One hour after ingestion, well-trained cyclists completed 15 min constant-load cycling at the power output equivalent to 80% maximal oxygen consumption, followed by 4 min active recovery, and then completed as much work as possible during a 15-min performance trial. Work relative to body mass completed during the performance test (Mean  $\pm$  SEM) was  $2.96 \pm 0.16$ ,  $2.94 \pm 0.12$ ,  $3.08 \pm 0.16$ , and  $3.05 \pm 0.17 \text{ kJ/kg BM}^{-1}$  for placebo, 1, 2, and 3  $\text{mg.kg BM}^{-1}$  caffeine conditions, respectively. Caffeine doses of 2 and 3  $\text{mg.kg BM}^{-1}$  improved performance by 3.9% (95% CI: -0.4 to 6.8,  $p=0.02$ ) trial and 2.9% (95% CI: -0.4 to 2.6,  $p=0.077$ ), respectively, compared with placebo; however there was no performance effect with 1  $\text{mg.kg BM}^{-1}$  (95% CI: -4.4% to 3.4%,  $p=0.80$ ). Conversely, Desbrow, Barrett, Minahan, et al., (2009) reported no effect of low and moderate caffeine doses on endurance performance. Trained cyclists ( $\dot{V}O_{2\text{peak}} 61.7 \pm 4.8 \text{ ml.kg.min}^{-1}$ ) ingested

capsules containing 0, 1.5, or 3 mg.kg BM<sup>-1</sup> one hour prior to commencing 15 min of steady state cycling at the power output equivalent to 70%  $\dot{V}O_{2peak}$ , followed by a 7 kJ.kg BM<sup>-1</sup> set-work cycle time-trial. The authors found no difference in mean performance time across all trials, however, there was a trend for mean performance time to be improved in the 3.0 mg.kg BM<sup>-1</sup> dose compared to the 1.5 mg.kg BM<sup>-1</sup> and placebo trials respectively (30:25 ± 3:10, 30:42 ± 3:41 and 29:51 ± 3:38 min for 0, 1.5, and 3.0 mg.kg BM<sup>-1</sup>, respectively).

In summary, it has been shown that caffeine doses of 2-3 mg.kg BM<sup>-1</sup> are sufficient for eliciting an ergogenic effect, and that performance subsequently plateaus when higher doses are administered despite attainment of higher plasma caffeine concentrations and an amplified hormonal and metabolic response to the higher doses. Lower caffeine doses are associated with a reduction in adverse side effects, and hence an impairment of performance, however there is currently a lack of research examining the efficacy of low caffeine doses during prolonged endurance exercise, independent to carbohydrate, and thus further research into this area is warranted.

#### *2.4.3.2. Timing of ingestion*

Researchers have suggested that the timing of ingestion and plasma caffeine levels influences caffeine's ergogenic effect. Following ingestion, elevated caffeine levels are detectible in the blood from 15-45 min following ingestion and peak at approximately 1 h (Harland, 2000). As such, it has become standard procedure for caffeine to be administered 1 h prior to exercise under the belief that ergogenic performance effects will be maximised by ensuring maximal saturation of hepatic caffeine metabolism and attainment of peak plasma caffeine concentrations (Burke, 2008; Desbrow et al., 2012b; Graham & Spriet, 1995), without clear physiological evidence to support such practice (Conway, Orr, & Stannard, 2003; Skinner, Jenkins, Taaffe, Leveritt, & Coombes, 2013)

Authors have shown that caffeine ingested 1 h prior to exercise can increase endurance capacity (Hoffman et al., 2007; E. M. Kovacs et al., 1998) and endurance performance (Ivy et al., 2009; Jenkins et al., 2008; Lane et al., 2013; McNaughton et al., 2008), but others have not shown an effect (Hadjicharalambous, Georgiades, Kilduff, et al., 2006; Jacobson, Febbraio, Arkinstall, & Hawley, 2001b). Although these studies did not assess plasma caffeine concentrations, Skinner, Taaffe, Leveritt, Coombes and Jenkins

et al. (2013) and Ryan, Kim, Fickes, et al. (2013) recently demonstrated that timing the commencement of exercise with peak plasma caffeine did not enhance the ergogenic response to caffeine, and moreover, in the study by Ryan et al., (2013) caffeine was most efficacious when administered immediately before exercise, compared with 1 and 2 h prior. Similarly, Paton, Lowe, and Irvine (2010) found that administering caffeine during high-intensity sprint cycling exercise reduced fatigue across subsequent sprints by 5.4% (90%CL  $\pm$ 3.6; ES: 0.25). Trained cyclists completed two sets of 5 x 30 s sprint/30 s active recovery, then received a caffeinated chewing gum before performing two further sprint sets. Mean power output (~400 W for caffeine and placebo) in the first 10 sprints versus the last 10 sprints declined by 0.4% (90%CL  $\pm$ 7.7) with caffeine compared to 5.8% (90%CL  $\pm$ 4.0) in the placebo trial. Finally, in another study by Beaven, Maulder, Pooley, et al., (2013), caffeine exposure via a mouth rinse immediately prior to and between high intensity sprint cycling bouts improved mean power in the first of five repeated 6s sprints (Cohen's  $d=0.71$ ). Thus, from a number of viewpoints it appears that the ergogenic effect of caffeine is not proportional to the plasma caffeine concentration and an alternative pathway may be responsible for mediating the rapid performance enhancing effects observed.

Of importance in these studies is that the rapid onset of ergogenic effects may be mediated via the oral cavity, possibly due to mediation of central activation of the brain in response to detection of caffeine by oral-receptors within the mouth (Haase, Cerf-Ducastel, Murphy, et al., 2009), or through a faster absorption and delivery of caffeine to adenosine receptor sites via the buccal mucosa, rather than hepatic pathways (Kamimori, Karyekar, Otterstetter, et al., 2002). It has been demonstrated that caffeine in the mouth results in central activation of the brain, namely the insula, thalamus and substantia nigra, hippocampus, parahippocampus, anterior cingulate, rolandic operculum, and amygdala (Haase et al., 2009). As previously mentioned, carbohydrate exposure to the mouth, via mouth-rinsing, increases central activation (Chambers et al., 2009; Gant et al., 2010a) and enhances endurance time-trial performance, without altering glucose metabolism (Carter et al., 2004; Chambers et al., 2009; Lane et al., 2013; Pottier et al., 2010; Rollo et al., 2010; Rollo et al., 2008; Sinclair et al., 2013). Consequently, this raises the possibility that caffeine exposure at the buccal cavity may facilitate changes in central activation prior to any observable change in caffeine plasma levels, and hence, may enable a more rapid onset of caffeine's ergogenic effects.

Alternatively, rapid onset of ergogenic effects may relate to the speed at which caffeine appears at adenosine receptor sites. Caffeine delivery via chewing gum has a high bioavailability with 85% of the delivered dose (Rassing, 1994) being absorbed rapidly through the buccal cavity; thus resulting in faster appearance (5 min vs. 15-45 min, respectively) and concentration rise of caffeine into the plasma compared with ingestion as caffeine is absorbed directly into the bloodstream, via the buccal mucosa, rather than hepatic pathways (Kamimori et al., 2002).

### ***2.5. Buccal caffeine delivery***

Suggestions that the ergogenic effects of caffeine may be mediated in response to the detection of caffeine in the mouth and/or increasing the speed at which caffeine enters the circulatory system has led authors to investigate the performance effects of buccal caffeine delivery. Therefore, this part of the review examines research that has assessed performance with caffeine delivery to the oral cavity.

The literature critiqued in this part of the review was retrieved using online search databases (i.e. PubMed and SportDiscus). Extensive searching was carried out using independent and combined use of key search terms, including 'caffeine', 'mouth rinse', 'chewing gum', 'endurance', 'performance', 'oral', 'central' and 'exercise'. From the database search, a total of nine peer-reviewed studies were found to exist in relation to caffeine mouth-rinse and chewing gum on exercise performance. Of the two caffeine mouth rinse studies, one examined high-intensity sprint cycling whilst one examined endurance performance. In the seven chewing gum studies, one examined high-intensity sprint cycling with the remaining six examining endurance performance. An overview of these studies and their findings are presented in *Table 2-2*.

**Table 2-2. Effect of buccal caffeine delivery methods on exercise performance.**

Authors (y)	Sample Size	Training status, Aerobic capacity	Mode/Test type	Post prandial status	Caffeine administration method, dose,	Oral stimulation: F x D	Performance Measure (Mean ± SD)	Effect
<b>Mouth-rinse studies</b>								
Beevan et al., (2013)	12M	RT	Cycle – HIT 5x6s (24s active recovery between)	2 h	CAF: water + AS + CAF (1.2% per rinse) PLA: water + AS.	Immediately prior to start of each sprint 5 x 5 s (25 ml)	Sprint 1 Performance: CAF ↑ PO 26.9 ± 26.9 W (ES: 0.71; <i>p</i> = 0.099)  Overall Performance PO: NS	CAF ↑ PO immediately; NS - overall PO
Doering et al., (2013)	10M	ET 59.8 ± 3.5	Cycle - set amount of work equivalent to cycling at 75% of PPO for 60min	1 h	CAF: water + AS + CAF (35 mg/rinse) PLA: water + AS.	30 s prior to start and then every 12.5% of TT. 8 x 10 s	Time (min): CAF: 65:18 ± 4:03; PLA: 65:40 ± 3:47	NS
<b>Chewing gum studies</b>								
Paton, Lowe, & Irvine, (2010)	9M	ET 62.5 ± 5.4	Cycle HIT – 50min with 4x(5x30s).	0 h (Fed)	CAF: 240 mg CAF + AS (spearmint flavour) PLA: AS (spearmint flavour)	Gum at after set 2 point - immediately prior to 3 <sup>rd</sup> set. 1 x 5min	Fatigue index (% ↓ PO) across sets CAF 0.4 ± 7.7%; PLA: 5.8 ± 4.0%.	CAF ↑ PO 5.4% (ES 0.25)
Ryan et al., (2012)	8M	RT 45.5 ± 5.7	Cycle – TTE at 85% $\dot{V}O_{2max}$	4 h	All CAF trials: 100 mg CAF + AS PLA: AS	Gum at -35, -5, +15 min relative to start. CAF-35 CAF-5 CAF+15 min PLA: no CAF	Time (min) CAF-35: 33.5 ± 9.4 min CAF-5: 33.8 ± 9.5 min CAF+15: 34.5 ± 14.6 min PLA: 33.2 ± 8.7 min	NS
Ryan et al., (2013)	8M	RT 50 ± 5	Cycle – 15min constant load at workload equal to 75% $\dot{V}O_{2max}$ , then 7kj.kg BM <sup>-1</sup> TT	3hr	CAF: 300 mg CAF + AS PLA: AS	Gum at time +/- min relative to start. CAF-120 CAF-60 CAF-5 PLA: no CAF	Time (min) CAF-120: 42.6 ± 2.2 min CAF-60: 41.8 ± 2.6 min CAF-5: 38.7 ± 1.2 min PLA: 40.7 ± 1.2 min	CAF-5 ↑ time 2.0%

Farhadi et al., (2011)	15M	RT	1500-m run TT	Not stated	CAF <sub>3</sub> : - 3 mg.kg BM <sup>-1</sup> CAF <sub>4</sub> - 4 mg.kg BM <sup>-1</sup> CAF <sub>5</sub> - 5 mg.kg BM <sup>-1</sup> PLA: AS	Gum delivered at time +/- min relative to start. -35 min, -5 min	Time (min) CAF <sub>3</sub> : 5:37 ± 0.14 min CAF <sub>4</sub> : 5:38 ± 0.24 min CAF <sub>5</sub> : 5:42 ± 0.34 min PLA: 5:52 ± 0.29 min	NS
Gharderi (2013)	15M	ET	1500-m run TT	Not stated	CAF: Gum 5 mg.kg BM <sup>-1</sup> PLA: noCAF	Gum delivered at time +/- min relative to start. -35 min, -5 min	Time (min) CAF: 5:42 ± 0:34 PLA: 5:52 ± 0:29	NS
Bashafaat et al., (2013)	15M	RT	1-km & 4-km cycle TT	Not stated	Gum containing CAF1: 180 mg CAF2: 300 mg PLA: noCAF	Gum delivered at time +/- min relative to start. -30 min, -5 min	1-km Time (min) CAF1: 1.09 ± 0.18; CAF2: 1.09 ± 0.20; PLA: 1.10 ± 0.23  4-km Time (min) CAF1: 5.36 ± 0.19; CAF2: 5.30 ± 0.19 PLA: 5.43 ± 0.25	NS
Lane et al., (2013)	12M 12F	ET M: 71.6 ± 4.6 F: 59.9 ± 5.1	London Olympic Games Simulation M: 43.83 km F: 29.35 km	0 h (fed) TT	Chewing gum in split dose CAF: 2 mg.kg BM <sup>-1</sup> and 1 mg.kg BM <sup>-1</sup> PLA: no CAF	Gum delivered at time +/- min relative to start. -40 min, -10 min	Time (min) CAF: 66.6 ± 5.4*; PLA: 64.1 ± 5.8  Power output (W) CAF: 260 ± 58*; PLA: 250 ± 57	CAF ↑ PO 4.0%.

AS – Artificial sweetener; CAF – caffeine; PLA – Placebo;

ET – endurance-trained; RT – recreationally-trained; M – male; F – female; mg.kg BM<sup>-1</sup> - milligrams per kilogram bodymass

PPO – Peak Peak Output; PO – mean power output; W – Watts;  $\dot{V}O_{2max}$  – maximal oxygen consumption.

TT – time-trial; TTE – time-to-exhaustion; +/- before/after; ↑ - improve; \* - statistically significant ( $p < 0.05$ ); NS – not statistically significant  $p > 0.05$

### ***2.5.1. Caffeine mouth-rinsing and exercise performance***

Two studies have investigated whether caffeine initiates an ergogenic effect via the oral cavity, through the use of a caffeinated mouth-rinse on immediately prior to and during cycle exercise. Beaven et al., (2013) used a repeated high-intensity cycle protocol, whilst the study of Doering et al., (2013) employed an endurance time-trial test.

Beaven et al., (2013) examined the effect of caffeine mouth-rinse on performance during a repeated high-intensity sprint cycle test. Twelve recreationally-trained males performed  $5 \times 6$  s sprints separated by 24 s of active recovery during which they received either 25 mL of a 1.2% caffeine mouth-rinse or taste-matched non-caloric placebo. Mouth rinse was swirled for 5 s prior to each sprint prior to expectorating. Although there was no significant difference evident on overall mean power output across the 5 trials performance for caffeine and placebo, a novel finding was that caffeine mouth-rinse, given immediately prior to exercise, without ingestion, elicited a rapid performance-enhancing effect on maximal voluntary power production (e.g., peak power output was increased by  $26.9 \pm 26.9$  W in sprint 1 with caffeine versus placebo; ES: 0.71;  $p = 0.099$ ), which lead the authors to suggest that a mechanism does exist by which caffeine can rapidly modulate physical capacity via the oral cavity.

Conversely, Doering et al. (2013) investigated the effect of a caffeine mouth-rinse on endurance performance. Well-trained male cyclists ( $\dot{V}O_{2\text{peak}}$ :  $59.8 \pm 3.5$  ml.kg<sup>-1</sup>.min<sup>-1</sup>) were given either 25 mL placebo or caffeine mouth-rinses (35 mg) to swirl for 10 s every 12.5% during ~1 h set work cycle time-trial equivalent to 60% maximal power output. Performance time was not statistically significantly for caffeine (65:18  $\pm$  4:03 min) versus placebo mouth-rinse (65:40  $\pm$  3:47 min) despite improving performance in seven of the ten participants. Additionally, the mean change in caffeine performance was 0.56%; which is considered a worthwhile improvement in cycling performance time (Paton & Hopkins, 2006). Of particular interest in the latter study was that in contrast to the rinsing methodology of Beaven et al., (2013), the authors doubled the caffeine rinsing duration from 5 s to 10 s in an effort to increase oral exposure time and thus a chance of eliciting a central effect.

Whilst one could speculate that an alternative pathway does not exist since both studies failed to find clear ergogenic effects when using a caffeine mouth-rinse, the differences

in the physiological demands of the aforementioned studies (i.e. substrate level phosphorylation vs. aerobic) along with variations in mouth-rinse duration, caffeine concentrations, and the presence of positive individual responses to caffeine, make conclusions on the possibility of an alternative pathway of action within the oral cavity possible. Thus, further investigations are needed to determine the effects of greater rinse frequency and duration, as well as the effect of higher caffeine concentrations and hence contact with oral-receptors, in order to identify whether alternative pathways initiated via the mouth, underlie ergogenic effects, independent to observable changes in plasma caffeine concentrations, when mouth-rinsing with caffeine.

### ***2.5.2. Caffeine chewing gums and exercise performance***

A novel strategy that has been suggested as a method for providing a rapid ergogenic effect, whilst also reducing the risk of suffering from adverse side effects and impaired performance that is commonly associated with ingestion of larger caffeine doses, is buccal delivery of caffeine via chewing gum. Seven studies have investigated the link between buccal caffeine delivery and repeated high-intensity sprint or endurance exercise performance on either short (<30 min) or prolonged (>30 min) duration. Performance findings have been inconsistent with three reporting improvements – one in repeated high-intensity cycling (Paton et al., 2010) and two in prolonged endurance cycling (Lane et al., 2013; Ryan et al., 2013); whilst the remaining four reported no effect – three in short duration endurance exercise (Bashafaat, 2013; Farhadi & Hadi, 2011; Farhadi, Hadi, & Sabegh, 2011) and one in prolonged endurance exercise (Ryan et al., 2012).

#### *2.5.2.1. Repeated high-intensity exercise*

Paton, Lowe, & Irvine, (2010) was the first to investigate the whether an ergogenic effect could be elicited when administering caffeine via a chewing gum during exercise, and without prior exercise administration. Trained cyclists completed a 10 min submaximal warm up followed by two sets of the high intensity cycle protocol (5 x 30 s sprint/30 s active recovery per set) separated by 5 min 100 W cycle recovery. On completion of second set, a commercially available spearmint flavoured gum containing either caffeine (240 mg) or placebo was chewed for 5 min, and then a further two sprint sets were performed. Mean power output in the first 10 sprints versus the last 10 sprints

declined by 0.4% (90%CL  $\pm$ 7.7) in the caffeine and 5.8% (90%CL  $\pm$ 4.0) in the placebo trials, respectively. Additionally, this improvement equated to a 5.4% (90%CL  $\pm$ 3.6%) performance enhancement with caffeine, and a small, but significant effect size (0.25). The performance results of this study highlight caffeine's ability to attenuate fatigue by exhibiting a rapid ergogenic effect when administered during exercise via a chewing gum.

#### 2.5.2.2. *Endurance exercise*

It is generally accepted that caffeine is effective for improving endurance capacity and performance (12.3 and 3.2% in time-to-exhaustion and time-trial tests, respectively). However, of the six chewing gum studies investigating endurance exercise only two reported significant performance enhancements (Lane et al., 2013; Ryan et al., 2013), whilst four reported no effect (Bashafaat, 2013; Farhadi, & Hadi, 2011; Ghaderi, 2013; Ryan et al., 2012).

To date, those using shorter duration time-trial tests have reported no significant performance effect during a 1500-m run (Bashafaat, 2013; Farhadi & Hadi, 2011; Ghaderi, 2013) and a 1-km and 4-km cycle time-trial (Bashafaat, 2013) despite similar studies finding performance effects with caffeine ingestion in exercise of similar duration and intensity (Anderson, Bruce, Fraser, et al., 2000; Bruce, Anderson, Fraser, et al., 2000; Wiles, Coleman, Tegerdine, & Swaine, 2006). However, performance outcomes tended to be greater in caffeine versus placebo trials in all studies regardless of the test mode. For example, Farhadi (2011) reported no effect of caffeine on 1500-m running performance though average time-trial time improved in all three caffeine conditions (3, 4, 5 mg.kg BM<sup>-1</sup>) versus placebo (5:37, 5:38, 5:42 vs. 5:52 min, respectively), and more importantly the associated change in performance (%) is considered worthwhile to track runners (Hopkins, 2001) at 0.3, 0.2, and 0.2%, respectively.

Additionally, the lack of findings in the current studies is likely attributable to differences in methodological procedures rather than inadequacy of the caffeine intervention itself. For example, the post-prandial status of an individual may influence the magnitude of caffeine's ergogenic effect when compared to placebo (Burke, 2008; Doherty & Smith, 2004); however all three of the aforementioned studies failed to

provide information on the postprandial status which makes the interpretation and transferability of their results highly problematic, and is also considered poor scientific practice.

In contrast, caffeine chewing gums have been shown to significantly improve performance time by 2.0% (Ryan et al., 2013) and power output by 4.0% (Lane et al., 2013) in prolonged cycle time-trials of ~40 and 70 min duration. Ryan et al. (2013) investigated the effect of providing 300 mg of caffeine in a single dose at various pre-exercise time points (-120, -60, and -5 min to start) before completing a 7 kJ.kg BM<sup>-1</sup> cycle time-trial (~40 min). Compared to placebo performance time was improved 2.0% when caffeine gum was administered immediately prior to exercise ( $38.7 \pm 1.2$  min vs.  $40.7 \pm 1.2$  min, respectively), whilst worsened when given 1 and 2 h prior ( $41.8 \pm 2.6$  min and  $42.6 \pm 2.2$  min, respectively). Further, in the latter study by Lane et al. (2013) the effect of providing placebo or 3 mg.kg BM<sup>-1</sup> caffeine chewing gum, in a split dose of 2 mg.kg BM<sup>-1</sup> and 1 mg.kg BM<sup>-1</sup> at -40 and -10 min respectively, relative to start of a simulated London Olympic Games cycle time-trial (~29 for females and 43-km for males). Results demonstrated a 4.0% (90% CL:  $\pm 1.7$ ) improvement in power output with caffeine compared with placebo. Collectively, these findings are of great interest as they support caffeine's ergogenic benefits being rapidly induced when delivered via a gum (i.e. -5 and -40 min) prior to prolonged exercise. Furthermore, the gains observed in both studies are in excess of the smallest worthwhile effect for endurance cycling - performance time and power output: 0.3-0.6% and 1.0-1.2%, respectively (Paton & Hopkins, 2006; Paton & Hopkins, 2001) – and therefore highlight the efficacy of such a practice to improve exercise performance in events of approximately 30 min to 1 h in duration.

Only one study has assessed the effect of caffeine chewing gum on endurance capacity via time-to-exhaustion. Ryan et al., (2012) examined the effect of administering low-dose caffeine in chewing gum at three time-points during a cycle time-to-exhaustion test at 85% of maximal oxygen consumption. Under double-blind conditions, eight physically active participants ( $\dot{V}O_{2\text{Max}}$ :  $45.5 \pm 5.7$  ml.kg<sup>-1</sup>.min<sup>-1</sup>) received an absolute dose of 200 mg at 1 of 3 time points (-35, -5, and +15 minutes) with a placebo gum at the other 2 points, whilst in the placebo trial all 3 points were non-caffeinated gums. Results demonstrated that there were no significant differences in performance (time-to-exhaustion for caffeine at -35 min, -5 min, +15 min, and placebo respectively =  $33.5 \pm$

9.4;  $33.8 \pm 9.5$ ;  $34.5 \pm 14.6$ ; and  $33.2 \pm 8.7$  min), which is in contrast to previous studies reporting benefits with low-dose caffeine of 1.5-2.5 mg.kg BM<sup>-1</sup> (Cox et al., 2002; Jenkins et al., 2008; Kovacs et al., 1998). Given the lower training status of the participants in their study, and hence lower reliability for repeated time-to-exhaustion performance, it is too early to rule out the ergogenic benefits of a low dose caffeine gum without further research.

Collectively, these findings highlight the efficacy of prior administration of caffeinated chewing gum for improving endurance exercise performance during events equal to or less than 1 hour. However, it remains unknown whether delivery of caffeine gum during exercise longer than 1 hour, without prior administration, could facilitate rapid ergogenic actions and thus improve fatigue and performance. Given the huge importance of a strong 'finishing-burst' in the last quarter of endurance events, determining whether providing caffeine late in exercise can assist in reducing fatigue and enhancing performance is a worthwhile avenue of exploration for the performance of elite athletes.

### ***2.5.3. Other proposed benefits with oral delivery***

Although caffeine has many desirable effects on physical and mental aspects of performance it also has a number of undesirable side effects that can impair performance (Maughan, Depiesse, & Geyer, 2007; Reilly & Edwards, 2007; Spriet, 1995). Impairments are largely attributed to large caffeine doses (Burke, 2008; Graham & Spriet, 1995) and the presence of caffeine in the gastrointestinal tract (Graham & Spriet, 1995). Thus, provision of caffeine via the oral cavity is an attractive delivery method as it may enable athletes to: 1) obtain faster stimulatory benefits with lower caffeine doses (due to high rate of absorption and bioavailability) (Chaudhary & Shahiwala, 2010; Yeo, Jentjens, Wallis, & Jeukendrup, 2005), and thus, lessen the risk of side effects associated with higher doses, and 2) reduce the risk of gastrointestinal distress via bypassing gastrointestinal absorption and the direct contact of caffeine with the stomach mucosa. This could make it an advantageous choice for high-level athletes that desire the ergogenic effects of caffeine without the impairments associated with larger doses and/or gastro-intestinal discomfort.

#### ***2.5.4. Summary of caffeine benefits on exercise performance***

Although current guidelines suggest ingestion of caffeine doses of 3-6 mg.kg BM<sup>-1</sup> taken 1 h prior to exercise to ensure maximal saturation of hepatic caffeine metabolism and peak plasma caffeine concentrations, ergogenic benefits have also been shown to occur with provision of caffeinated chewing gum in lower caffeine doses of 1.5-2.5 mg.kg BM<sup>-1</sup> provided shortly before exercise (35 and 5 min prior) and in the absence of peak plasma concentrations of caffeine.

Additionally, though existing literature has provided insight into the mechanistic action and performance benefits of caffeine when athletes ingest caffeine prior to exercise in a non-fatigued state, few have investigated the provision of caffeine during exercise and without administration of a dose prior to exercise, despite it being common practice for endurance athletes to consume caffeine-gels and drinks during exercise to overcome sensations of fatigue and enhance performance. Thus, whether an ergogenic effect can induced late in exercise, when exposed to exercise-induced fatigue, is an area that requires further investigation and would provide valuable insight into whether the effects of fatigue can be reduced/reversed and allow for a stronger finishing 'burst' and thus, overall performance.

Finally, despite the high prevalence of adverse side effects when consuming caffeine in large singular doses, there has been little research on independent use of lower doses per se or in a cumulative manner. Given that a gum results in more rapid absorption and onset of stimulatory effects, it possible that lower doses provided in a cumulative manner could mediate ergogenic effects in the absence of adverse side effects. However there is a gap in the current research investigating such practice and therefore further research is required.

### ***2.6. PART III – COMBINED EFFECTS OF CARBOHYDRATE AND CAFFEINE***

It is common practice for athletes to co-ingest carbohydrate and caffeine supplements, prior to and during endurance competition and training, as a means of combating fatigue and enhancing exercise performance (Burke, 2008). Additionally, scientific evidence has shown that intergration of caffeine into existing carbohydrate supplementation strategies provides an small but significant (ES: 0.26;  $\pm 95\%$  CI 0.15 – 0.38,  $p < 0.001$ ) additive effect than that observed with carbohydrate or caffeine alone (For meta-

analysis see: Conger, Warren, Hardy, & Millard-Stafford, 2011). Underlying improved performance effects when both supplements are co-ingested is that caffeine may improve gastrointestinal membrane permeability, and thus increase the rate of carbohydrate absorption, plasma appearance, and availability for skeletal muscles (Van Nieuwenhoven, Brummer, & Brouns, 2000; Yeo et al., 2005). However, whether this physiological effect initiates additive ergogenic effects on performance through peripheral changes or reductions in central fatigue remains unclear.

Given that peripheral factors are not always performance-limiting during endurance exercise, and the recent findings of enhanced performance with central stimulation when administering carbohydrate mouth-rinses (Carter et al., 2004; Chambers et al., 2009) or caffeine chewing gums (Lane et al., 2013; Ryan et al., 2013), a combined oral-stimulation strategy could be a worthwhile practice for athletes to adopt. To our knowledge, only Beaven et al. (2013) has investigated the synergistic effects of combined oral stimulation. In part A of the study they showed an improvement in mean power output during an all-out sprint following rinsing with either carbohydrate ( $27 \pm 27$  W; ES: 0.71) or caffeine ( $29 \pm 26$  W; ES: 1.08) compared with placebo. In part B of the study, combined carbohydrate and caffeine improved peak power output compared to carbohydrate alone ( $36 \pm 37$  W; ES: 0.81) suggesting a combined oral stimulation may have an additive synergistic effect on central performance mediators. However, that they did not directly investigate the independent and combined effects in a single study, making conclusions difficult. Additionally, whether additive central ergogenic effects could be mediated during endurance exercise remains to be explored.

There is a need for further research to better understand the physiological and performance effects of combined central stimulation, in the absence of peripheral interactions, in order to determine whether acute caffeine and carbohydrate oral-presence could synergistically counteract the negative effects of exercise-induced fatigue. Furthermore, insight into dual central stimulation could be beneficial to athletes at the end of endurance events where the ability to replenish endogenous energy stores may not be sufficient or desirable.

### *2.6.1. Other benefits with non-ingestion*

In addition to ergogenic benefits, the provision of oral carbohydrate and/or caffeine may improve exercise outcomes through limiting impairments associated with gastrointestinal distress. Traditionally, the most common method of carbohydrate consumption prior to exercise training and competition has been through ingestion of sports bars, gels, and sports drinks; whilst caffeine consumption has generally been through ingestion of capsules, or mixed in with carbohydrate containing gels and fluid (Desbrow & Leveritt, 2006, 2007b). These mediums require entry into the stomach, absorption via the mucosa of the intestine, and first passing of hepatic metabolism, before they can initiate an ergogenic effect. As such, a major limitation of their administration relates to the timing of ingestion and the risk of gastrointestinal distress. Following ingestion of carbohydrate and/or caffeine supplements there is an increased incidence of exercise-induced gastrointestinal symptoms such as: nausea, cramping, vomiting, heartburn, abdominal pain, and bloating (Brouns & Beckers, 1993) (Jeukendrup, 2004; Pfeiffer, Cotterill, Grathwohl, Stellingwerff, & Jeukendrup, 2009; van Nieuwenhoven, Brouns, & Kovacs, 2005) all of which invariably have an adverse effect on exercise performance. Thus, delivery of both of these ingredients to the oral cavity, in the absence of ingestion, may improve performance by lowering the risk of gastrointestinal disturbance, and hence associated impairments to performance.

The use of a carbohydrate mouth-rinse during exercise of around 1 hour or less appears to be an effective means for enhancing performance by improving central function. In contrast, a caffeine mouth-rinse is yet to be proven effective in endurance exercise; however provision via a chewing gum does appear to be effective for improving performance outcomes. It is currently unknown whether a carbohydrate containing chewing gum could provide a similar or greater ergogenic effect through greater time in the oral cavity, and hence central stimulation and motor performance.

### *2.7. Summary of reviewed literature*

There is growing evidence to support the carbohydrate and caffeine mediating central ergogenic effects within the oral cavity and buccal mucosa. This interaction at the mouth is suggested to exert central ergogenic effects on endurance performance by manipulating the 'central' governor and its regulation of pacing via changes in central regions associated with perceived effort, pain sensations, and motor output. Given these

central changes there is a possibility that combined carbohydrate and caffeine may interact within the mouth to provide an additive central effect on performance.

Carbohydrate mouth-rinsing has been shown to result in enhanced exercise performance, however there appears to be a dose-response relationship with longer rinse exposure times providing superior performance outcomes compared with shorter exposures. No previous research has examined the use of a carbohydrate chewing gum and the subsequent effect of endurance performance. Similarly, the lack of clear efficacy of caffeine mouth-rinsing appears to be related to a reduced buccal contact time versus those adopting a chewing gum strategy.

Traditionally, the provision of carbohydrate and/or caffeine has been via ingestion, and absorption via the gastrointestinal tract, however a downside to this method of delivery is its common association with gastrointestinal disturbances that can negatively impact on performance. A novel alternative that can enhance performance and alleviate gastrointestinal disturbance risks, by removing contact with the intestinal mucosa, whilst also allowing for a more rapid onset of ergogenic effects is with buccal delivery via the mouth.

### ***2.8. Proposed area for investigation***

Existing literature has provided insight into the performance benefits of exposing carbohydrate and caffeine to the oral cavity during endurance exercise approximately 1-hour duration and in a non-fatigued state; however, none have investigated whether ergogenic effects can be elicited when carbohydrate and/or caffeine are exposed to the oral cavity at a later stage of exercise, when endogenous carbohydrate stores are reduced and exercise-induced fatigue is present. However, that it has been shown that athletes frequently consume less than recommended amounts of carbohydrate during 1) competition - which may be the result of the exercise intensity, gastrointestinal intolerance, and/or the implications of the event itself (i.e. movement constraints, limited ability to carry fuel, etc) (Burke et al., 2005); and 2) in training – which is a deliberate practice carried out for improved physiological adaptations (Hulston Venables, Mann, et al., 2010; Yeo et al., 2010), investigation into the possibility of enhancing exercise performance under exercise-induced fatigue states, and in the

absence of carbohydrate ingestion appears worthwhile and may provide insight into the performance enhancing benefits of caffeine when endogenous carbohydrate stores are reduced.

## Chapter Three: Methods

The following methods are applicable to the study completed as part of this thesis. This chapter includes a detailed description of: 1) participants recruited; 2) equipment used and its calibration; 3) exercise tests and protocols; 4) data analysis techniques and 5) methods of statistical analysis.

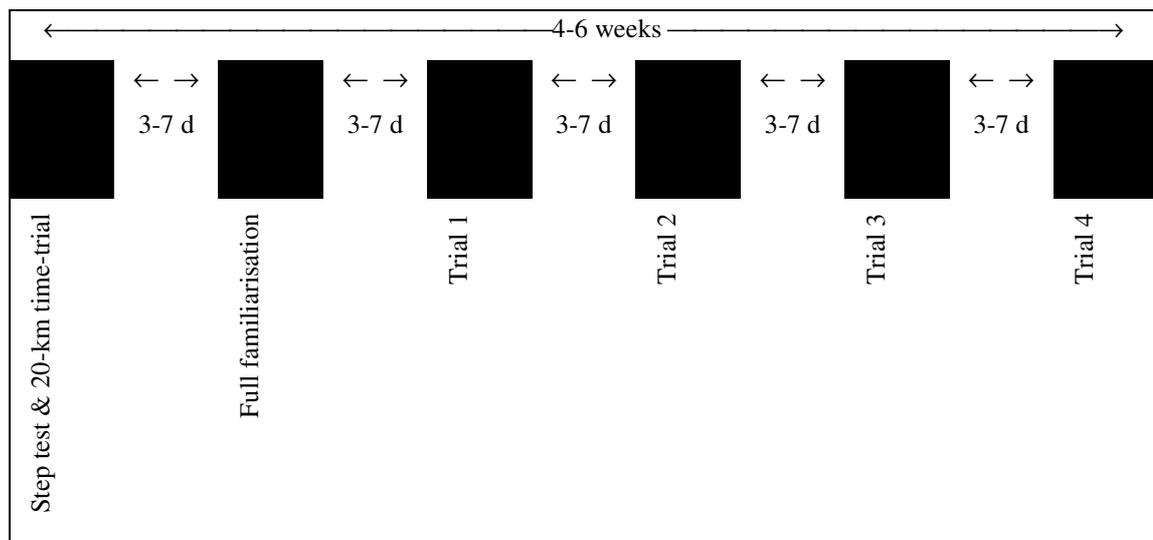
### *3.1. Research Design and outline*

The study used a controlled, double-blind, repeated-measures, cross-over experimental design, whereby participants served as their own control, under the following conditions:

- 1) Chewing gum consisting of carbohydrate (4 x ~1.8 g sucrose per piece + artificial sweeteners).
- 2) Chewing gum consisting of caffeine (4 x 50 mg caffeine per piece + artificial sweeteners).
- 3) Chewing gum consisting of carbohydrate and caffeine (4 x ~1.8 g sucrose + 50 mg caffeine per piece + artificial sweeteners).
- 4) Chewing gum consisting of artificial sweeteners (PLA) (4 x artificial sweeteners).

Participants were required to visit the laboratory six times over a period of 4-6 weeks (see *Figure 3-1*). The first visit involved completion of the pre-screening medical questionnaire, measurement of height and body mass (in riding clothes, without shoes), skinfold measurement, and an incremental cycle step test to volitional exhaustion. So long as the participant achieved the minimum entry criteria ( $\dot{V}O_{2\text{peak}} \geq 55.0 \text{ ml.kg}^{-1}.\text{min}^{-1}$ ), an initial 20 kilometre time trial (20-km time-trial) was performed to familiarise participants with the distance and exercising to full-capacity when exposed to fatigue from prior exercise. The second visit was a full familiarisation test. The two familiarisation sessions had the purpose of allowing the participants to become familiar with the following aspects of the 20-km time-trial: 1) riding on the Velotron ergometer, 2) pre-existing fatigue experienced prior to commencement; 3) the high intensity nature of the test; 4) establish their individual pacing strategy, and 5) to determine the fixed-gear participants would start in for subsequent experimental trials. Visits three to six

involved the experimental trials, each performed under one of the four experimental gum conditions in a randomised order.



**Figure 3-1. Timeline for study.**

All tests were performed in the Sports Physiology laboratory at the Sports Performance Research Institute New Zealand, AUT Millennium. The laboratory was well-ventilated and temperature controlled allowing environmental conditions to be held consistent (Mean  $\pm$  SD:  $18.6 \pm 0.8^{\circ}\text{C}$  and  $60 \pm 7\%$  rh for temperature and relative humidity, respectively).

### **3.2. Participants**

Eleven endurance-trained male cyclists and triathletes were recruited for this study from various cycling and triathlon clubs within the greater Auckland region. Participant characteristics are presented in *Table 3-1*. The majority of participants regularly competed in road cycle races and were in training for either cycle and/or triathlon events lasting longer than 2 hours (i.e. 160 km Lake Taupo Cycle Challenge, K2 200 km cycle race, or Ironman consisting of 3.8 km swim, 180 km cycle, and 42.2 km run). Participants were all in well-established training programs, commenced at least six months prior to study entry, and were training regularly at the time of testing, with an average weekly cycle training volume range of 8-14 hours (Mean  $\pm$  SD:  $10 \pm 2$  h/wk). All participants were informed, verbally and in written form, of the risks associated with the testing and the requirements of their participation, and were given the opportunity to have any questions answered. Prior to participation, all participants provided written,

informed consent in accordance with the Research Ethics Committee at Auckland University of Technology, and completed a medical questionnaire.

***Table 3-1. Participant anthropometric characteristics (N=11).***

<b>Measure</b>	<b>Mean <math>\pm</math> SD</b>
Age (yr)	32.2 $\pm$ 7.5
Height (m)	1.8 $\pm$ 0.6
Body mass (kg)	74.3 $\pm$ 6.8
Sum of 8 skinfolds (mm)	67.8 $\pm$ 13.3
Body fat % (Yuhasz)	8.2 $\pm$ 1.0
$\dot{V}O_{2peak}$ (ml.kg <sup>-1</sup> .min <sup>-1</sup> )	60.2 $\pm$ 4.0

### ***3.3. Equipment***

#### *3.3.1. Ergometer*

An electro-magnetically braked cycle ergometer (Veletron, Racermate Inc, Seattle, Washington USA) was used for all cycling-related tests. This model of cycle ergometer uses an electromagnetic braking system to control resistance by increasing or decreasing the amount of force applied to the flywheel in response to the pre-determined demands entered into the computer-controlled software (Velotron Coaching Software, Version 1.5). The programme allows for the design of different ‘protocols’ as the assessor can predetermine the level of resistance on the flywheel independent of pedaling cadence, such as for the incremental cycle step test, 90 min ‘pre-load’ phase, and 20-km time trial (20km-TT) used in the present study. In addition, this ergometer was chosen as it features fixed gear ratios and gear shifting procedures that closely mimic the feel of actual road riding, as well as a proven ability to provide accurate measurements of power output during prolonged cycling time trials (< 1 % error) (Abbiss, Quod, Levin, Martin, & Laursen, 2009), and high reproducibility (Sporer & McKenzie, 2007).

#### *3.3.2. Pulmonary gas exchange*

An automated metabolic gas analysis system (ParvoMedics TrueOne 2400, Salt Lake City, UT) connected to a Dell Optiplex 790 computer running Windows 7 and ParoMedics OUSW 4.3.4 (v.20111228) data acquisition/analysis software, was used to record pulmonary gas exchange measures during the initial incremental test. This system has been assessed as highly reliable and accurate when compared to the criterion

Douglas bag method (Crouter, Antczak, Hudak, DellaValle, & Haas, 2006; Macfarlane & Wu, 2013).

Ambient temperature, barometric pressure, and relative humidity (rh) were entered into the computer programme from the system's corresponding weather station (Perception II 7400; Ambient Weather Station, Hayward, CA, USA). The system was turned on at least 30 min prior to testing and calibrated using a two-step process for flow-volume and gas analysis, in accordance with the manufacturer's instructions.

### *3.3.3. Heart rate*

Heart rate (HR) measurements were carried out during all testing and experimental sessions using an RS800CX Polar heart rate monitor (Polar Electro Oy, Kempele, Finland), set to record HR data every five seconds. These monitors have been shown to be reliable and accurate when compared to ECG (Achten & Jeukendrup, 2003; Laukkanen & Virtanen, 1998). On completion of each experimental trial, HR data was downloaded using the appropriate computer software program (Polar Protrainer 5 Performance software, Kempele, Finland).

### *3.3.4. Blood lactate and glucose*

Capillary blood samples were obtained to determine blood concentrations of lactate and glucose. Samples were collected from the right ear lobe at rest, on completion of the 90-min steady-state phase, and 3 min after the time trial. The lobe was thoroughly cleaned using an alcohol swab to ensure the sample was not contaminated by sweat.

Blood lactate concentration was measured using a Lactate Pro analyser (Akray, Tokyo, Japan). The Lactate Pro is a hand-held portable analyser that uses a small blood sample (5µl) to measure lactate via a reagent strip. The device precision and reliability has been established between devices ( $CV = 0.99$ ) and when compared to the 'gold standard' laboratory criterion devices such as the Radiometer Abl 700 Series Acid-Base Analyser ( $CV = 0.98$ ) (Pyne, Boston, Martin, & Logan., 2000). Before use, the device was calibrated using the magnetic strip provided by the manufacturer. The same Lactate Pro device was used throughout the study.

Blood glucose concentration was measured using the CareSens II glucose analyser (i-SENS Inc., Korea); a device which has been established against International Standards for glucose meter accuracy and reliability (International Organization for Standardization: ISO15197, 2003). This device has also demonstrated high accuracy and reliability ( $CV = 2.83$ ) when compared with the laboratory 'gold standard' YSI Glucose Analyser ( $CV = 0.99$ ) (Cohen, Boyle, Delaney, & Shaw, 2006). The same CareSens II device was used throughout the study.

### ***3.4. Methodological procedures***

#### *3.4.1. General procedures*

Prior to the first assessment, the participant's own bicycle dimensions were measured and recorded so that the Velotron cycle ergometer closely resembled the rider's favoured set-up for: crank height, reach and height of the handle bars, and the height, fore and back position of the saddle. The participants own pedals were fitted to the cranks of the ergometer to allow them to ride in their own cycling shoes. Participants were then instructed to ride at a low to moderate resistance on the initial set-up for up to five minutes, or until they deemed the set-up comfortable, and to request any final minor adjustments before the final set-up was confirmed. Following confirmation, the set-up was recorded and repeated across all testing sessions.

#### *3.4.2. Specific procedures*

##### *Visit 1: Incremental Cycling Step Test and Time Trial familiarisation*

The purpose of the incremental step test to volitional exhaustion was to determine each participant's maximal oxygen uptake ( $\dot{V}O_{2\max}$ ), first ventilatory threshold ( $VT_1$ ), second ventilatory threshold ( $VT_2$ ) and associated maximum and threshold powers (PPO, PPO at  $VT_1$  and  $VT_2$ , respectively).

Following the initial ergometer set-up, the heart rate monitor, headpiece and pneumotachometer mouth piece were fitted to the participant. Heart rate and gas variables - oxygen consumption ( $\dot{V}O_2$ ), carbon dioxide consumption ( $\dot{V}CO_2$ ), minute ventilation (VE), ventilatory equivalents for oxygen ( $VE/\dot{V}O_2$ ) and carbon dioxide ( $VE/\dot{V}CO_2$ ), respiratory exchange ratio (RER) - were recorded throughout the test for use in post-test analysis and identification of ventilatory thresholds.

The test started at a power output of 100 W and consisted of a continuous step protocol with 5 min stages. Power output was progressively increased by 50 W at the end of each 5-min stage until volitional exhaustion. Participants cycled at their individualised and self-selected optimal cadence, so that an accurate reflection of maximum aerobic power could be determined (Zavorsky et al., 2007b). The test was terminated (*a*) voluntarily by the subject, or (*b*) when cadence dropped below 60 rev.min<sup>-1</sup> (Åstrand, 2003). Participants were permitted to stand-up out of the saddle intermittently if a drop in cadence occurred, but were encouraged to remain seated in the saddle for the majority of each stage while maintaining a relatively constant cadence.

On completion of the incremental test, participants were encouraged to remain on the ergometer and ‘spin’ against a very low resistance (~50 W) for five minutes, followed by ten minutes full recovery off the bike. This recovery strategy was designed to facilitate some recovery from the incremental assessment in order to allow effective participation in the 20-km time-trial familiarisation.

For the 20-km time-trial, the Velotron was set to the time-trial mode and performance feedback (power output, cadence, speed, and heart rate) was covered so that only the amount of work completed (i.e. distance) and gear ratios were visible. The 20-km time-trial began from a standing, stationary-start and participants were instructed to perform each trial in the fastest time possible. Throughout the 20-km time-trial participants’ were able to freely adjust their gear ratio and pedalling cadence as required. Participants were each given the same minimal verbal encouragement at time points corresponding to each kilometre, which included phases such as “3 kilometres done, you’re doing well”, and “5 kilometres to go, you can do it”.

#### *Visits 2-6: Familiarisation and Experimental procedures*

The timeline of the main experimental trial is presented in *Figure 3-2*.



Throughout the 20-km time-trial participants' were able to freely adjust their gear ratio and pedalling cadence as required. Participants were provided instantaneous feedback for distance, but were blinded from power output, cadence, speed, and heart rate. On completion, participants were verbally asked to guess which gum they believed they received, and whether they experienced gastrointestinal discomfort with the chewing gum.

To minimise the effects of hydration and heat strain on exercise performance, a small fan (windspeed:  $2.8 \pm 0.3 \text{ m.s}^{-1}$ ) was positioned in front to the participant. Water consumption was *ad libitum* during both the 90-min constant-load phase and 20-km time-trial, as this practice is shown to maximise endurance performance through optimising the body's self-regulation of plasma osmolarity, and hence, extra cellular fluid volume homeostasis (Goulet, 2011).

#### 3.4.3. Dietary and exercise control

All testing sessions were separated by at least 3 days (mean  $\pm$  SD:  $5 \pm 3$ ). To minimise sources of variation in performance, time of the day ( $\pm 1 \text{ h}$ ), nutrition and physical activity in the 24-h period prior to each trial were kept consistent. Participants were instructed to avoid consumption of caffeinated products in the 12-h period preceding each test and to abstain from exhaustive or prolonged exercise in the 24-h period prior to each test. Prior to their second visit, participants were provided with a dietary guidebook and recording sheet to ensure they obtained a minimum of 6 g carbohydrate per kilogram bodyweight on the day before each trial and 1 g carbohydrate per kilogram body weight in the meal prior to each trial to replicate racing nutrition. The amount and type of food consumed was recorded, along with the duration and intensity of physical activity, if any, and this was requested to be replicated across all future trials to minimise inter-trial variations in levels of endogenous carbohydrate and pre-existing fatigue. The diaries of participants confirmed adherence to these criteria.

#### 3.4.4. Intervention information

Table 3-2 presents the manufacturer's ingredients for the chewing gums provided in each of the four experimental conditions – carbohydrate (CHO), caffeine (CAF), combined carbohydrate and caffeine (CHO+CAF), and placebo (PLA).

**Table 3-2. Chewing gum ingredients.**

<b>Key ingredients in all gums (1 piece = 3g)</b>	<b>Content (mg/tablet)</b>
<b>Sweeteners</b>	
- Sorbitol	1600
- Isomalt	300
- Mannitol	60
- Aspartame	7.5
- Acesulfame K	3.5
- Gum base	75
<b>Flavours</b>	
- Grapefruit symrise	60
<b>Additional Specific Ingredients for each experimental gum condition</b>	
<b>Carbohydrate</b>	
- Sucrose (CHO)	1800
<b>Caffeine</b>	
- Caffeine	50
<b>Carbohydrate + Caffeine</b>	
- Sucrose (CHO)	1800
- Caffeine	50

One piece of chewing gum (3 g) was provided immediately before the start of the 20-km time-trial and again for every 25% of the time-trial completed (i.e. 0, 5, 10, 15km). The delivery procedure of the gum and time between oral stimuli being presented (i.e. approximately every 7.5-8 minutes) was similar to existing designs in carbohydrate mouth rinse studies (Carter et al., 2004; Gam et al., 2013; Lane, et al., 2013). Participants were instructed to chew for 3-km (~5-min) before expelling the contents into a container held by the investigator.

### **3.5. Data Analysis**

#### *3.5.1. Performance calculations*

Time, power output, and cadence were automatically recorded at a frequency of 1 Hz by the Velotron software (Velotron Coaching Software, Racermate, USA). For comparison purposes, the data was extracted and entered into an Excel spreadsheet where values were converted to 1km averages. Further, the performance time and average power output for each individual time trial was recorded for analysis.

### 3.5.2. Physiological variables

During all experimental 20-km time-trial's, blood lactate and glucose were recorded at rest, immediately post the 90-minute constant-load cycle, and 3 minutes after completion of the 20-km time-trial. Throughout the trial, heart rate was recorded continuously throughout the 90-min constant load and 20-km time trial at a sampling rate of 5 seconds.

### 3.5.3. Statistical analysis

Simple descriptive statistics are shown as mean  $\pm$  between-subject standard deviations. Performance power output values for each subject were entered into an MS Excel statistics spreadsheet designed by Hopkins (Hopkins, 2006) and data were log-transformed to reduce bias arising from non-uniformity of error and back-transformed to obtain changes in means as percentages. To make inferences about the true (population) values of carbohydrate and/or caffeine chewing gum on cycling performance the uncertainty of the effect was expressed as 90% confidence limits, with probabilities of the true value representing a substantial change in performance (Batterham, 2006). An estimate of the smallest substantial change was required to make these inferences. For performance measures, represented as 20-km time-trial time, the estimate was based on the endurance time-trial performance variability in power output for competitive cyclists (0.5-1.5%) (Paton, & Hopkins, 2006; Paton & Hopkins, 2001). As such, the smallest substantial change in endurance time-trial performance was assumed to be a reduction or increase in performance power output of 1% or greater. Magnitude-based inferences were used to indicate whether the effect was substantially positive or negative, and beneficial or harmful. Clinical inferences were assessed for performance measures and mechanistic for heart rate, and blood lactate and glucose concentrations (Hopkins, Marshall, Batterham, & Hanin, 2009). With clinical inferences, an effect with possible benefit (>25% chance) was clear if harm was very unlikely (odds ratio of benefit/harm >66) and considered unclear if otherwise (i.e. its confidence interval overlapped thresholds for substantial change). For lactate and glucose concentrations, a standardised change of 0.2 was assumed for between-subject standard deviations, with the thresholds for moderate and large effects being 0.6 and 1.2, respectively.

## Chapter Four: Results

### 4.1. Physiological characteristics

The physiological characteristics determined from the incremental step test are presented in *Table 4-1*. All participants met the entry criteria by possessing a  $\dot{V}O_{2\text{peak}} \geq 55 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ .

**Table 4-1. Participant physiological characteristics at baseline (N=11).**

Measure	Mean $\pm$ SD
$\dot{V}O_{2\text{peak}}$ ( $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ )	60.2 $\pm$ 4.0
HR <sub>peak</sub> ( $\text{b}\cdot\text{min}^{-1}$ )	183 $\pm$ 10
W <sub>peak</sub> (W)	331 $\pm$ 34
W <sub>peak</sub> (W/kg)	4.4 $\pm$ 0.3
Power at VT <sub>1</sub> (WVT <sub>1</sub> )	195 $\pm$ 30
Power at VT <sub>1</sub> (%W <sub>peak</sub> )	59 $\pm$ 6
$\dot{V}O_{2\text{peak}}$ at VT <sub>1</sub> ( $\text{L}\cdot\text{min}^{-1}$ )	3.0 $\pm$ 0.4
$\dot{V}O_2$ at VT <sub>1</sub> (% $\dot{V}O_{2\text{peak}}$ )	66 $\pm$ 4
HR at VT <sub>1</sub> ( $\text{b}\cdot\text{min}^{-1}$ )	146 $\pm$ 12
Power at VT <sub>2</sub> (WVT <sub>2</sub> )	259 $\pm$ 38
Power at VT <sub>2</sub> (%W <sub>peak</sub> )	78 $\pm$ 5
$\dot{V}O_2$ at VT <sub>2</sub> ( $\text{L}\cdot\text{min}^{-1}$ )	3.7 $\pm$ 0.5
$\dot{V}O_2$ at VT <sub>2</sub> (% $\dot{V}O_{2\text{peak}}$ )	82 $\pm$ 5
HR at VT <sub>2</sub> ( $\text{b}\cdot\text{min}^{-1}$ )	164 $\pm$ 12

HR<sub>peak</sub> – highest heart rate obtained in test; W<sub>peak</sub> – highest power output recorded;

$\dot{V}O_{2\text{peak}}$  – peak oxygen consumption for 30-s. VT<sub>1</sub> – first ventilatory threshold;

VT<sub>2</sub> – second ventilatory threshold;

### 4.2. Performance measures (mean power output, time)

The performance data from each trial are shown in *Table 4-2*.

**Table 4-2. Performance measures obtained during the 20-km time-trial for each condition (Mean  $\pm$  SD).**

Measure	PLA	CHO	CAF	CHO+CAF
Time (m:s)	32:27 $\pm$ 1:57	32:25 $\pm$ 1:45	32:20 $\pm$ 1:57	32:26 $\pm$ 1:51
Mean Power Output (W)	270 $\pm$ 37	271 $\pm$ 35	273 $\pm$ 40	270 $\pm$ 37

CAF – caffeine; CHO – carbohydrate, CHO+CAF – carbohydrate and caffeine; PLA – placebo.

Comparative PLA, CHO, CAF, and CHO+CAF time-trial performance outcomes are summarised in *Table 4-3*. The data presented show the percentage change in equivalent time-trial performance between treatments and chances of real improvement for elite athletes using one treatment relative to another. The pairwise comparison of placebo versus experimental trials showed that all experimental treatments produced positive insubstantial improvements relative to placebo. Inferences for improvements in mean power output (Mean;  $\pm 90\%$ CL), compared with PLA, were *possibly trivial* with all experimental treatments - CHO (0.2;  $\pm 2.0$ ), CAF (0.1;  $\pm 2.2$ ), and CHO+CAF (0.1;  $\pm 1.8$ ). Additionally, differences between experimental gums (CAF vs. CHO; 0.3;  $\pm 1.6$ ) were *possibly trivial* or *unclear*, whilst differences in both independent conditions (CHO or CAF) versus combined (CHO+CAF) were insubstantial with an *unclear* effect on performance for CHO (-0.1;  $\pm 1.2$ ) and for CAF (-0.4;  $\pm 1.5$ ).

**Table 4-3. Pairwise comparisons quantifying the magnitude of effect of different chewing gum contents on 20-km time-trial mean power output (see Table 4-2).**

	Treatment effect <sup>a</sup>	
	% effect Mean $\pm 90\%$ CL <sup>b</sup>	Qualitative inference <sup>c</sup>
<b>Experimental treatment effects vs. placebo</b>		
CHO vs. PLA	0.2 $\pm 2.0$	Possibly trivial
CAF vs. PLA	0.4 $\pm 2.2$	Unclear
CHO+CAF vs. PLA	0.1 $\pm 1.8$	Possibly trivial
<b>Within treatment effects - Independent and Combined</b>		
CAF vs. CHO	0.3 $\pm 1.6$	Possibly trivial
CHO+CAF vs. CAF	-0.4 $\pm 1.5$	Unclear
CHO+CAF vs. CHO	-0.1 $\pm 1.2$	Unclear

CAF – caffeine; CHO – carbohydrate, CHO+CAF – carbohydrate and caffeine; PLA – placebo.

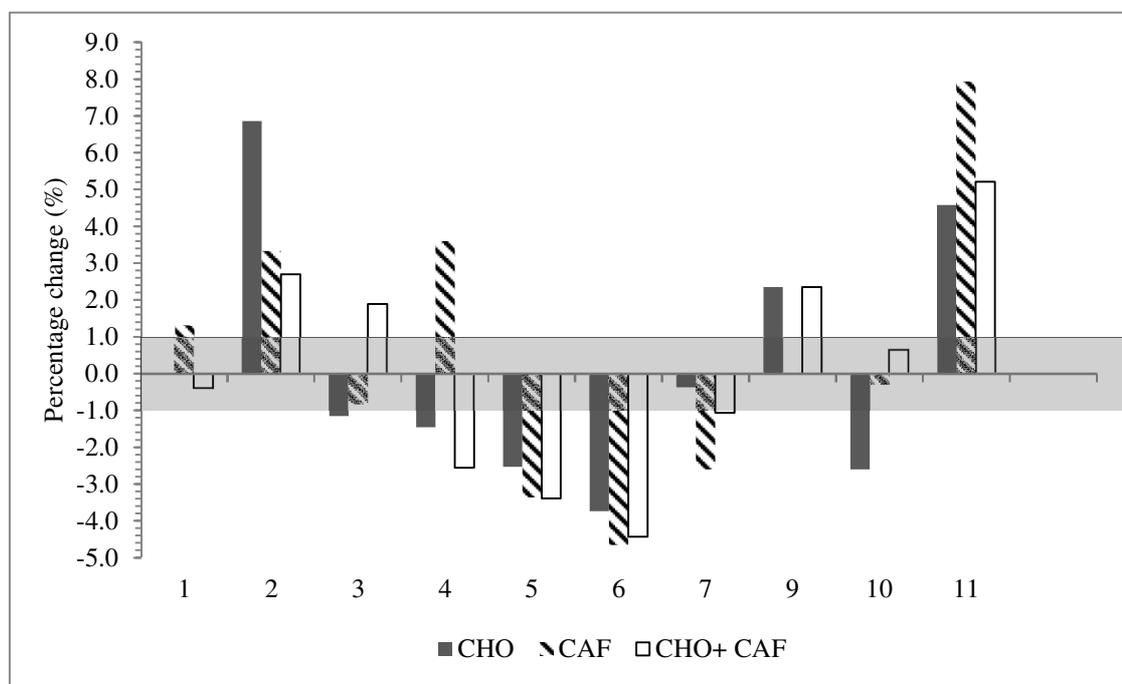
<sup>a</sup> units of change are % for all measures derived from back-transformed log data.

<sup>b</sup> CL: add and subtract this number to the difference to obtain the 90% confidence limits for the true difference.

<sup>c</sup>Based on smallest beneficial or harmful change in performance of 1%.

Individual responses for mean power output in experimental treatments compared to placebo are presented in *Figure 4-1*. Three participants substantially improved mean power output with CHO versus PLA (6.9, 2.4, and 4.6%), however six had substantial reductions (-1.2, -1.5, -2.5, -3.7, and -2.6) and two had trivial differences (0.0 and -0.4%). With CAF, four had a substantial improvement (1.3, 3.3, 3.6, and 7.9) compared to PLA, however three had a substantial negative effect (-3.4, -4.7, and -2.6) while the remaining three showed trivial differences (-0.8, 0.0, and -0.3). In the combined

CHO+CAF condition, four participants showed substantial improvement (1.3, 5.1, 2.3, and 3.4), whilst three substantially worsened (-3.5, -2.2, and -2.3) and the remaining three presented with trivial differences (0.3, -0.8, and -0.9).



**Figure 4-1. Individual responses to experimental treatments relative to placebo for percentage change in mean 20-km time-trial power output.**

CAF – caffeine; CHO – carbohydrate, CHO+CAF – carbohydrate and caffeine;  
Grey Bar = Smallest worthwhile change of 1%.

NB – where no bars are shown = no different to placebo trial

#### **4.3. Pacing measures (mean power output, time)**

Mean performance outcomes for each 5-km quarter are presented in *Table 4-4*. In PLA, CHO, and CHO+CAF mean power output was highest in the first quarter of the 20-km time-trial compared to all other quarters, whilst in the CAF trial, performance was highest in the final quarter. The third quarters had the lowest mean power output of all trials.

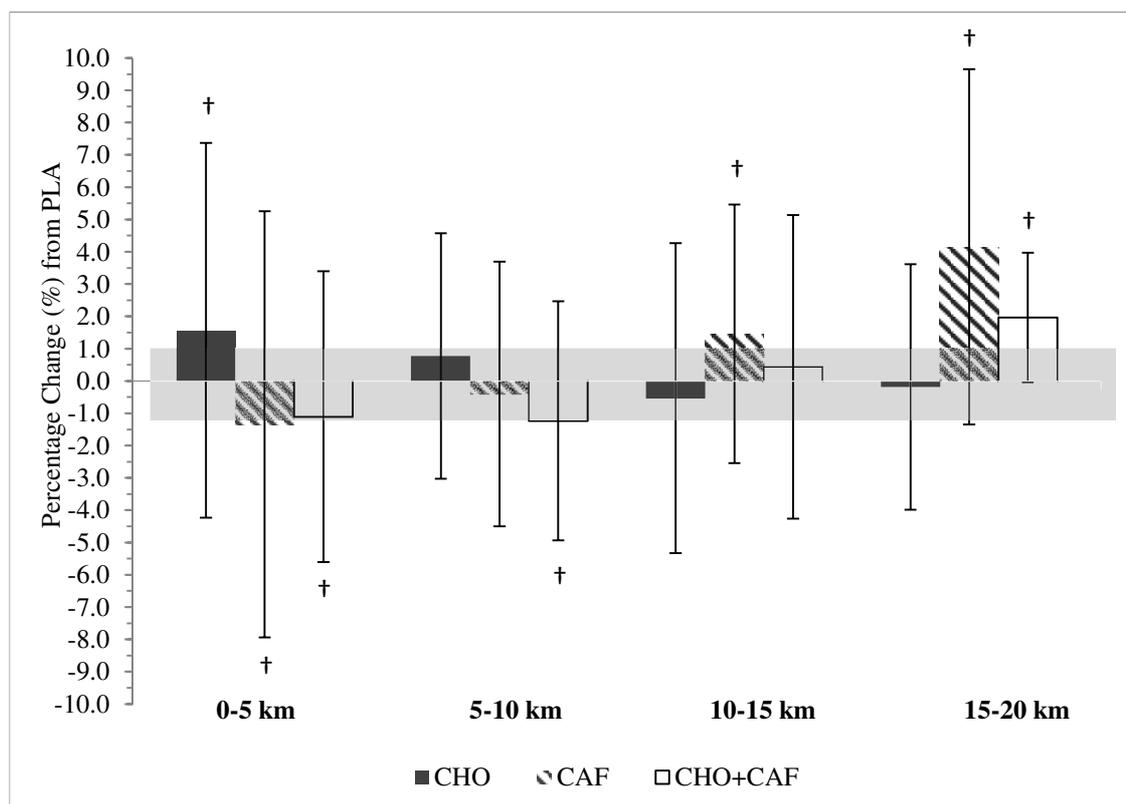
**Table 4-4. Performance outcomes for each 5-km quarter during the 20-km time-trial (Mean  $\pm$  SD).**

	PLA	CHO	CAF	CHO+CAF
<b>Quarter 1 (0-5km)</b>				
Time (m:s)	8:01 $\pm$ 0:31	7:58 $\pm$ 0:26	7:59 $\pm$ 0:32	8:02 $\pm$ 0:28
Mean Power Output (W)	284 $\pm$ 40	288 $\pm$ 37	281 $\pm$ 47	280 $\pm$ 38
<b>Quarter 2 (5-10km)</b>				
Time (m:s)	8:09 $\pm$ 0:28	8:07 $\pm$ 0:25	8:09 $\pm$ 0:29	8:10 $\pm$ 0:26
Mean Power Output (W)	264 $\pm$ 35	266 $\pm$ 35	264 $\pm$ 40	261 $\pm$ 35
<b>Quarter 3 (10-15km)</b>				
Time (m:s)	8:08 $\pm$ 0:28	8:07 $\pm$ 0:26	8:08 $\pm$ 0:29	8:10 $\pm$ 0:26
Mean Power Output (W)	259 $\pm$ 35	258 $\pm$ 36	263 $\pm$ 39	260 $\pm$ 35
<b>Quarter 4 (15-20km)</b>				
Time (m:s)	8:12 $\pm$ 0:29	8:14 $\pm$ 0:27	8:11 $\pm$ 0:29	8:12 $\pm$ 0:28
Mean Power Output (W)	273 $\pm$ 41	272 $\pm$ 38	284 $\pm$ 42	279 $\pm$ 43

CAF – caffeine; CHO – carbohydrate, CHO+CAF – carbohydrate and caffeine; PLA – placebo.

NB - All results were statistically indifferent.

Percentage difference for experimental versus PLA trial for mean power output (mean  $\pm$ 90%CL) relative to the smallest worthwhile change of 1% are presented in *Figure 4-2* for each 5-km quarter of the 20-km time-trial. Mean power output was higher in CHO versus PLA for the 0-5km quarter (1.6%), 5-10km (0.8%) and 10-15km, (0.5%), but less in the final 15-20km quarter (-0.2%). Additionally, the difference in mean power output was only greater than the smallest worthwhile change in the first quarter. Percentage difference for mean power output in CAF versus PLA was lower for the 0-5km (-1.3%) and 5-10km quarter (-0.4%), but higher in the 10-15km and 15-20km quarters (1.5 and 4.2%, respectively). The difference in mean power in the first quarter was greater than the smallest worthwhile change in the negative direction, whilst positive in the third and fourth quarters. In the CHO+CAF trial, mean power output difference was lower in the 0-5km and 5-10km quarters (-1.1 and -1.2%, respectively), and higher in the 10-15km (0.4%) and 15-20km quarter (2.0%). The difference in mean power output in the first and second quarters were greater than smallest worthwhile change in the negative direction, whilst positive in the fourth quarter.



**Figure 4-2. Performance change (%) for mean power output obtained during each 5-km quarter for experimental versus placebo condition (Mean  $\pm$ 90% CL).**

CAF – caffeine; CHO – carbohydrate, CHO+CAF – carbohydrate and caffeine; PLA – placebo.

† = Mean substantially different from PLA based on smallest beneficial or harmful change in performance of 1%.

Pairwise comparisons quantifying the magnitude of effect of different chewing gum contents on mean power output (see *Table 4-4*) for each 5km quarter are summarised in *Table 4-5*. Pairwise comparisons for CHO to PLA revealed *unclear* effects on the difference in mean power output across the first (Mean  $\pm$  SD:  $288 \pm 37$  and  $284 \pm 40$  W for CHO and PLA, respectively), second ( $266 \pm 35$  vs.  $264 \pm 35$  W), and fourth quarters ( $272 \pm 38$  vs.  $273 \pm 41$  W), and *possibly harmful* effects in the third quarter ( $258 \pm 36$  vs.  $259 \pm 35$ W) . When comparing CAF to PLA, there was a *possibly harmful* effect of CAF on the first two quarters ( $281 \pm 47$  and  $264 \pm 40$  vs.  $284 \pm 40$  and  $264 \pm 35$  W, for CAF and PLA, respectively) , an *unclear* effect on the third quarter ( $263 \pm 39$  vs.  $259 \pm 35$  W), and a *very likely beneficial* effect on the final quarter ( $284 \pm 42$  vs.  $273 \pm 41$  W). Results comparing the difference in mean power output for CHO+CAF to PLA revealed *possibly harmful* effects across the first two quarters ( $280 \pm 38$  and  $261 \pm 35$  vs.  $284 \pm 40$  and  $264 \pm 35$  W for CHO+CAF vs. PLA, respectively), *unclear* effects on the third quarter ( $260 \pm 35$  vs.  $259 \pm 35$  W), and *likely beneficial* effects on the final quarter ( $279 \pm 43$  vs.  $273 \pm 41$  W).

Among independent experimental conditions (CAF vs. CHO), pairwise comparisons revealed a *possibly trivial* effect on the difference in mean power output for the first quarter (Mean  $\pm$  SD:  $281 \pm 47$  vs.  $288 \pm 37$  W for CAF vs. CHO, respectively), a *possibly harmful* effect on the second quarter ( $264 \pm 40$  vs.  $266 \pm 35$  W), and *likely beneficial* and *very likely beneficial* effects on performance in the final two quarters ( $263 \pm 39$  and  $284 \pm 42$  vs.  $258 \pm 36$  and  $272 \pm 38$  W). Comparisons of combined versus independent treatments of CHO+CAF vs. CAF showed *unclear* effects on performance in the first 0-5km quarter, *possibly harmful* effects in the second and third quarters, and *likely harmful* effects on performance in the final quarter. Additionally, CHO+CAF vs. CHO revealed *likely harmful* effects on the first two quarters, *unclear* effects on the third quarter, and a *likely beneficial* effect on the final quarter of the trial.

**Table 4-5. Pairwise comparisons quantifying the magnitude of effect of different chewing gum contents on 5-km quarters during the time-trial for mean power output (see Table 4-4).**

	Quarter 1 (0-5km)		Quarter 2 (5-10km)		Quarter 3 (10-15km)		Quarter 4 (15-20km)	
	Mean <sup>a</sup> ±90% CL <sup>b</sup>	Qualitative inference <sup>c</sup>						
<b>Experimental treatment effects vs. placebo</b>								
CHO vs. PLA	1.6 ±3.1	Unclear	0.8 ±2.0	Unclear	-0.5 ±2.6	Possibly harmful	-0.2 ±2.1	Unclear
CAF vs. PLA	-1.3 ±3.6	Possibly harmful	-0.4 ±2.2	Possibly harmful	1.5 ±2.2	Unclear	4.2 ±3.0	Very likely beneficial
CHO+CAF vs. PLA	-1.1 ±2.4	Possibly harmful	-1.2 ±2.0	Possibly harmful	0.4 ±2.5	Unclear	2.0 ±1.8	Likely beneficial
<b>Inter-experimental treatment effects - Independent and Combined</b>								
CAF vs. CHO	-2.9 ±3.1	Possibly trivial	-1.2 ±1.5	Possibly harmful	2.0 ±1.8	Likely beneficial	4.3 ±2.6	Very likely beneficial
CHO+CAF vs. CAF	0.2 ±3.1	Unclear	-0.8 ±2.0	Possibly harmful	-1.0 ±1.6	Possibly harmful	-2.1 ±1.7	Likely harmful
CHO+CAF vs. CHO	-2.6 ±3.1	Likely harmful	-2.0 ±2.0	Likely harmful	1.0 ±2.2	Unclear	2.2 ±2.4	Likely beneficial

CAF – caffeine; CHO – carbohydrate, CHO+CAF – carbohydrate and caffeine; PLA – placebo.

<sup>a</sup> units of change are % change derived from back-transformed log data

<sup>b</sup> CL: add and subtract this number to the difference to obtain the 90% confidence limits for the true difference

<sup>c</sup>Based on smallest beneficial or harmful change in performance of 1%.

#### 4.4. Physiological measures

##### 4.4.1. Heart rate

Average and maximal heart rates achieved for the 20-km time-trial in each condition are presented in *Table 4-6*. There was no substantial difference in either average or maximal heart rates across all conditions with Cohen’s effect sizes being  $<0.2$  between conditions and inferences being *likely trivial*.

**Table 4-6. Average and maximal heart rate measures during the 20-km time-trial for each condition (Mean  $\pm$  SD).**

	PLA	CHO	CAF	CHO+CAF
Average HR (bpm)	163 $\pm$ 13	164 $\pm$ 11	162 $\pm$ 12	163 $\pm$ 13
Average HR as %HR <sub>peak</sub>	89 $\pm$ 7	89 $\pm$ 6	89 $\pm$ 7	89 $\pm$ 7
Maximal HR (bpm)	176 $\pm$ 11	176 $\pm$ 10	178 $\pm$ 12	176 $\pm$ 10
Maximal HR as %HR <sub>peak</sub>	96 $\pm$ 6	96 $\pm$ 5	97 $\pm$ 7	96 $\pm$ 5

HR – heart rate; HR<sub>peak</sub> – Highest heart rate attained in maximal step test; PLA – placebo; CAF – caffeine; CHO – carbohydrate; CHO+CAF – carbohydrate and caffeine.

Average heart rates for each 5-km segment during the 20-km time-trial are presented for each condition in *Table 4-7*. Heart rate increased steadily across each of the quarters during the 20-km time-trials. Pairwise comparisons quantifying the magnitude of effect of different chewing gum contents on average heart rate for each 5km quarter showed insubstantial differences with CHO, CAF, and CHO+CAF versus PLA for the first quarter, with associated Cohen’s effect sizes being less than the 0.2 threshold for a small effect (ES  $\pm$ 90%CL of 0.18  $\pm$ 1.23; 0.08  $\pm$ 0.5; -0.13  $\pm$ 0.43, respectively). Difference in average heart rate in the second quarter was small for CHO vs. PLA (ES: 0.27  $\pm$ 1.98), and insubstantial for CHO and CAF vs. PLA (0.15  $\pm$ 0.82 and -0.12  $\pm$ 1.19, respectively). However, there was an insubstantial difference between CHO+CAF vs. PLA during the second quarter with associated effect sizes being less than small (-0.12  $\pm$ 0.82). Differences in average heart rate for CHO and CAF vs. PLA during the third and fourth quarters were associated with small effect sizes (0.43  $\pm$ -1.91 and 0.34  $\pm$ 0.62; 0.33  $\pm$ -1.49 and 0.40  $\pm$ -0.73, for third and fourth quarters of CHO and CAF vs. PLA, respectively). However, there was an insubstantial difference between CHO+CAF vs. PLA with associated effect sizes being less than small in the third (-0.04  $\pm$ 1.25), and fourth quarters (0.14  $\pm$ 1.37).

Among independent experimental conditions (CAF vs. CHO), pairwise comparisons of differences in average heart rate during each 5-km quarter revealed insubstantial differences across all four quarters with associated Cohen's effect size of less than small (ES  $\pm$ 90%CL:  $-0.10 \pm 0.69$ ;  $-0.12 \pm 1.19$ ;  $-0.09 \pm 1.30$ ;  $0.07 \pm 0.78$  for the first through to fourth quarter, respectively). Comparisons CHO+CAF vs. CHO showed small effect sizes for the difference in average heart rate for the first ( $-0.31 \pm 1.01$ ), second ( $-0.39 \pm 1.40$ ), and third quarter ( $-0.47 \pm 1.09$ ); however there was an insubstantial difference in the final quarter ( $-0.19 \pm 0.72$ ). The difference in average heart rate for CHO+CAF vs. CAF showed small effects on the difference in average heart rate for all four quarters ( $-0.21 \pm 0.34$ ;  $-0.27 \pm 0.34$ ;  $-0.38 \pm 0.77$ ;  $-0.26 \pm 0.7$  for the first through to fourth quarter, respectively).

**Table 4-7. Average heart rate measures for each 5-km quarter of the 20-km time-trial for each condition (Mean  $\pm$  SD).**

Pacing effects	PLA	CHO	CAF	CHO+CAF
Quarter 1 (0-5km)	159 $\pm$ 7	161 $\pm$ 6 $\partial$	160 $\pm$ 6 $\partial$	157 $\pm$ 8
Quarter 2 (5-10km)	167 $\pm$ 6	169 $\pm$ 6* $\partial$	168 $\pm$ 3 $\partial$	166 $\pm$ 5
Quarter 3 (10-15km)	169 $\pm$ 5	172 $\pm$ 5*#	171 $\pm$ 3* $\partial$	168 $\pm$ 5
Quarter 4 (15-20km)	173 $\pm$ 5	175 $\pm$ 3*	176 $\pm$ 3* $\partial$	174 $\pm$ 6

CAF – caffeine; CHO – carbohydrate, CHO+CAF – carbohydrate and caffeine; PLA – placebo.

\* - substantially different from PLA (ES>0.2)

$\partial$  - substantially different from combined CHO+CAF (ES >0.2)

#### 4.4.2. Blood glucose and lactate concentrations

Average pre and post 20-km time-trial blood glucose and lactate concentrations are presented in *Table 4-8* for each condition.

**Table 4-8. Blood glucose and lactate measures before and after the 20-km time-trial for each condition (Mean  $\pm$  SD).**

Measure	PLA	CHO	CAF	CHO+CAF
<b>Glucose (mmol.L<sup>-1</sup>)</b>				
Pre-TT	4.8 $\pm$ 0.4	4.5 $\pm$ 0.8*	4.3 $\pm$ 0.7*	4.8 $\pm$ 1.1
Post-TT	6.4 $\pm$ 0.9	5.6 $\pm$ 0.7*	5.9 $\pm$ 1.2*	6.5 $\pm$ 1.3
<b>Lactate (mmol.L<sup>-1</sup>)</b>				
Pre-TT	1.2 $\pm$ 0.3	1.5 $\pm$ 0.4* $\partial$	1.5 $\pm$ 0.5* $\partial$	1.8 $\pm$ 0.4*
Post-TT	6.7 $\pm$ 2.4 $\partial$ #	6.6 $\pm$ 1.5 $\partial$ #	8.4 $\pm$ 0.9*	8.2 $\pm$ 1.8*

TT – time-trial; PLA – placebo; CAF – caffeine; CHO – carbohydrate; CHO+CAF – carbohydrate and caffeine.

\* - substantially different from PLA (ES>0.2)

# - substantially different from CAF (ES>0.2)

$\partial$  - substantially different from combined CHO+CAF (ES >0.2)

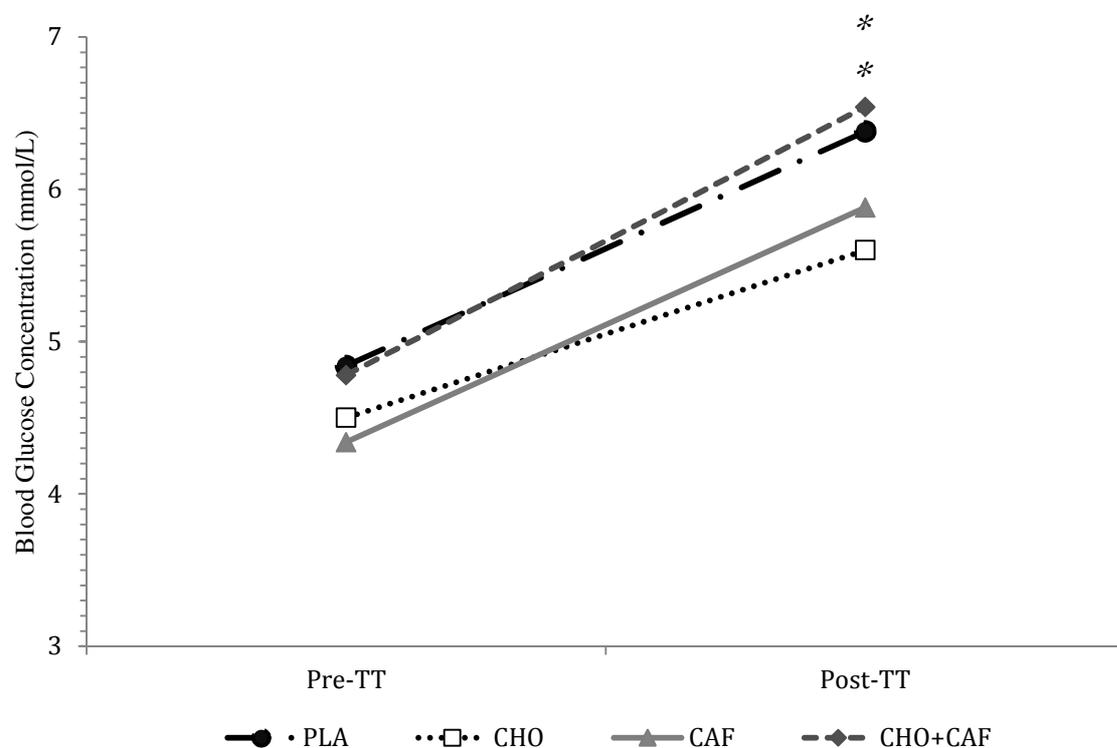
##### 4.4.2.1. Blood glucose concentrations

Blood glucose was slightly lower pre 20-km time-trial in CHO and CAF trials compared with PLA and CHO+CAF trials, which represented a small Cohen's effect size for CHO and CAF vs. PLA (ES  $\pm$ 90%CL: -0.40  $\pm$ 0.54 and -0.57  $\pm$ 0.58, respectively), and for CHO and CAF vs. CHO+CAF (0.26  $\pm$ 0.54 and 0.43  $\pm$ 0.57, respectively). However, there was insubstantial differences between PLA and CHO+CAF (-0.14  $\pm$ 0.54) or CAF and CHO (-0.17  $\pm$ 0.53).

Blood glucose concentrations post 20-km time-trial showed higher levels for PLA and CHO+CAF compared with CHO and CAF trials, which represented Cohen's effect sizes of moderate and small for CHO and CAF vs. PLA (ES  $\pm$ 90%CL: -0.63  $\pm$ 0.15 and -0.44  $\pm$ 0.31, respectively), and moderate and small for CHO and CAF vs. CHO+CAF (0.53  $\pm$ 0.51 and 0.72  $\pm$ 0.52, respectively). However, there were insubstantial differences between PLA and CHO+CAF (ES: 0.10  $\pm$ 0.56) or CAF and CHO (0.19  $\pm$ 0.37).

Changes in blood glucose concentrations pre and post 20-km time-trial are presented in *Figure 4-3*. There was a clear increase in blood glucose concentrations across all trials.

However, the increases in blood glucose concentration from pre to post 20-km time-trial were greatest in the CHO+CAF trial (+1.7 mmol/L), slightly less for both PLA (+1.6) and CAF (+1.6), and lowest for CHO (+1.1).



**Figure 4-3. Blood glucose levels pre and post 20-km time-trial for each condition.**

PLA – placebo; CAF – caffeine; CHO – carbohydrate; CHO+CAF – carbohydrate and caffeine.

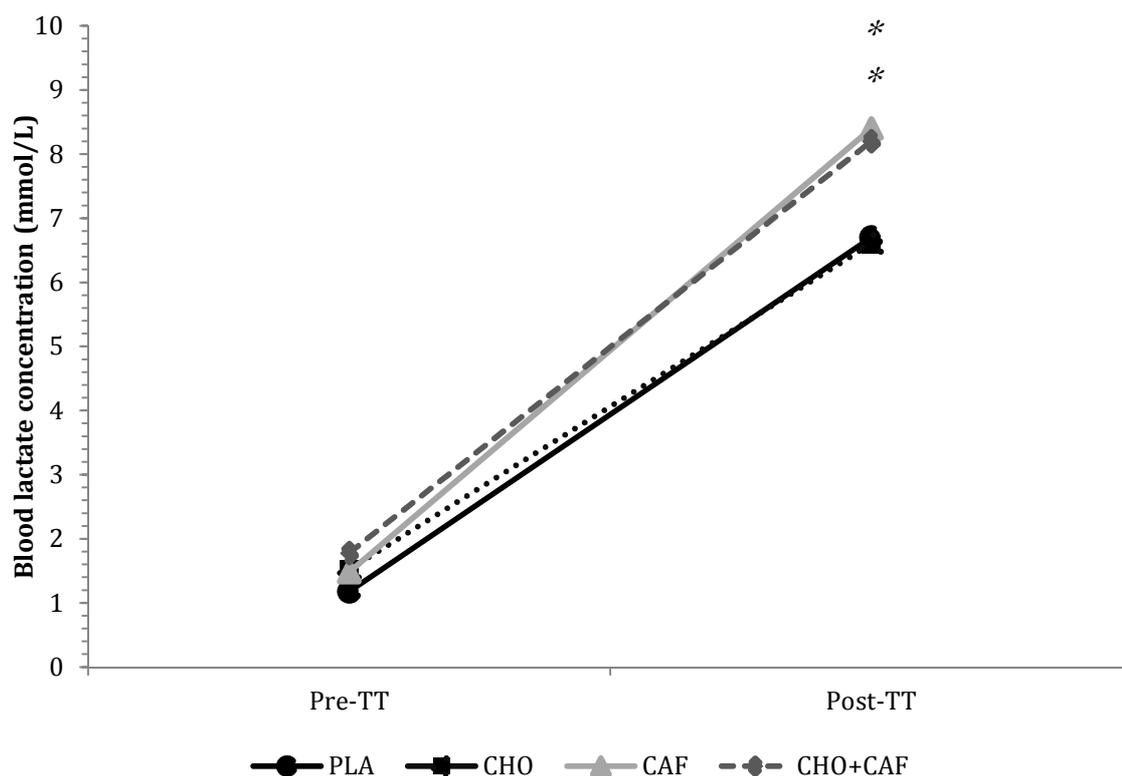
\* - substantially different from PLA (ES>0.2)

#### 4.4.2.2. Blood lactate concentrations

Blood lactate was slightly higher prior to the start (pre-TT) of the 20-km time-trial in CHO, CAF, and CHO+CAF trials compared with PLA. The difference in pre-TT lactate represented small Cohen's effect size for CHO vs. PLA (ES  $\pm$ 90%CL:  $-0.70 \pm 0.83$ ), moderate effect size for CAF vs. PLA ( $0.55 \pm 1.12$ ) respectively), and large effect size for CHO+CAF vs. ( $1.16 \pm 0.72$ ). Within experimental conditions, blood lactate was highest prior to the time-trial in the CHO+CAF trial compared with CHO and CAF, which represented a Cohen's effect size of moderate and small respectively ( $0.61 \pm 0.90$  and  $0.46 \pm 0.67$ ). However, there were insubstantial differences between CAF and CHO ( $-0.15 \pm 1.47\%$ ).

Blood lactate concentrations following completion of the 20-km time-trial (post-TT) showed higher concentrations for CAF and CHO+CAF compared with PLA and CHO trials, which represented moderate Cohen's effect sizes for CAF vs. PLA and CHO (ES  $\pm$ 90%CL:  $0.90 \pm 1.09$  and  $0.85 \pm 0.55$ , respectively), and for CHO+CAF vs. PLA and CHO ( $0.78 \pm 1.14$  and  $0.72 \pm 0.62$ , respectively). However, there were insubstantial differences between CAF vs. CHO+CAF (ES:  $-0.12 \pm 0.68\%$ ), and PLA vs. CHO ( $0.05 \pm 0.77\%$ ).

Changes in blood lactate concentrations pre and post 20-km time-trial are presented in *Figure 4-4*. There was a clear increase in blood lactate concentrations across all trials. However, the increases in blood lactate concentration from pre to post 20-km time-trial were greatest in the CAF (+6.9 mmol/L) and CHO+CAF trials (+6.4) compared to CHO (+5.1) and PLA trials (+5.5).



**Figure 4-4. Blood lactate concentrations pre and post 20-km cycle time-trial in each condition.**

PLA – placebo; CAF – caffeine; CHO – carbohydrate; CHO+CAF – carbohydrate and caffeine.

\* - substantially different from PLA (ES>0.2).

#### 4.7. Perceptual measures

##### 4.7.1. Gastrointestinal Discomfort

Subjective feedback on gastrointestinal discomfort and symptoms are presented in *Table 4-9*. A total of 6 of the 44 time-trials featured minor gastric upsets. Half (50%) of the time-trials with gastric distress (2 PLA, 1 CAF) were the participant's best performance trial. There were no serious gastric distresses reported at the end of any of the trials.

**Table 4-9. Participant feedback on gastrointestinal distress and associated symptoms following the 20-km time-trial.**

	PLA	CHO	CAF	CHO+CAF
<b>GI distress (#)</b>	3	1	2	0
<b>Symptoms</b>	Nausea, Belching	Nausea	Nausea, Belching	

PLA – placebo; CAF – caffeine; CHO – carbohydrate; CHO+CAF – carbohydrate and caffeine; GI – gastrointestinal.

##### 4.7.2. Perceptual effects

Perceptual feedback on the chewing gum contents are presented in *Table 4-10*. Following completion of the 20-km time-trial, participants were able to correctly identify the exact contents of the chewing gum 25% of the time. Within the carbohydrate containing trial conditions (CHO and CHO+CAF), participants were able to correctly identify the presence of carbohydrate 41% of the time. In caffeine containing trial conditions (CAF and CHO+CAF), participants were able to correctly identify the presence of caffeine 68% of the time.

**Table 4-10. Participant feedback on gastrointestinal distress and associated symptoms following the 20-km time-trial.**

	Ratio Correct	Percentage (%)
<b>Exact identification of gum content</b>	12/44	25
<b>Identification of carbohydrate</b>	9/22	41
<b>Identification of caffeine</b>	15/22	68

## **Chapter Five: Discussion**

The primary aim of this study was to examine the independent and combined effects of carbohydrate and caffeine chewing gums on self-paced cycling time-trial performance under the influence of exercise-induced fatigue. A secondary aim was to examine the effects of the gums on pacing and physiological responses in order to provide mechanistic support for any potential differences found. Given that each of the ergogenic aids investigated are proposed to elicit their performance-enhancing effect via central mechanisms, it was hypothesised that 1) acting independently, carbohydrate and caffeine would enhance exercise performance compared with placebo, and 2) that the combination of carbohydrate and caffeine together would elicit a synergistic effect on performance that would be greater extent than the effect of either independent substance alone. The main finding was that the oral presence of carbohydrate and caffeine in chewing gum, either independently or combined, did not enhance mean power output in the 20-km cycle time-trial after 90-mins of prior exercise compared with placebo condition. However, carbohydrate and caffeine chewing gums did appear to subconsciously alter motor output and the distribution power output across the time-trial despite adoption of a maximal self-selected intensity across all trials.

To the best of the author's knowledge, this is the first study to investigate the independent and combined effects of the oral presence of carbohydrate and caffeine on endurance performance in athletes under conditions of exercise-induced fatigue. As such, it is not possible to directly compare the findings of the present study in the context of those that have been previously reported. However, where appropriate, present results have been evaluated against other studies that have attempted to modify performance through oral stimulation, via mouth-rinsing or chewing gum, with carbohydrate or caffeine. Additionally, in some instances, reference has been made to studies that have attempted to quantify the effect of carbohydrate and caffeine ingestion on performance under low glycogen conditions.

## 5.1. Performance measures

### 5.1.1. Mean performance effect

There was no 'clear' beneficial effect of using independent carbohydrate (Mean  $\pm 90\%CL$ :  $0.2 \pm 2.0\%$ ), caffeine ( $0.1 \pm 2.2\%$ ), or together in combination ( $0.1 \pm 1.8\%$ ) on mean power output during the 20-km time-trial compared with the placebo condition. As such, these results did not meet the criteria for smallest worthwhile change in performance, measured via power output (0.5-1.5%), for high level cyclists, as estimated by Paton and Hopkins (2001). A possible explanation for the lack of an observable performance effect in the present study is the unexplainable higher variability in placebo trial performance compared with experimental trials, as evidenced by the larger confidence limits (1.8-2.2%) across pairwise experimental-placebo comparisons (compared to 1.2-1.6% across experimental conditions; *Table 4-3*).

Evaluating the findings of the present study with previous work is difficult, due to subtle differences in study design, including supplementation medium, dosage, and timing, as well as the duration and intensity of different performance measures. In terms of changes in mean 20-km time-trial power output (Mean  $\pm 90\%CL$ :  $0.2 \pm 2.0\%$ ) with carbohydrate chewing gum versus placebo, the possibly trivial performance effects are in contrast to previous carbohydrate mouth-rinse studies that report clear worthwhile enhancements in cycling time-trials over 40-km (Carter et al., 2004; Chambers et al., 2009; Gam et al., 2013; Lane et al., 2013a; Pottier et al., 2010) and 20-km (Sinclair et al., 2013). However, in contrast to many of the previous studies that have had participants present with likely full endogenous muscle glycogen stores, the current study exposed participants to a 90 min of constant-load cycling to simulate the fatigue experienced late in endurance events. Although we did not take physiological measures of glycogen, previous research has shown that 100 min of constant-load cycling at 63% of peak power output (same as the current study) depletes muscle glycogen by 50% in well-trained cyclists (Coyle, Coggan, Hemmert, & Ivy, 1986; Yeo et al., 2008), and therefore participants' are likely to have been ~45-50% depleted prior to commencing the 20-km time-trial. Thus, a possible explanation for these contrasting results could be that the centrally-mediated ergogenic effects of carbohydrate may be less efficacious after more prolonged exercise due to the breaching of an allowable 'glycogen-depletion threshold level', leading to a more conservative anticipatory pacing strategy that could not be overridden by energy-detecting oral receptors during the time-trial.

Likewise, the findings of an unclear performance effect ( $0.4 \pm 2.2\%$ ) with caffeine chewing gum compared to placebo are in contrast to other similar studies. For example, both Ryan et al., (2013) and Lane et al. (2013) demonstrated clear performance improvements with caffeine gum in endurance cycling time-trials of approximately 25, and 30 and 49 km, respectively. A possible explanation for the observed discrepancies is that performance may be due to the higher caffeine doses, shorter nature of their adopted time-trial, lack of pre-loading, or the maintenance of endogenous carbohydrate levels during exercise; thus, allowing caffeine to exhibit secondary effects on peripheral and/or metabolic functions of performance (Spriet et al., 1992). Therefore, it may be more practical to compare the current results to similar duration studies that have employed endurance tests under conditions of lowered endogenous energy stores, and without the presence of carbohydrate.

Under the conditions of lowered endogenous carbohydrate stores, the current findings also contrast several recent studies that have shown caffeine to act independently of glycogen levels, and significantly enhance high-intensity endurance performance during a 4-km time-trial (Silva-Cavalcante et al., 2013) and high-intensity aerobic interval training (Lane et al., 2013b). Of particular interest is the performance findings of Lane et al. (2013) who employed a similar glycogen-reducing protocol to the current study (100-min at  $\sim 63\%$  peak power output) 4 h prior to performance of a 1 h high-intensity cycling test consisting of 8 x 5 min at maximal self-selected pace intervals with 1 min active recovery. That the authors found significant performance enhancements (mean power output increased 3.5%,  $p = 0.05$ ; qualitative inference 'likely positive') is in contrast to findings from the present study. However it is likely attributable to differences in the performance test (i.e. interval-based vs. constant) and methodological differences in caffeine administration within the current study (i.e. ingestion of a single dose of  $3 \text{ mg.kg BM}^{-1}$  1 h prior compared with the current studies' buccal delivery of 4 x 50 mg for a total dose  $\sim 2.7 \text{ mg.kg BM}^{-1}$  at the start and then every 25% of distance completed). Given that caffeine doses of  $2.0\text{-}3.0 \text{ mg.kg BM}^{-1}$  are effective for improving endurance performance with ingestion (Cox et al., 2002; Desbrow et al., 2012b) and buccal delivery (Lane et al., 2013), it is possible that the ergogenic effects usually obtained with caffeine were unattainable during the time-trial due to the provision of the late, smaller divided dose (see section on pacing). A possible explanation is that

caffeine's initiation of ergogenic effects may require breaching of a 'threshold effect' in relation to 1) plasma caffeine concentrations and 2) the number of adenosine receptor sites occupied by caffeine, since the last quarter could be hypothesised to have occurred concomitantly with breaching of a certain 'threshold' for caffeine plasma levels and/or actions at adenosine sites due to receipt of the full 200 mg of caffeine. However, there is currently no known way of measuring the occupancy of caffeine at receptor sites and we chose not to measure serum caffeine concentration during the time-trial due to the negative implications for performance. As such, the extent to which the relationship between caffeine concentration and exercise performance can be assessed from the current and previous studies is limited and future research should investigate the physiological responses to single versus divided doses on the ergogenic effect of caffeine provided *during* exercise.

Also of interest in the present study was the difference in magnitude of the independent effects of caffeine or carbohydrate compared with placebo and when provided in combination. Several studies have shown improved performance with caffeine over carbohydrate alone during endurance exercise (Cox et al., 2002; Hulston & Jeukendrup, 2008; Kovacs et al., 1998; Lane et al., 2013). However, less is known when combined supplementation occurs without ingestion and thus, negates the secondary effects of caffeine, such as increased gastrointestinal permeability and exogenous carbohydrate oxidation (Yeo et al., 2005) that occur alongside the ergogenic effects. Due to the central mechanisms of action proposed to underlie carbohydrate (Carter et al., 2004; Carter, Jeukendrup, Mann, et al., 2004; Chambers et al., 2009) and caffeine (Davis et al., 2003; Jones, 2008), along with research demonstrating enhanced cortico-excitability (Specterman et al., 2005) and endurance performance with combined ingestion in non-peripherally limiting exercise (Conger et al., 2011), it was thought that carbohydrate and caffeine in combination would elicit a greater ergogenic influence compared with each substance independently and versus placebo. However, in the present study there were trivial and unclear performance effects for combined carbohydrate and caffeine versus placebo (Mean  $\pm$  90%CL: 0.1  $\pm$ 1.8%), carbohydrate (-0.1  $\pm$ 1.2), and caffeine (-0.4  $\pm$ 1.5), respectively. It is unclear as to why the current study observed insubstantial effects, however a likely explanation relates to the previously mentioned methodological differences between studies.

Previous research examining the caffeine and carbohydrate use (Cox et al., 2002; Hulston & Jeukendrup, 2008; Kovacs et al., 1998; Lane et al., 2013), is flawed in that they have failed to assess the independent effects of caffeine, and thus it is not possible to determine the relative importance of each. In the current study, trivial differences were observed for the effects of carbohydrate or caffeine alone versus placebo ( $0.2 \pm 2.0$  and  $0.1 \pm 2.2\%$ , respectively) and with respect to each other ( $0.3 \pm 1.6\%$ ). Previous research has given clear support for these two substances when provided independently of the oral cavity; however there is currently a paucity of research examining the interactive effects of combined oral delivery. To date, only Beaven et al., (2013) has investigated the centrally-mediated performance effects via use of combined and independent carbohydrate and caffeine mouth-rinsing prior to maximal sprint cycling. However, a major limitation of their study was that they did not directly compare the independent, combined, and placebo trials in one single study; and thus, it is not possible to interpret the interaction of the different ingredients with certainty for comparison to the current study findings. Further research is needed to better understand independent and combined central ergogenic mechanisms in order to elucidate whether additive effects can be mediated via the oral cavity.

### *5.1.2. Individual performance effects*

Research investigating the efficacy of ergogenic aids and nutritional supplements frequently demonstrates considerable individual variations in the observed performance effect in response to the receptiveness of the individual (Astorino & Roberson, 2010; Bruce et al., 2000; Cook, Beaven, Kilduff, & Drawer, 2012; Jenkins et al., 2008). In agreement, the individual performance responses observed in the current study revealed considerable inter and intra-individual variation to the independent and combined oral presence of carbohydrate and caffeine (*Figure 4-1*).

In regards to carbohydrate chewing gum, three participants performed substantially better with carbohydrate compared to placebo, with increases in mean power output of 2.4-6.9%, whilst six participants experienced substantial reductions in mean power output of 1.2-3.7%. Interestingly, those that demonstrated enhanced performance with carbohydrate only also had substantially enhanced performance with the carbohydrate and caffeine gum of 1.3-3.4%, which suggests that these individuals may have been

'responders' to carbohydrate. Similarly, in the caffeine chewing gum condition, four participants demonstrated substantial improvements in time-trial performance, with increases in mean power output of 1.3-7.9%, whilst three went substantially worse by 2.6-4.7%. Additionally, of those that performed substantially better with caffeine, two went substantially better with combined caffeine and carbohydrate by 2.7 and 5.2%, respectively, which suggest that these individuals may have been positive responders to caffeine. Also, of those that went substantially worse with caffeine, two of these participants also performed substantially worse with the combined carbohydrate and caffeine gum by -3.5 and -2.2%, respectively, which suggests that these individuals may have been adverse responders to caffeine. An explanation for this inconsistency in performance responses may be due to the small sample size, a possible sampling error variance, and/or the presence of non-responders/adverse caffeine responders. Thus, future research investigating the efficacy of ergogenic aids should aim to identify positive responders prior to research entry in order to better understand the magnitude of ergogenic performance effects in this sub-group and therefore allow practitioners to provide more accurate prescriptive advice when using ergogenic aids.

## ***5.2. Pacing measures***

Although there was no substantial difference observed for mean power output during any of the 20-km time-trials, there were notable differences in subconscious regulation of motor output during the 20-km time-trial in response to the experimental gum ingredients.

Some of the pacing results from the present study are similar to those previously reported for carbohydrate mouth-rinse studies. Carter et al., (2004) found carbohydrate mouth-rinse significantly ( $p < 0.05$ ) improved mean power output during the first three quarters of the 1 h time-trial compared with placebo, and although not significant, carbohydrate also improved performance in the last quarter. Nevertheless, in contrast to the findings of Carter et al. (2004), Chambers et al. (2009), and Lane et al., (2013), whereby mouth-rinse improved performance in the second half of the 1 h time-trial, the carbohydrate gum in the current study did not improve performance in the latter two quarters compared with placebo ( $-0.5 \pm 2.6$  and  $-0.2 \pm 2.1\%$  for 10-15km and 15-20km respectively), and of concern, may have in fact had a 'possibly harmful' effect on

performance in the third quarter of the trial from 10-15km. In light of these findings, our results provide some indication that the oral presence of carbohydrate late in endurance exercise may alter motor output, possibly through increased central stimulation and an amelioration of the reduction in motor output that typically results from central feedback of lowered endogenous stores in the early stages of the time-trial. However, this overriding of the anticipatory strategy may have subsequently had a detrimental effect on pacing and allowable motor output by causing participants to ‘over-pace’ the first half of the time-trial. Perhaps the most practical approach to enhancing prolonged endurance performance capacity would be to ingest a small amount of carbohydrate early on in exercise and then in the latter stages use a carbohydrate chewing gum, thus allowing for avoidance of gastrointestinal upset with higher carbohydrate consumption (Burke et al., 2005; Pfeiffer, Stellingwerff, Hodgson, et al., 2012), lessening endogenous depletion, and enabling mediation of a central stimulatory effect that can be supported by adequate energy stores.

In contrast, caffeine chewing gum exhibited almost the opposite effect on power output distribution compared to carbohydrate. Compared to the placebo chewing gum, caffeine exhibited a ‘possibly harmful’ effect on mean power output for the first two quarters (Mean  $\pm$ 90%CL:  $-1.3 \pm 3.6$  and  $-0.4 \pm 2.2\%$  for 0-5km and 5-10km, respectively), and an ‘unclear’ effect in the third quarter ( $1.5 \pm 2.2\%$ ). However, a ‘very likely beneficial’ effect of caffeine on performance was observed in the final quarter ( $4.2 \pm 3.0\%$ ) of the time-trial. The lack of immediate performance effects are in contrast to previous caffeine gum studies of Paton et al., (2010) and Ryan et al., (2013), who both demonstrated ergogenic effects with administration of a caffeine gum ~5 min prior to performance of high-intensity cycling tests. However, a possible explanation for these discrepancies and the improvement of pacing in the last quarter of the time-trial may be due to the smaller, divided caffeine dose used in the present study (200 mg total – 50 mg at each 5-km time-points vs. 300 mg in one dose in the studies by Paton et al. (2010) and Ryan et al. (2013), resulting in an insufficient delivery of caffeine to the plasma and adenosine receptor site early on in the time-trial. However, of particular interest is that performance was altered substantially compared with placebo, in the final quarter of the trial, when endogenous stores would have been at their lowest, and conversely fatigue levels highest. This suggests that providing caffeine during endurance exercise may enable cyclists’ to ‘override’ fatigue signals associated with exercise-induced fatigue

which is in alignment with studies showing improved endurance performance with caffeine ingestion in a glycogen-reduced state (Lane et al., 2013; Silva-Cavalcante et al., 2013). Collectively, these findings add support for the mechanistic action of caffeine as a central-mediator that can play a role in altering pacing strategies by attenuating negative afferent muscle feedback, allowing for increased motor unit recruitment and force for a given maximal work rate (Davis et al., 2003; Doherty, Smith, Hughes, & Davison, 2004); however this did not result in an improvement in performance in the current study.

Additionally, pacing results for the combined carbohydrate and caffeine chewing gum demonstrated a similar power output distribution profile to the independent caffeine gum condition; with a ‘possibly harmful’ effect on mean power output for the first two quarters (Mean  $\pm$ 90%CL:  $-1.1 \pm 2.4$  and  $-1.2 \pm 2.0\%$  for 0-5km and 5-10km, respectively), an ‘unclear’ effect in the third quarter ( $0.4 \pm 2.5\%$ ), and a ‘likely beneficial’ effect in the final quarter from 15-20km ( $2.0 \pm 1.8\%$ ). The findings of a possible negative effect during the first two quarters with the combined gum are perplexing given the findings of an improvement in mean power output in the first two quarters in the independent carbohydrate gum condition in the current study, whilst the findings of enhanced performance in the latter quarter are in agreement of those seen during the independent caffeine gum condition. That the current carbohydrate gum findings and previous research has shown immediate increases in motor output in response to carbohydrate in the mouth (Beaven et al., 2013; Carter et al., 2004; Gam et al., 2013; Gant, Stinear, et al., 2010a), it is surprising that the presence of carbohydrate in the combined gum did not facilitate a similar improvement in motor output in the early phases of the time-trial. A possible explanation for these confounding findings may be that the presence of both carbohydrate and caffeine in the oral cavity caused an interactive effect within the mouth, which subsequently negated the positive effects of carbohydrate. In terms of the observed performance enhancement during the latter stages of the time-trial, these may be attributable to breaching of an ‘accumulative caffeine threshold’ and hence, initiation of caffeine’s ergogenic effect late in exercise (discussed previously). Further research is needed to better understand 1) the physiological responses to buccal caffeine delivery during endurance exercise in order to determine factors that regulate the initiation of ergogenic effects; and 2) the independent and combined effects of the oral presence of caffeine and carbohydrate to

elucidate whether interactive effects within the mouth are synergistic or antagonistic.

### **5.3. Physiological measures**

#### *5.3.1. Heart rate*

In the current study, there was no effect of experimental gum conditions on average or maximal heart rate during the 20-km time-trial (*Table 4-6*), which is in agreement with previous research that has reported no effect on exercise-induced elevations in heart rate with carbohydrate mouth-rinsing (Carter et al., 2004; Gam et al., 2013; Rollo et al., 2008; Sinclair et al., 2013), and caffeine provided in a mouth-rinse (Beaven et al., 2013; Doering et al., 2013), chewing gum (Ryan et al., 2013), or an ingested capsule (Jenkins et al., 2008). A possible explanation for this lack of difference in heart rate between conditions may be that the maximal self-selected intensity tests used in these studies, as in the current one, elicit near maximal heart rate values and as such, no substantial differences were observed between conditions.

However, in contrast to the caffeine studies mentioned previously, several authors have shown that caffeine ingestion increases average heart rate values for high-intensity aerobic exercise (Bridge & Jones, 2006; Kovacs et al., 1998), which are typically associated with increases in the work output during exercise (Kovacs et al., 1998). A probable explanation for the lack of an observable difference in average heart rate in the current study may be the late onset of caffeine's ergogenic effect during the 20-km time-trial for independent caffeine and combined carbohydrate and caffeine conditions (see section on pacing), and therefore a lack of an observable difference in average heart rate throughout the time-trial.

#### *5.3.2. Blood glucose concentrations*

In the current study, there was a small difference in blood glucose concentrations measured before the time trial in the independent carbohydrate and caffeine trials compared with placebo (ES  $\pm$ 90%CL:  $-0.40 \pm 0.54$  and  $-0.57 \pm 0.58$ , respectively) and combined carbohydrate and caffeine ( $0.26 \pm 0.54$  and  $0.43 \pm 0.57$ , respectively). However, it is unlikely that these small differences would have had any effect on performance during the 20-km time-trial, as 1) all participants were likely to be euglycemic, and 2) previous research has demonstrated that despite variations in pre-

exercise blood glucose concentrations at the commencement of a 40-min cycle time-trial (as a result of various pre-event feeding times) there were no differences in rate of perceived exertion, heart rate, or performance (Moseley, Lancaster, & Jeukendrup, 2003). Furthermore, that power output and pacing was similar in the independent caffeine and combined carbohydrate and caffeine conditions, despite small differences in the pre time-trial blood glucose concentrations, suggests that it is unlikely that the marginal differences observed prior to the time-trial would have influenced performance capabilities during the time-trial.

Blood glucose concentration showed clear increases across all 20-km time-trials by 1.1-1.7 mmol.L<sup>-1</sup> (*Figure 4-4*). However, the observed changes were not reflective of differences in performance or pacing despite being associated with moderate and small Cohen's effect sizes for differences in the independent carbohydrate and caffeine trials compared with placebo (ES  $\pm$ 90%CL: -0.63  $\pm$ 0.15 and -0.44  $\pm$ 0.31, respectively) and combined carbohydrate and caffeine trials (0.53  $\pm$ 0.51 and 0.72  $\pm$ 0.52, respectively). Additionally, these findings are in line with previous carbohydrate mouth-rinse (Chong, Guelfi, & Fournier, 2011; Gam et al., 2013) and caffeine gum studies (Bashafaat, 2013; Farhadi & Hadi, 2011; Farhadi, Hadi, & Sabegh, 2011), which show that plasma glucose concentrations increase as a result of exercise *per se*, rather than in response to the oral presence of carbohydrate or caffeine.

### 5.3.3. Blood lactate concentrations

The largest physiological change observed in the present study was the difference in blood lactate concentration after completion of the 20-km time-trial in the independent and combined caffeine trials compared with the carbohydrate and placebo trial (*Figure 4-5*). The current study showed that during the independent caffeine and combined carbohydrate and caffeine gum trials, blood lactate concentrations were higher than with the placebo and carbohydrate gum on completion of the 20-km time-trial (Mean  $\pm$  SD: 8.4  $\pm$  0.9 and 8.2  $\pm$  1.8 versus 6.7  $\pm$  2.4, 6.6  $\pm$  1.5 mmol.L<sup>-1</sup>, respectively), which represented moderate Cohen's effect sizes for caffeine versus placebo and carbohydrate (ES  $\pm$ 90%CL: 0.90  $\pm$ 1.09 and 0.85  $\pm$ 0.55, respectively), and carbohydrate and caffeine versus placebo and carbohydrate (0.78  $\pm$ 1.14 and 0.72  $\pm$ 0.62, respectively). Research investigating the effect of caffeine on blood lactate concentrations is equivocal (Davis & Green, 2009). The current findings are in agreement with previous studies

demonstrating increased lactate levels with caffeine administration (Bell, Jacobs, & Ellerington, 2001; Jenkins et al., 2008), but contrast others finding no effect (Bashafaat, 2013; Farhadi & Hadi, 2011; Farhadi, Hadi, & Sabegh, 2011). It is thought that an increase in blood lactate levels with caffeine reflects a heightened aerobic (Jenkins et al., 2008) and anaerobic metabolism during exercise (Silva-Cavalcante et al., 2013), probably as a result of increased adrenaline and central nervous system activity (Davis & Green, 2009). This may reduce pain perception, improve exercise tolerance and motor output (Doherty et al., 2004), and hence culminate in the higher end-exercise lactate levels observed at the point of completion (Doherty et al., 2004). The current study supports this theory as increases in blood lactate during caffeine-containing time-trials were associated with substantial increases in mean power output during the final quarter of the 20-km time-trial (Mean  $\pm$  SD: 284  $\pm$  42 and 279  $\pm$  43 W for CAF and CHO+CAF, respectively) compared to trials without caffeine (273  $\pm$  41 and 272  $\pm$  38 W for PLA and CHO, respectively). These corresponded with ‘very likely beneficial’ and ‘likely beneficial’ changes in performance compared with placebo (Mean  $\pm$  90%CL: 4.2  $\pm$  3.0 and 2.0  $\pm$  1.8% for CAF and CHO+CAF, respectively) and carbohydrate (4.3  $\pm$  2.6 and 2.2  $\pm$  2.4% for CAF and CHO+CAF, respectively).

#### **5.4. Perceptual measures**

##### *5.4.1. Gastric comfort*

The intake of carbohydrate and caffeine during endurance exercise performance is often associated with reported gastrointestinal distress (Burke, 2008; Burke et al., 2005; Graham & Spriet, 1995; Pfeiffer et al., 2009; Pfeiffer et al., 2012). It has been suggested that use of oral mouth-rinses and/or chewing gum delivery methods might serve to reduce the incidence of gastrointestinal distress whilst still eliciting ergogenic effects (Paton et al., 2010; Sinclair et al., 2013). In the current study, there were a total of 6 time-trials that featured minor gastrointestinal distress symptoms, including nausea and burping; however half of these were associated with the participant’s best time-trial performance. Consequently, these results suggest that the gastrointestinal distress reported was associated with the higher intensity exercise, and the possible redirection of gastric blood flow (ter Steege & Kolkman, 2012), rather than in response to the intervention itself.

#### 5.4.2. *Perceptual effects*

In the current study, as with previous carbohydrate and caffeine mouth rinse and gum studies, all participants were blinded to the composition of each gum, but they were aware that one trial would be a placebo. On completion of the time-trials, participants were only able to correctly identify the exact contents of the gums 25% of the time (*Table 4-10*), which is no more than the odds of chance alone; however, when considering the identification of either carbohydrate and/or caffeine, participants were able to correctly identify the contents 41 and 68%, respectively. Collectively, these results and the observation of no effect on overall performance outcomes for experimental or placebo time-trials, suggest that blinding was sufficient in terms of ensuring maximal effort in each trial, as the exact contents were unidentifiable. Additionally, that caffeine was more identifiable than carbohydrate and placebo time-trials provides further support for the previous discussion (see section 5.1 mean performance effects) around the lack of a pharmacologically-induced ergogenic effect of caffeine in small, divided 50mg dosages.

Interestingly, although not asked specifically, several participants also commented on the ability of the chewing gum to reduce perceptions of hunger that were induced by the 90 min constant-load phase. For example, two participants stated that “the gum made me feel less hungry” and “the gum took away my hunger” on completion of the time-trial when provided with carbohydrate and placebo gums. From a practical stand-point, this finding may be particularly useful for elite athletes performing “train low” practises – i.e. after an overnight fast or in the absence of carbohydrate supplementation – which are often associated with a reduction in power output due to increased feelings of hunger, lethargy, and fatigue (Johnson, Stannard, Chapman, & Thompson, 2006). The use of gum in such circumstances may help sustain higher power outputs by reducing perceptions of fatigue and hunger, and thus, promote superior training adaptations in metabolic efficiency and mitochondrial biogenesis (Cox, Clark, et al., 2010; Hawley, Burke, Phillips, & Spriet, 2011; Hulston et al., 2010; Yeo et al., 2008). However, future research is needed to fully elucidate the benefits of using chewing gum containing artificial sweeteners, carbohydrate and/or caffeine, on prolonged endurance exercise performance, hunger, and feelings of fatigue.

### 5.5. Limitations

The findings of the present thesis are considered unique in that this is the first study to investigate the use of independent and combined oral carbohydrate and caffeine presence for enhancing endurance performance under exercise-induced fatigue conditions. Consequently, there were no direct methodological blueprints to guide the direction of this study. On retrospective analysis therefore, a number of limitations in this study can be observed.

The placebo effect positively influences performance outcomes, as participants are fuelled by the expectation (i.e., belief) that an advantageous treatment has been received. Hence, in addition to 'true' pharmacological or nutritional effects observed with ergogenic aids, the benefit of knowingly or deceptively ingesting caffeine (Beedie, Stuart, Coleman, & Foad, 2006), carbohydrate (Clark, Hopkins, Hawley, & Burke, 2000), or other ergogenic aids (Nybo & Secher, 2004) has been shown to be in part, attributable to the placebo effect. For example, Beedie et al., (2006) demonstrated that highly trained cyclists ( $\dot{V}O_{2\max}$   $57.9 \pm 9$  ml.kg.min<sup>-1</sup>) increased power output during a 10-km cycle time-trial by ~2-3% when told they had received caffeine, but actually ingested a placebo, compared to when they were told they had received placebo. Consequently, a possible explanation for the lack of a detectable overall performance effect in the current study may be due to the placebo effect since 1) participants knew there was a high chance of receiving an experimental gum (i.e. 75% of the time), and 2) when they knowingly ingested the placebo, as in the second familiarisation trial, performance was substantially lower than when blinded to receiving the placebo (Mean  $\pm$  SD:  $252 \pm 36$  and  $270 \pm 37$  W, respectively; Percentage change  $\pm 90\%$ CL:  $6.7 \pm 3.4\%$ ; ES  $\pm 90\%$ CL:  $0.43 \pm 0.22$ ). Future research investigating the oral presence of carbohydrate and/or caffeine during endurance exercise should aim to include a true control trial in order to determine the magnitude of the placebo effect on centrally-mediated performance responses.

The mechanism for performance enhancement with carbohydrate and/or caffeine ingestion is suggested to be due to their effect on the central nervous system and the subsequent effect this has on the telo-anticipatory strategy for exercise, which results in a weakened subjective interpretation of effort for a given exercise intensity, despite a higher power output (and hence working capacity). This phenomenon has been shown

to occur with oral carbohydrate mouth rinses (Carter et al., 2004; Chambers et al., 2009; Pottier et al., 2010) and the ingestion of caffeine (Astorino, Cottrell, & Talhami et al., 2012; ). For example, Pottier et al., (2010) observed a higher power output - 3.7% improvement in 1-hour cycling time-trial performance - despite rating of perceived exertion remaining unchanged ( $15.44 \pm 1.39$  vs.  $15.52 \pm 1.69$  Borg) when rinsing with a carbohydrate solution versus placebo solution. In the current study, all participants were instructed to perform maximally in each time-trial and rating of perceived exertion was not measured. This measure was excluded deliberately for two reasons – 1) perceived exertion is shown to be constant during time-trial exercise as effort intensity is determined by prior exercise experience and knowledge of the event distance (Mihevic, 1993), and 2) that the obtainment of external measures results in a constant distraction to the athlete during the time-trial. Consequently, it is unknown whether the effort perception was same across trials and whether changes observed in the pacing were the result of carbohydrate and/or caffeine influencing feelings of effort and fatigue, and hence, future research is needed to better understand this area.

The current study did not use a no-gum control trial, nor did it address the possibility that an ergogenic effect was mediated in response to the presence of ‘sweet’ tasting artificial sweeteners. Previous research has demonstrated that the oral presence of saccharin stimulates some of the same cortical areas of the brain associated with the presence of carbohydrate in the mouth, such as the insula/frontal operculum and prefrontal cortex of the brain, however activation of these areas did not result in enhanced endurance performance as with glucose and maltodextrin mouth-rinses (Chambers et al., 2009). Additionally, artificial sweeteners within placebo mouth-rinses did not enhance performance compared with carbohydrate in several other mouth-rinse studies (Carter et al., 2004; Fares & Kayser, 2011; Lane et al., 2013; Pottier et al., 2010; Rollo et al., 2010; Rollo et al., 2008) and moreover, the magnitude of the difference appeared to be similar to reported enhancements of maltodextrin versus water only mouth-rinses (Carter et al., 2004; Fares & Kayser, 2011; Gam et al., 2013). As such, authors have suggested that the presence of artificial sweeteners in the mouth is not associated with an increase in exercise performance. Still, it should also be considered that in previous mouth-rinse studies, performance tests have been approximately 1 h or less in duration, whilst in the current study the participants performed for 90 min before commencing the time-trial. Thus, in the current study it is possible that reduced muscle

glycogen stores and the onset of hunger – as subjectively mentioned by most participants prior to start of the time-trial – may have altered the central activation response to the presence of artificial sweeteners in the mouth, and hence exercise perceptions and performance capabilities, since cortical activation is enhanced during periods of hunger (Haase et al., 2009). As such, future research investigating the centrally-mediated effects of carbohydrate and/or caffeine during endurance exercise should aim to include a true control trial in order to determine the magnitude and implications of the presence of artificial sweeteners on prolonged endurance performance when exposed to exercise-induced fatigue and hunger.

### ***5.6. Practical applications***

The current study demonstrated no enhancements in time-trial performance when using a carbohydrate and/or caffeine chewing gum and therefore making evidence based practical applications that are relevant to enhancing endurance performance in competition and training are challenging.

In line with previous carbohydrate mouth-rinse studies, the current findings of improved performance at the beginning of the time-trial with carbohydrate gum support the ability of oral carbohydrate to facilitate increases in motor output. Further, the current study adds to existing findings by demonstrating that this effect can be induced even under the conditions of reduced endogenous glycogen stores and exercise-induced fatigue. However probably of most importance is the finding of a reduced performance later in exercise, which highlights the importance of ensuring adequate endogenous carbohydrate stores to support a centrally-induced change in the anticipatory strategy and subsequent increase in motor output. Consequently, one may speculate that the most practical approach to enhancing prolonged endurance performance capacity, particularly in those susceptible to gastrointestinal upset with higher carbohydrate consumption (Burke et al., 2005; Pfeiffer et al., 2012), would be to ingest a small amount of carbohydrate (i.e. 30-60 g/h) early on in exercise and then in the latter stages, use a carbohydrate chewing gum. Such a strategy might allow for the avoidance of adversely lowered endogenous carbohydrate stores, thereby enabling mediation of a central stimulatory effect that can be physiologically supported.

Additionally, in line with previous caffeine studies showing improved endurance performance with caffeine ingestion in a glycogen-reduced state (Lane, Areta, et al., 2013; Silva-Cavalcante et al., 2013), the current study suggests that the use of caffeine may be beneficial to performance even when endogenous stores are reduced and fatigue levels highest, such as in the final stages of a long distance race and when adopting ‘train-low’ methods in training. However, in order to induce ergogenic effects more rapidly than in the current study, it may have been better for the caffeine to be delivered in a larger, single gum dose, as in the studies of Paton et al.(2010) and Ryan et al. (2013), since these studies have showed the rapid onset of ergogenic effects.

Finally, another anecdotal finding of the present study was that the use of a flavoured chewing gum improved perceptions of hunger during extensive endurance exercise without supplementation, which may be beneficial for athletes wishing to partake in “train-low” training sessions for weight loss (i.e. fasted and/or extensive endurance training) and/or superior training adaptations (fasted and second session with lowered endogenous stores).

### ***5.7. Conclusion***

In conclusion, the results of the present study showed that 20-km cycle time-trial performance, under conditions of reduced endogenous glycogen stores and exercise-induced fatigue was not improved by the oral presence of carbohydrate and caffeine in chewing gum, either independently or combined. It appears that both carbohydrate and caffeine chewing gums were able to subconsciously alter motor output, probably through central effects on the brain and anticipatory regulation strategy for distribution of power output, across the time-trial despite adoption of a maximal self-selected intensity across all trials. Specifically carbohydrate appeared to facilitate an immediate increase in power output, whilst caffeine exhibited effects later in exercise. Additionally, the interactive effects of carbohydrate and caffeine in the mouth appeared to negate the immediate effects of carbohydrate whilst, the latter effects of caffeine were displayed. The increase in blood lactate concentrations in caffeine trials appears to be ergogenic to performance, as mean power output was increased in the final quarter of the time-trial. The experimental conditions had no effect on other physiological variables (heart rate and blood glucose) and did not appear to negatively influence

gastrointestinal discomfort. In an attempt to improve athletic performances in training and competition, further work utilising chewing gum delivery strategies from the current study with provision of small amounts of carbohydrate during the pre-loading phase and a larger single caffeine dose during exercise is required to further determine if oral presence of carbohydrate and/or caffeine during endurance exercise positively affects performance.

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## Appendices

### *Appendix 1: Participant Information Sheet*



## Participant Information Sheet



Date Information Sheet Produced: 16<sup>th</sup> July 2012.

### **Project Title**

**“Athletic performance when using an ergogenic chewing gum in trained cyclists and triathletes”**

### **An Invitation**

Hi, my name is Katherine Prumm and I am a Post Graduate student at AUT University. Along with Adjunct. Prof Paul Laursen, Assoc. Prof. Andrew Kilding and Dr Rodney Siegel, I am inviting you to help with a project that looks at the use of a chewing gum to enhance performance when fatigued.

It is entirely your choice whether or not you would like to be involved in the study, and if you choose to be involved you can withdraw from the study at any time.

### **What is the purpose of this research?**

Sport Scientists are always looking for ways to enhance the performance of athletes. Recently, the use of mouth rinses and chewing gums that contain legal and commonly used performance enhancing substances have been shown to be an effective way of improving athletic performance in cycling and running. The purpose of this research is to determine the effect of a legal performance enhancer, provided via a chewing gum, on cycling time trial performance in trained cyclists and triathletes.

### **Why was I chosen for this invitation?**

As a trained cyclist and/or triathletes you have been asked to take part in this study.

### **What will happen in this research?**

Prior to the research commencing you will come to the AUT University lab at the Millenium Institute of Sport and Health in Mairangi Bay, Auckland for an aerobic capacity ( $\dot{V}O_{2max}$ ) test to assess your fitness level. This test involves cycling on a cycle ergometer in stages of 5 minutes. The test will start at 100 W and after each stage there

will be an increase in intensity (50 W) until you can no longer maintain the required power output. During the incremental test we will measure your oxygen consumption ( $\dot{V}O_2$ ) using a metabolic cart and heart rate using a heart rate monitor. This will involve wearing a snorkel-like apparatus so we can measure your breathing, and these measures will help us define your aerobic capacity, peak power output, cycling economy, your aerobic and anaerobic thresholds and current level of fitness. Also on visit 1, we will measure your body dimensions using skinfold callipers and a tape measure.

Following the fitness test and on meeting the entry criteria to the research trials ( $>55$  ml.kg.min  $\dot{V}O_2$  max) you will complete a 20 km time trial to become familiar with the duration of the trial. Following the first visit you will be required to report to the University lab at AUT Millennium in Mairangi Bay five times for one familiarisation trial and four time trials (each trial will be separated by 3-7days). To help you become familiar with the 20-km time trial procedure following a bout of cycling, you will perform a familiarization performance time trial which will consist of 90minutes cycling at the power output corresponding to 80% of your anaerobic threshold and then within 4 min of completing the steady state cycle you will complete a 20km time trial.

On each of the time trial days, you will complete a 90 minute cycle at the power output corresponding to 80% of your aerobic threshold (determined by anaerobic capacity test) followed by a 20 km time trial. During the time trial we will measure heart rate and power output. Before and after we will take a small sample of blood from the ear lobe to measure blood glucose and lactate concentrations. The time-trials will simply require you to complete the trials as fast as possible and during the trials you will be provided with a piece of chewing gum every 5 km, with a total of 4 pieces over the entire trial. During the trial you will be required to chew the gum and keep it in your mouth for the duration of 3 km. Also prior to each trial you will be required to refrain from heavy exercise and ensure you consume a diet that is high in carbohydrates (same as you would for competition).

### **What are the discomforts and risks?**

You may experience some temporary discomfort (exertion) during the time trial assessment and maximal aerobic tests. This will be similar to what you feel during hard training and racing (heavy breathing, tired muscles). However, if you experience any excessive discomfort you will be able to stop the test at any time.

### **How will these discomforts and risks be alleviated?**

The primary researcher is a qualified first aid responder and a medical clinic is located within the building where the lab testing will take place. Cool water will be offered throughout the assessments and adequate measures will be taken if you feel at all dizzy during the assessments. You will have sufficient time to warm-up prior to starting the assessments. You will also be offered sports drink following the completion of the exercise trial.

**What are the benefits?**

You will benefit from this study by understanding how a ergogenic aid effects competition performance which may potentially enhance your competitive ability and racing strategies. You will also establish markers of fitness ( $\dot{V}O_2$  max, cycling economy, threshold levels) at this current period in your cycling/triathlon career.

One of the research team for this project is involved in the development and assessment of the gum used in this study. Pending the outcome of this study, the gum may become commercially developed and eventually will become available to use it in competition.

**What compensation is available for injury or negligence?**

In the unlikely event of a physical injury as a result of your participation in this study, rehabilitation and compensation for injury by accident may be available from the Accident Compensation Corporation, providing the incident details satisfy the requirements of the law and the Corporation's regulations.

**How will my privacy be protected?**

All information related to you will be coded in order to ensure that you cannot be identified. The information will remain in locked storage and will only be accessible to the people of the researchers of this project (mentioned above). No-one will be able to identify you from any of the summary findings for the report of the project.

**What are the costs of participating in this research?**

The only cost to you is that of time. On the first day, the aerobic capacity testing session will take approximately 40-50 minutes, and after a period of rest will be followed by the first familiarisation 20 km time trial. The second familiarisation session (visit 2), which is used to ensure that you feel comfortable with the equipment, the process, and the testing procedures As well as the testing sessions (visits 3- to 6) will require 150 minutes of your time (90 minute cycle followed by 20km time trial (~30 minutes).

**What opportunity do I have to consider this invitation?**

You may take the time you need and decide whether or not you would like to be involved.

You can stop being involved in the project at any point.

**How do I agree to participate in this research?**

If you agree to participate please fill in the attached consent form and return to address/email below.

**Will I receive feedback on the results of this research?**

Yes, the outcomes of this study will be provided to you, as well as a report containing the results from your  $\dot{V}O_2$  max test (aerobic capacity, cycling economy, thresholds and precise training zones).

**What do I do if I have concerns about this research?**

Any concerns regarding the nature of this project should be notified in the first instance to the Project Supervisor:

Adjunct. Prof. Paul Laursen, High Performance Sport New Zealand (HSPNZ), Millennium Campus, 17 Antares Place, Mairangi Bay, Auckland 0632. Ph (09) 477 5427, Mob 021 303 153, [paul.laursen@hpsnz.org.nz](mailto:paul.laursen@hpsnz.org.nz).

Concerns regarding the conduct of the research should be notified to the Executive Secretary, AUTEK, Madeline Banda, [madeline.banda@aut.ac.nz](mailto:madeline.banda@aut.ac.nz), Ph 921 9999 ext 8044.

**Whom do I contact for further information about this research?**

***Researcher Contact Details:***

Katherine Prumm, Sport Performance Research Institute New Zealand, School of Sport and Recreation, AUT University, Auckland 0637, Ph 0274273857, [katherineprumm@hotmail.com](mailto:katherineprumm@hotmail.com).

***Project Supervisor Contact Details:***

Adjunct Prof. Paul Laursen, High Performance Sport New Zealand (HSPNZ), AUT Millennium Campus, 17 Antares Place, Mairangi Bay, Auckland 0632. Ph (09) 477 5427, Mob 021 303 153, [paul.laursen@hpsnz.org.nz](mailto:paul.laursen@hpsnz.org.nz).

***Project Co-supervisor Contact Details:***

Dr Rodney Siegel, High Performance Sport New Zealand (HSPNZ), AUT Millennium Campus, 17 Antares Place, Mairangi Bay, Auckland 0632. Ph (09) 477 5427, Mob 027 669 9991, [rod.siegel@hpsnz.org.nz](mailto:rod.siegel@hpsnz.org.nz).

Assoc. Prof. Andrew Kilding, Sport Performance Research Institute New Zealand, School of Sport and Recreation, AUT University, Private Bag 92006, Auckland 1020, Ph 921 9999 ext. 7056, [andrew.kilding@aut.ac.nz](mailto:andrew.kilding@aut.ac.nz)

**Approved by the Auckland University of Technology Ethics Committee on 13 August 2012, AUTEK Reference number 12/187.**

*Appendix 2: Consent Form*

## Consent to Participation in Research



Title of Project: **“Athletic performance when using an ergogenic chewing gum in highly trained cyclists and triathletes.”**

Project Supervisor: **Adjunct Professor Paul Laursen**

Researcher: **Katherine Prumm**

- 
- |  |        |
|--|--------|
| • I have read and understood the information provided about this research project (Information Sheet dated 16 July 2012)   | Yes/No |
| • I have had an opportunity to ask questions and to have them answered   | Yes/No |
| • I am not suffering from any injury or illness which may impair my physical performance   | Yes/No |
| • I understand that I may withdraw myself or any information that I have provided for this project at any time prior to completion of data collection, without being disadvantaged in any way  | Yes/No |
| • If I withdraw, I understand that all relevant information will be destroyed  | Yes/No |
| • I understand that the personal information collected will be used for academic and conditioning guidance purposes only and identifiable individual information will not be published in any form outside of this project without my written permission | Yes/No |
| • I agree to take part in this research  | Yes/No |
| • I wish to receive a copy of the report from the research:  | Yes/No |

Participant signature: .....

Participant name:.....

Date: .....

Participant's Contact Details:

.....  
.....

***Project Supervisor Contact Details:***

Adjunct Professor Paul Laursen  
High Performance Sport New Zealand (HSPNZ)  
AUT Millenium Campus - Level 3  
17 Antares Place  
Mairangi Bay  
Auckland 0632  
Ph: (09) 477 5427 / Mob: 021 303 153  
[paul.laursen@hpsnz.org.nz](mailto:paul.laursen@hpsnz.org.nz)

***Approved by the Auckland University of Technology Ethics Committee Date 25-August-2012 - AUTEK Reference number 12/187***

*Appendix 3: Medical Pre-screening Questionnaire*

**Medical Pre-screening Questionnaire**

Name: .....  
 Address:.....  
 Phone Number: .....  
 Email Address: .....  
 Birth date: .....  
 Gender (M/F): .....

**Health History:**

Please tick (√) any of the following for which you have been diagnosed or treated by a physician or health professional:			
<ul style="list-style-type: none"> <li>• High Blood Pressure</li> <li>• Thyroid Problem</li> <li>• High Cholesterol</li> <li>• Heart Attack</li> <li>• Hypoglycemia</li> <li>• Epilepsy</li> <li>• Osteoarthritis</li> </ul>		<ul style="list-style-type: none"> <li>• Heart Problem</li> <li>• Emphysema</li> <li>• Heart Disease</li> <li>• Asthma</li> <li>• Diabetes/Pre-Diabetes</li> <li>• Stroke</li> <li>• Other (please specify)</li> </ul>	

**Please mark YES or No to the following:                      YES    NO**

- Has your doctor ever said that you have a heart condition and recommended supervised physical activity?
- Do you frequently have pains in your chest when you perform physical activity?
- Have you had chest pain when you were not doing physical activity?
- Do you lose your balance due to dizziness or do you ever lose consciousness?
- Do you have a bone, joint or any other health problem that causes you pain or limitations that must be addressed when completing exercise?
- Have you had a recent surgery?

If you have marked YES to any of the above, please elaborate below:

- Do you have any chronic illness or physical limitations such as Asthma, diabetes? Yes/No
  - Do you have any injuries or orthopaedic problems such as bursitis, bad knees, back, shoulder, wrist or neck issues?    YES/ NO, If yes please specify

- Do you take any medications, either prescription or non-prescription, on a regular basis? Yes/No. What is the medication for?
- Does this medication affect your ability to exercise?

**Lifestyle Related Questions:**

- 1) Do you smoke? YES NO If yes, how many?\_\_\_\_\_
- 2) Do you drink alcohol? YES NO If yes, how many glasses per week?\_\_\_\_\_
- 3) Do you regularly consume caffeine (i.e. No doz, coffee, tea, coke, etc) YES / NO  
How much would you consume in a typical day?  
Have you ever had any adverse responses to caffeine in your diet?
- 4) Describe your job:  Sedentary  Active  Physically Demanding
- 5) Does your job require frequent travel that would prevent you from completing the study? YES NO

**I have understood all questions and answered them to the best of my knowledge and I certify that I have disclosed fully any conditions that may affect my participation in physical exercise.**

**Name and signature:.....**  
**Date:.....**

*Appendix 4: Dietary and Physical Activity Standardisation Instructions***DIETARY AND PHYSICAL ACTIVITY  
STANDARDISATION INSTRUCTIONS****Athletic performance when using an ergogenic chewing  
gum in trained cyclists and triathletes**

Chief investigator: Katherine Prumm (Masters Candidate)

Sport Research Institute of New Zealand, School of Sport and Recreation,

Auckland University of Technology

Auckland 0637,

Ph 0274273857 / email: katherineprumm@hotmail.com.

In this study, we will be investigating the effect of several legal performance enhancer, provided via a chewing gum, on cycling time trial performance in trained cyclists and triathletes. To do this effectively, we need to reduce the “day to day variability” in cycling performance that might otherwise mask small, alterations in exercise performance. One tactic is to standardise all the conditions under which trials are performed – including physical activity in the 24hours prior and dietary preparation. Important factors you should adhere to include:

- Performing only low intensity (<70%max heart rate) exercise training of less than 2hours in the 24hours prior to each trial
- Being consistent with the amount of carbohydrate and energy eaten during the 24 hours before the trial
- Being consistent with your fluid intake on the day before and morning of the trial
- Avoiding caffeine in the 12hours prior to each trial
- Standardising your pre-trial meal

These instructions will help you to achieve a similar preparation for each trial.

**Exercise goals**

Aim: prior to each trial we want you to feel fresh and free of fatigue as you would for competition. To ensure that fatigue is not a limiting factor at any of the trials and ensure that you perform maximally in each trial it is advised that you refrain from heavy physical exercise – both aerobic and resistance based – in the 24 hours prior to your trial. Should you be required complete physical activity on the day before your trial, it is advised that it is of a low intensity (<70% heart rate max) and of less than 2hours in duration.

## Carbohydrate and fluid goals

Aim: we want you to eat at least 6 g of carbohydrate per kg of your body weight on the day before each trial, and the same pre-trial meal on the morning of your trial (providing at least 1 g carbohydrate/kg). We also want you to consume at least 2 litres of fluid on this day (including all drinks consumed at meals or during training), and 400 ml of fluid at the meal consumed just before the trial. Additionally, it is essential that you avoid caffeine in the 12 hours prior to each trial as this may influence the results of each trial – foods to avoid include: coke, coffee, no-doz tablets, and energy drinks.

Steps:

1. Fill in your name..... and  
current body weight?.....kg
2. Calculate your carbohydrate intake (minimum) for the day before the trial:  
 $6 \times \text{BM} = \dots\dots\dots\text{g}.$   
Calculate your carbohydrate intake (minimum) for the last meal, eaten 2 hours  
before you start the trial:  $1 \times \text{BM} = \dots\dots\dots\text{g}.$
3. Keep a food record for the day before your first trial, concentrating on the carbohydrate-rich foods found in the table over the page, and the amount of fluid consumed. Use the table on the following page to add up how much carbohydrate is eaten at each meal or snack. Aim for the targets of at least 6 g/kg and at least 1 g/kg. Each of these “blocks” of food provides approximately 50 g of carbohydrate. It is not necessary to eat a whole block, or round numbers of blocks. Try to keep count in terms of quarter or half blocks
4. Once you have completed the first day’s record, this sets the amount that you need to eat for the next trials. It is simplest to try to repeat a very similar meal pattern for each of these days – i.e. stick to the same type and amount carbohydrate foods. If this is impractical, use the carbohydrate counter to replace one carbohydrate food with the amount of another carbohydrate choice that provides a similar amount of carbohydrate.  
**Example**, on day one you might have eaten 2 rounds of cheese and salad sandwiches (4 thin slices of bread) for lunch, with a Juice (unsweetened orange juice). The carbohydrate counter tells you that this is equal to 1 block (50 g carbohydrate) for the bread and just under a half block (or about 20 g of carbohydrate) for the juice. If you want to swap the lunch menu, this same amount of carbohydrate could be found in 2 english muffins (with a similar kind of filling) and one carton of low fat flavoured yoghurt.
5. Keep a record of each day’s food intake so that we can check how well you were able to duplicate your carbohydrate intake and fluid intake for the next trials.
6. Repeat the same process for the meal eaten ~ 2 hours before the trial

## Index of 50g carbohydrate serves from common foods

Professor Louise Burke, Australian Institute of Sport

### CEREALS

Wheat biscuit cereal (e.g. Weetbix)	60g (5 biscuits)
'Light' breakfast cereal (e.g. Cornflakes, Weeties)	60 g (2 cups)
'Muesli' flake breakfast cereal (e.g. Sustain)	65 g (1.5 cups)
Toasted muesli	90 g (1 cup)
Porridge - made with milk	350 g (1.3 cups)
Porridge - made with water	550 g (2.5 cups)
Rolled oats	90 g (1 cup)
Cereal bar	2.5 x 30 g bar, 3 x 25 g bar
Rice cakes	6 thick or 10 thin
Rice, boiled	180g (1 cup)
Pasta or noodles, boiled	200 g (1.3 cups)
Canned spaghetti	440 g (large can)
Crispbreads and dry biscuits	6 large or 15 small
Fruit filled biscuits	5
Plain sweet biscuits	8-10
Cream filled/chocolate biscuits	6
Bread	110 g (4 slices white or 3 thick wholegrain)
Bread rolls	110 g (1 large or 2 medium)
Pita and lebanese bread	100 g (2 pita)
Chapati	150 g (2.5)
English muffin	120 g (2 full muffins)
Crumpet	2.5
Cake-style muffin	115 g (1 medium)
Pancakes	150 g (2 medium)
Scones	125 g (3 medium)
Iced fruit bun	105 g (1.5)
Croissant	140 g (1.5 large or 2 medium)
Rice-cream or creamed rice	330 g (1.5 cups)

### FRUIT

Fruit crumble	1 cup
Fruit packed in heavy syrup	280 g (1.3 cups)
Fruit stewed/canned in light syrup	520 g (2 cups)
Fresh fruit salad	500 g (2.5 cups)
Bananas	2 medium-large
Mangoes, pears, grapefruit and other large fruit	2-3
Oranges, apples and other medium size fruit	3-4
Nectarines, apricots and other small fruit	12
Grapes	350 g (2 cups)
Melon	1,000 g (6 cups)
Strawberries	1,800 g (12 cups)
Sultanas and raisins	70 g (4 Tbsp)
Dried apricots	115 g (22 halves)

### VEGETABLES AND LEGUMES

Potatoes	350g potato (one very large or 3 med)
Sweet potato	350 g (2.5 cups)
Corn	300 g (1.2 cups creamed corn or 2 cobs)
Green Beans	1,800 g (14 cups)
Baked beans	440 g (1 large can)

Lentils	400 g (2 cups)
Soy beans and kidney beans	400 g (2 cups)
Tomato puree	1 liter (4 cups)
Pumpkin and peas	700 g (5 cups)
<b>DAIRY PRODUCTS</b>	
Milk	1 liter
Flavored milk	560 ml
Custard	300 g (1.3 cup)
'Diet' yogurt and natural yogurt	800 g (4 individual tubs)
Flavored non-fat yogurt	350 g (2 x 200 g individual tubs)
Ice-cream	250 g (5 scoops)
<b>SUGARS AND CONFECTIONERY</b>	
Sugar	50 g
Jam	3 Tbsp
Syrups	4 Tbsp
Honey	3 Tbsp
Chocolate	80 g
Mars Bar (~ 60 g bar)	1.5 bars
Jelly confectionery	60g
<b>MIXED DISHES</b>	
Pizza 200 g (medium -1/4 thick or 1/3 thin)	
Hamburgers	1.3 Big Macs
Lasagna	400 g serve
Fried rice	200 g (1.3 cups)
<b>DRINKS</b>	
Fruit juice - unsweetened	600 ml
Fruit juice - sweetened	500 ml
Cordial	800 ml
Soft drinks and flavored mineral water	500 ml
Fruit smoothie	250-300 ml
<b>SPORTS FOODS</b>	
Sports drink	700 ml
Carbohydrate loader supplement	250 ml
Liquid meal supplement	250-300 ml
Sports bar	1-1.5 bars
Sports gels	2 sachets
Glucose polymer powder	60 g

## NUTRITION AND PHYSICAL ACTIVITY LOG

**TRIAL # \_\_\_: DAY BEFORE                      date:                      name.....**

**PHYSICAL ACTIVITY LOG FOR DAY PRIOR TO TRIAL**

Time of day	Type of activity	Duration	Intensity (heart rate if used or rate on a scale of 1-10 with 1 being easy and 10 hardest)

**NUTRITION**

Meal	FOOD AND DRINKS	CALCULATION OF CARBOHYDRATE CONTENT	CALCULATION OF ML OF FLUID CONSUMED
Breakfast			
Lunch			
Dinner			
Snacks			

--	--	--	--

Total carbohydrate (AIM = g).....

Total fluid (aim = > 2000 ml) .....

**TRIAL # \_\_\_: MORNING OF TRIAL / LAST MEAL (2 HOURS PRE TRIAL)**

**date: name.....**

**\*\*\*\*\*please refrain for consuming foods that contain caffeine on the day of your trial\*\*\*\*\***

Meal	FOOD AND DRINKS	CALCULATION OF CARBOHYDRATE CONTENT	CALCULATION OF ML OF FLUID CONSUMED
		AIM = g	AIM = 400 ML

Note: if you have a late morning/early afternoon trial, you may choose to eat an early breakfast, followed by this last meal. If so, please record the breakfast and repeat for all subsequent trials

Meal	FOOD AND DRINKS	CALCULATION OF CARBOHYDRATE CONTENT	CALCULATION OF ML OF FLUID CONSUMED
		AIM = g	