CALORIC CONTENT HAS GREATER LEVEL OF BRAIN ACTIVATION DURING CARBOHYDRATE MOUTH RINSING

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CALORIC CONTENT HAS GREATER LEVEL OF BRAIN ACTIVATION DURING CARBOHYDRATE MOUTH RINSING

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LIST OF ABRREVIATIONS

AAL	automated anatomical labelling
ACC	anterior cingulate cortex
AMDI	Advanced Medical and Dental Institute
CHO	carbohydrate
CTC	clinical trial complex
DLPC	dorsal lateral prefrontal Cortex
DP	degree of polymerization
e	electrolyte
EPI	echo planar imaging
fMRI	functional magnetic resonance imaging
FOV	field of view
Fru	fructose
GI	gastrointestinal
Glu	glucose
Malto	maltodextrin
NS	not significant
NSPs	non-starch polysaccharides

OFC	orbitofrontal cortex
SD	standard deviation
SPM	statistical parametric mapping
Suc	sucrose
SVC	small volume correction
T	tesla
T1R2	taste receptor type 1 member 2
T1R3	taste receptor type 1 member 3
TR	time repetition
TT	time trail
TTE	time to exhaustion
U_{sg}	urine specific gravity
VAS	visual analogue scale
VO_2max	volume of maximum oxygen consumption
WFU	Wake Forest University

LIST OF SYMBOLS

α	alpha
β	beta
+	plus
-	dash
=	equal
%	percentage
>	more than
<	less than
/	or
~	approximately

LIST OF UNITS

°C	degree celcius
cm	centimetre
g	gram
hr	hour
kcal	kilocalorie
kg	kilogram
kJ	kilojoules
km	kilometre
m	metre
min	minute
mL	millilitre
L	litre
mm	millimetre
mmoL	millimole
s	second

KANDUNGAN KALORI MEMBERI KESAN YANG LEBIH KE ATAS PENGAKTIFAN OTAK KETIKA BERKUMUR DENGAN CECAIR KARBOHIDRAT

ABSTRAK

Berkumur dengan larutan karbohidrat dipercayai dapat mengaktifkan reseptor di dalam rongga mulut yang berkait dengan ganjaran dan pusat kenikmatan otak untuk meningkatkan prestasi sukan jangka masa panjang. Walau bagaimanapun, pencerahaan tentang pengaktifan otak yang disebabkan oleh kandungan kalori atau tahap kemanisan ketika berkumur masih kurang jelas. Oleh itu, objektif utama kajian ini adalah untuk mengenal pasti sama ada pengaruh kandungan kalori atau tahap kemanisan yang memberi kesan ke atas pengaktifan otak. Sebelas orang peserta lelaki yang sihat (Umur: 20 ± 1 years; ketinggian: 168.7 ± 6.1 cm; jisim badan: 61.4 ± 6.1 kg; dan kadar penggunaan oksigen yang paling tinggi (VO_2max): 51.7 ± 2.5 $mL.kg.min^{-1}$) telah terlibat dalam kajian ini secara sukarela. Peserta dikehendaki melalui 10 sesi ujian berkumur dengan 10 larutan karbohidrat yang berbeza secara rawak. Setiap kali ujian berkumur, peserta perlu berkumur selama 10 saat ketika pengimejan resonans magnet kefungsian (fMRI) dijalankan. Empat set larutan kandungan kalori telah disediakan: 1) 19 kcal/g (6% glukosa, 5.3% fruktosa dan 3.8% maltodextrin); 2) 59 kcal/g (18% glukosa, 15.9% fruktosa dan 11.4% maltodextrin); 3) 79 kcal/g (24% glukosa, 21.2% fruktosa dan 15.4% maltodextrin); 4) 0 kcal/g (10% sukralosa). Keputusan imbasan neuro menunjukkan bahawa ke semua tiga kepekatan larutan maltodextrin (berkalori tetapi tiada manis) memberi pengaktifan otak yang lebih tinggi berbanding dengan ke dua-dua jenis larutan glukosa dan fruktosa (berkalori dan manis). Sementara itu, 21.2% fruktosa (berkalori dan manis) menunjukan pengaktifan otak yang lebih tinggi berbanding dengan 10% sukralosa (tiada kalori tetapi manis). Tiada perubahan signifikan ke atas status hidrasi sebelum imbasan MRI dan juga paras glukosa darah dan tahap keselesaan gastrousus (GI) ketika sebelum dan selepas imbasan MRI. Hasil daripada data imbasan, kesimpulannya, kandungi kalori dan bukannya tahap kemanisan yang berpotensi menjadi penentu kepada pengaktifan otak.

CALORIC CONTENT HAS GREATER LEVEL OF BRAIN ACTIVATION DURING CARBOHYDRATE MOUTH RINSING

ABSTRACT

Mouth rinsing a carbohydrate (CHO) solution has been shown to activate receptors within the oral cavity which is related to reward and pleasure centres of the brain for the enhancement of endurance exercise performance. However, it remains unclear whether the caloric content or the sweetness level of a solution may influence the level of brain activation during mouth rinsing. Therefore, the aim of this study was to examine the influence of caloric content or the sweetness level on brain activation when performing CHO mouth rinsing. Eleven healthy male participants (Age: 20 ± 1 years; height: 168.7 ± 6.1 cm; body mass: 61.4 ± 6.1 kg; and peak rate of oxygen consumption (VO_2max): 51.7 ± 2.5 $mL.kg.min^{-1}$) volunteered for this study. Participants were randomly assigned to 10 mouth rinsing trials with 10 different CHO solutions. During each trial, participants rinsed a CHO solution for 10 seconds while functional magnetic resonance imaging (fMRI) was performed. Four sets of CHO solutions with different calorie contents were prepared: 1) 19kcal/g (6% of glucose, 5.3% of fructose and 3.8% of maltodextrin); 2) 59 kcal/g (18% of glucose, 15.9% of fructose and 11.5% of maltodextrin); 3) 79 kcal/g (24% of glucose, 21.2% of fructose and 15.4% of maltodextrin); 4) 0 kcal/g (10% of sucralose). The neuroimaging results showed that the three concentration levels of maltodextrin solutions (calorie without sweet) produced a greater level of brain activation when compared with both glucose and fructose (sweet with calorie). Meanwhile, the 21.2% of fructose (sweet with calorie) showed higher brain activation as compared with 10% of sucralose (sweet without calorie). There were no significant changes in hydration status in pre MRI scans and also the blood glucose level and gastrointestinal (GI) comfort level for pre and post of MRI scans. Based on the imaging data, as a conclusion, the caloric contents and not the level of sweetness potentially be the main determinant of brain activation.

CHAPTER 1

INTRODUCTION

1.1 Introduction

The positive effect of carbohydrate (CHO) ingestion before, during and after exercise has been extensively investigated (Jeukendrup, 2008; Temesi et al., 2011). Carbohydrate ingestion improves prolonged moderately (>90 minutes, 45-75% of VO_2max) endurance exercise performance (Carter et al., 2003; Febbraio et al., 2000; Maughan et al., 1996; Mitchell et al., 1989). The improvement in endurance exercise has been linked to two possible mechanisms. The first suggests that CHO ingestions maintains blood glucose availability for the extended duration of exercise which provides an alternative source of energy when muscle glycogen storage is diminished (Duckworth et al., 2013). The second mechanism suggests that ingestion of CHO during exercise will reduce the rate of utilisation of muscle glycogen (Boulay, 1990). These two factors will delay the depletion of vital energy source for exercise which therefore delays fatigue (Benton, 2002; Duckworth et al., 2013).

While the ergogenic benefit of CHO ingestion during prolonged aerobic exercise has been well documented and accepted, it remains controversial for shorter (15 minutes) to moderate (1 hour) period of exercise. Another study have shown that for shorter to moderate duration exercise, a performance benefit of CHO ingestion can be observed compared to placebo (Carter et al., 2003) while others have shown no improvement (Desbrow et al., 2004; Jeukendrup et al., 2008). Glucose level in the blood does not decrease at the first hour of endurance exercise even when there is no exogenous CHO intake (Romijn et al., 1993). Therefore, the ergogenic effect of

CHO cannot be entirely explained by CHO oxidation and maintenance of blood glucose concentration as reported in prolonged aerobic activity bout since CHO oxidation and blood glucose availability are not the limiting factor during shorter duration exercise among well trained athletes.

Based on this notion, CHO ingestion during exercise may well have a central effects relating to motivation or motor output through an oral or gastric mechanism. Carter et al., (2004a) was among the first to test this notion by a glucose free saline solution or infusing 20% glucose-saline solution to cyclist exercising at 75% VO_2max. The findings indicated that there was no improvement in performance related with the increased glucose level in the blood despite the increased glucose uptake into the skeletal muscle and carbohydrate (Carter et al., 2004a). This observation proposed that ergogenic benefit of CHO ingestion may be a centrally mediated factor and not entirely due to elevated blood glucose levels. Following this study, Carter et al. (2004b) experimented on the on a 1 hour cycling time-trial exercise during CHO mouth rinsing and recorded a 2.9% increment in cycling performance when mouth rinsing a CHO solution compared to placebo solution.

In recent years, positive ergogenic effects of CHO mouth rinse have been exposed as new intervention to improve time trial exercise (Carter et al., 2004b; Chambers et al., 2009; Che Muhamed et al., 2014; Lane et al., 2013; Pottier et al., 2010; Sinclair et al., 2014) and distance covered during endurance exercise (Fraga et al., 2015; Rollo et al., 2010; Wright & Davison, 2013). The occurrence of CHO in the mouth is able to activate a novel energy signalling pathway capable of improving exercise performance (Turner et al., 2014). This signalling situation has been prove to enhance corticomotor output (Gant et al., 2010). Equally important, the corticol response on tasteless glucose solution also has been investigated to observe the brain activation. Further verification of this premise was provided by Frank et al., (2008), where CHO solutions influenced the enhancement in corticol activation compared to equivalently sweet artificially sweetened solutions that acted as placebo.

In exploring the notion of enhanced brain activation with mouth rinse, Chamber et al., (2009) examined the level of brain activation from the effects CHO mouth rinse containing glucose, maltodextrin and a placebo solution containing saccharin. Their study reported that the mouth rinse containing glucose (sweet) and maltodextrin (non-sweet) improved the performance compared to placebos. It is also reported that glucose and maltodextrin activates the anterior cingulated cortex (ACC), an area related to ratings of perceived exertion (RPE).

To date, only one study has evaluated brain activation using mouth rinse with 18% of CHO solution (Chambers et al., 2009) while 6 – 8% of CHO solution has been used for other studies on performance test (Beelen et al., 2009; Carter et al., 2004b; Chambers et al., 2009; Fraga et al., 2015; Pottier et al., 2010; Rollo et al., 2008; Trommelen et al., 2015). Limited studies have systematically investigated higher levels of concentration and the sweetness of CHO mouth rinse. The speculations whether the sweetness or the caloric stimulates the brain activation are still remains unclear. For this reason, the objective of this research is to examine the influence of caloric content and the sweetness level on brain activation when rinsing with mouth rinse containing CHO.

1.2 Purpose of study

The purpose of the study is to examine the influence of caloric content and the sweetness level on brain activation when performing CHO mouth rinsing.

1.3 Objectives of study

Preliminary study:

1. Independent triangle sensory taste match test - To test for any possible differences in taste of the sweetest solution among two different solutions.
2. Visual Analogue Scale for perceived sweetness levels - To determine the percieved levels of sweetness of 10 different solutions subjectively.

Main study:

1. The objective of the main study is to determine the influence of caloric contents or the sweetness level on brain activation when rinsing with CHO.

1.4 Hypothesis

It is hypothesized that a higher caloric content of a CHO solution will result in greater brain activation when performing mouth rinsing.

1.5 Study terminologies

Mouth rinse	- Mouth rinse is defined as a fluid distribution around the oral part for about 5 to 10 seconds and followed by expulsion by spitting (de Ataide e Silva et al., 2014).
Carbohydrates	- Carbohydrates is one of the main nutrients that help in providing energy to the human body. A CHO is a biological molecule consisting of carbon (C), hydrogen (H) and oxygen (O) atoms, usually with hydrogen–oxygen atom ratio of 2:1 (Seager & Slabaugh, 2013).
Caloric	- The amount of heat necessary to raise the temperature of 1 gram of water by 1°C (Piper et al., 2005).
fMRI	- A functional neuroimaging process that uses magnetic resonance imaging (MRI) technology which is mainly used to perform brain activation studies by looking at the neural activity which relies on the fact that cerebral blood flow and neuronal activation are coupled (Singleton, 2009).

CHAPTER 2

LITERATURE REVIEW

2.1. Carbohydrate as a source of energy and its influences on endurance exercise performance

Since the early 1980s through to recent years, numerous studies have investigated the exercise performances during CHO mouth rinsing (Below et al., 1995; Bjorkman et al., 1984; Carter et al., 2003; Coyle et al., 1983; J. L. Ivy et al., 1983; Jeukendrup et al., 1997; Maughan et al., 1996; Mitchell et al., 1989). These studies have shown the positive ergogenic effect of CHO ingestion on endurance exercise performance by increasing the capacity to perform endurance exercise, measured via time to exhaustion, total amount of work performed and the physiological stress.

During exercise, CHO ingestion helps to improve endurance exercise capacity by preventing hypoglycemia and provide a ready fuel for the working muscles (Coyle, 1992). By maintaining blood glucose concentration and the rate of CHO oxidation necessary to exercise strenuously, CHO consumption throughout exercise may delays fatigue by 30 – 60 minutes in endurance-trained athletes (Coyle, 1992).

Below et al., (1995) reported that cycling exercise performance in the heat (31.2 ± 0.1°C and 54 ± 3% relative humidity) was 6.3% faster with CHO ingestion as compared to water ingestion. In another study by Jeukendrup et al., (1997), 19 endurance-trained cyclists were randmoly assigned to a cycling time trial while ingesting a total of 14 mL/kg of either a 7.6% CHO-electrolyte solution or artificially flavoured and coloured water as placebo. The time-trial performance was significantly faster by 2.3% in the trail when CHO-electrolyte drink was ingested. In addition, Carter et al., (2003) reported that the CHO supplementation improves moderate and high-intensity exercise in the heat. Eight endurance-trained men were asked to cycle until fatigue twice at two different intensities (60% of VO_2max and 73% of VO_2max) at an ambient temperature of 35°C. During the exercise trials, subjects ingested either 6.4% of maltodextrin solution or an artificial placebo. The time to exhaustion was significantly improved with CHO ingestion at both intensities of 60% and 73% of VO_2max, by 14.5% and 13.5%, respectively. A more recent study by Rollo et al., (2011) also found that CHO-electrolyte ingestion showed an improvement in endurance running exercise performance. In the study, runners were able to cover a greater distance of 320 metres when CHO-electrolyte was ingested during exercise as compared with the placebo trial. A systematic result on the effect of CHO ingestion on endurance exercise performance is presented in Table 2.1.

Table 2.1 Summary of studies in the literature that investigated the effects of CHO ingestion on exercise performance

Authors	**Sample size (n)**	**Performance test**	**CHO type**	**Fed or fasted**	**Effect (+ indicates improvement**	**Performance effect (statistical significant)**
Mitchell et al., (1989)	10	2hr cycling	a) 6% CHO b) 12% CHO c) 18% CHO	3hr	a) +6% b) +13.4% c) +8%	a) NS b) Improved c) NS
Below et al., (1995)	8	1hr cycling	a) 6% CHO-e b) 40% MALTO-e	Overnight fast	+6.3%	Improved
Jeukendrup et al., (1997)	19	1hr TT cycling	7.6% CHO-e	1hr	+2.3%	Improved
El-sayed et al., (1997)	8	1hr TT cycling	8% GLU	3hr	+1.5%	Improved
Carter et al., (2003)	8	a) 60% of VO_2max TTE cycling b) 73% of VO_2max TTE cycling	a) 6.4% MALTO b) 6.4% MALTO	a) Overnight fast b) Overnight fast	a) +14.5% b) +13.5%	a) Improved b) Improved

Table 2.1 Continued

Authors	**Sample size (n)**	**Performance test**	**CHO type**	**Fed or fasted**	**Effect (+ indicates improvement**	**Performance effect (statistical significant)**
Rollo et al. (2011)	10	1hr running	6.4% CHO-e	14hr	+2.2%	Improved

*Note: TT = time trial, TTE = time to exhaustion, Hr = hour, CHO = carbohydrate, CHO-e = carbohydrate-electrolyte, MALTO = maltodextrin, GLU = glucose, SUC = sucrose, FRU = fructose

2.2 Possible mechanisms of carbohydrate ingestion during prolonged exercise

CHO ingestion during performing endurance exercise that is believed to be an ergogenic aid has comprehensively acknowledged (Jeukendrup, 2004). Endogenous CHO are stored as glycogen, primarily in muscle and liver (Gonzalez et al., 2016). Higher basal muscle glycogen availability may delay the muscle glycogen depletion which can lead to fatigue (Gonzalez et al., 2016). However, in trained athletes, higher absolute and relative exercise intensities can be sustained for a prolonged period of time (Coyle et al., 1988), making it still possible to attain a critically low level of muscle glycogen (Gonzalez et al., 2016). Hence, greater muscle glycogen storage may be dependable for greater performance during prolonged endurance exercise (Gonzalez et al., 2016).

The potential mechanism of endurance-type exercise training would be derived by hormonal response (Gonzalez et al., 2016). Endurance type exercise training will blunt the rise of glucagon (Coggan et al., 1990), norepinephrine and epinephrine hormones and lead to the decrease in plasma insulin at 60% of VO_2max (Coggan et al., 1995).However, this hormonal response can be prevented if the CHO solution is ingested immediately before (Snyder et al., 1983) and after beginning the exercise (Ivy et al., 1979). Since liver glycogen metabolism has only been studied at exercise intensities at below 80% of VO_2max, the hormonal response and alteration of liver glycogen utilisation during exercise by the endurance-trained athletes still need further research (Gonzalez et al., 2016).

During prolonged exercise that lasts longer than approximately of 90 to 150 minutes, the liver glycogen stores may compromise, and as a result, the blood glucose concentration depletes (Boulay, 1990). One of the mechanisms behind the

CHO ingestion that helps in improving the endurance performance is by maintaining the blood glucose level to prevent the occurrence of hypoglycaemic state (Duckworth et al., 2013). Hypoglycaemia (blood glucose level > 3.3 mmol/l) believed to influence the mental alertness negatively and it leads to fatigue and lethargy (Benton, 2002; Duckworth et al., 2013). In addition, CHO ingestion prior and during endurance exercise is proposed to maintain and sustain optimal functioning of central nervous system which may improve the perceptual response as outcomes (Welsh et al., 2002) and parts of the brain such as the motor cortex will remain fully activated (Nybo, 2003).

2.3 Types of carbohydrate

CHO provides fuel to the human body not easily absorbed (Cummings et al., 1997). The dietary components of CHO are diverse with a different range of physical, physiological and chemical properties (Cummings & Stephen, 2007). Like other micronutrients, the primary classification of CHO dietary components is determined by the degree of polymerisation (DP), molecular size, the character of individual monomers and the type of linkage (α or non-α) (Cummings & Stephen, 2007).

Table 2.2 Classification of major dietary CHO (Cummings & Stephen, 2007)

Class (DP[a])	Subgroup	Principal components
Sugars (1–2)	Monosaccharides	Glucose, fructose, galactose
	Disaccharides	Sucrose, lactose, maltose, Trehalose
	Polyols (sugar alcohols)	Sorbitol, mannitol, lactitol, xylitol, erythritol, isomalt, maltitol
Oligosaccharides (3–9) (short-chain carbohydrates)	Malto-oligosaccharides (α-glucans)	Maltodextrins
	Non-α-glucan oligosaccharides	Raffinose, stachyose, galacto and fructo oligosaccharides, polydextrose, inulin
Polysaccharides (≥ 10)	Starch (α-glucans)	Amylose, amylopectin, modified starches
	Non-starch polysaccharides (NSPs)	Cellulose, hemicellulose, pectin, arabinoxylans, β-glucan, glucomannans, plant gums and mucilages, hydrocolloids

*Note: (DP[a]) - [a]Degree of polymerization or number of monomeric (single sugar) units.

Table 2.2 shows the classification of major dietary CHO. Along with chemical approach, CHO is divided and classified into three main groups, which are simple sugars (DP 1–2), oligosaccharides which is also known as short-chain CHO (DP 3-9) and polysaccharides (DP ≥ 10). The subgroups for sugar are monosaccharides, disaccharides, and polyols (sugar alcohols). Oligosaccharides consist of malto-oligosaccharides (α-glucans), principally occurring from the hydrolysis of starch (Cummings & Stephen, 2007) and non-α-glucan such as raffinose, stachyose, fructooligosaccharides and galactooligosaccharides, polydextrose and inulin. Meanwhile, polysaccharides can be divided into two small groups, namely (α-glucans) and non-starch polysaccharides (NSPs).

2.3.1 Glucose

Glucose is common CHO that has been used in many studies of mouth rinsing and exercise performance (Carter et al., 2004b; Chambers et al., 2009; Fraga et al., 2015; I. Rollo et al., 2008). Glucose is classified as a monosaccharide (simple sugar) because the degree of polymerization or number of monomeric unit is one (Cummings & Stephen, 2007). There are three principal monosaccharides namely glucose, fructose and galactose, and they are the building blocks of naturally occurring disaccharides, oligosaccharides and polysaccharides (Cummings & Stephen, 2007). Glucose absorbed from the small intestine, give rapid glycemic responses and provide a ready source of fuel and energy (Cummings et al., 1997).

It is generally accepted for a long time ago that sugar and other low molecular weight CHOs are more rapidly absorbed and digested in the small intestine compared to starch, the only digestible polysaccharide or complex sugar (Asp, 1995). Fascinatingly, glucose drink is believed to induce the connectivity function between hypothalamus and striatum suggesting that glucose improves the communication between appetite control centres (Page et al., 2013).

2.3.2 Fructose

Fructose is physically present in many fruits and usually used as an additional sweetener in some beverages (Dolan et al., 2010; Lowette et al., 2015). Fructose is classified as monosaccharide which is the same group as glucose and also known as fruit sugar (Basaranoglu et al., 2015).

In addition, fructose is in monosaccharide group because it has same molecular formula as glucose (Cummings & Stephen, 2007). Furthermore, this sweet tasting sugar can be found naturally in vegetables and fruits (Lowette et al., 2015). Equally important, fructose is two times as sweet as glucose (Lowette et al., 2015). Fructose drinks are believed to motivate and increase the connectivity between hypothalamus and thalamus which is thought to be inadequate to induce satiety (Page et al., 2013).

2.3.3 Maltodextrin

Maltodextrin is a nutritive polysaccharide with no sweet characteristic (Moore et al., 2005). It is broadly used in the food industry as sweeteners, fat substitutes and to modify the texture of food products (Cummings & Stephen, 2007). It consists of glucose units primarily linked by α-1, glucosidic bonds with dextrose equivalent values of lower than 20 (Moore et al., 2005). Maltodextrin derived from starch and most are readily digested and absorbed in the small bowel (Cummings et al., 1997; Moore et al., 2005). Corn starch has been widely used in maltodextrin manufacture but recently some consideration has been called to other starches such as potato, wheat, rice and cassava (Guzman-Maldonado & Paredes-Lopez, 1995).

2.3.4 Sucralose

Sucralose, a replacement of disaccharide (Index, 2006), is a non-nutritive compound that is synthesised by selective chlorination of sucrose (Grotz & Munro, 2009) and a non-caloric sweetener (Grice & Goldsmith, 2000). It is a free-flowing, white crystalline solid that is freely soluble in water and stable both in its crystalline form and in solution (Grice & Goldsmith, 2000). Sucralose is a synthetic trichlorinated disaccharide with a chemical name 1, 6-dichloro-1, 6-dideoxy-*β*-*D*-fructofuranosyl-4-chloro-4-deoxy-*α*-*D*-galactopyranoside (Grice & Goldsmith, 2000; Index, 2006).

The sweetness potency of sucralose is approximately 600 times sweeter than sucrose (table sugar), depending upon the specific food or beverage application (Grice & Goldsmith, 2000; Schiffman et al., 2008). Sucralose has been used by thousands of food, beverage, and pharmaceutical products in North America, Latin America, Europe, the Asian Pacific and the Middle East region (Davies, 2010). A vigilant assessment of the data has led to the conclusion that sucralose is secure for its intended purpose of use (Grice & Goldsmith, 2000).

2.4 Carbohydrate mouth rinsing

The studies by Carter and colleagues (2004a, 2004b) were the first to test the hypothesis to rule out the role of a greater CHO availability for oxidation on endurance performance. In their first study, Carter et al (2004a) had examined the effect of increased glucose availability during 1 hour cycling exercise by infusing a 20% glucose-saline solution or a glucose–free solution to six endurance athletes cycling at 75% Watt$_{max}$. No performance enhancement with increased blood glucose level was observed despite the increased glucose uptake into the skeletal muscle and carbohydrate oxidation. Thus, it leads to a conclusion that the role of CHO in short (up to 1 hour) endurance exercise performance is centrally modulated and is signaling through the mouth or gastric region. In a follow up study, Carter et al., (2004b), tested the hypothesis of centrally mediated effect on CHO while rinsing. Similar exercise protocol was tested, however, the participants rinsed using a 6.4% maltodextrin solution or a placebo (match to taste) for 5 seconds before expectorating into a bucket at every 7.5 minutes interval of the 1 hour time trial. The main finding of this study was the time to complete the set amount of work (measure of performance) was shorter by 2.8% when participants rinsed using the CHO solution. This was the first evidence to show the positive ergogenic benefit of CHO mouth rinse. It was postulated from this study that the improvement in performance was related to enhanced brain activation.

Since the work by Carter et al (2004a, 2004b), many other studies have been conducted to examine the effects of CHO mouth rinse on exercise performance. Summary of these studies are presented in Table 2.3.

Table 2.3 Summary of studies in the literature that investigated the effects of CHO mouth rinse on exercise performance

Authors	**Sample size (n)**	**Characteristic of subject**	**Performance test**	**CHO type**	**Fed or fasted**	**Rinse Duration (s)**	**Performance effect (statistical improvement)**
Carter et al., (2004b)	9	Endurance-trained cyclist	1hr cycling TT	6.4% MALTO	4hr	5s	Improved (+ 2.9%)
Whitham & Mckinney (2007)	7	Recreationally active	1hr running	6% MALTO	4hr	5s	NS
Rollo et al., (2008)	10	Endurance-trained runner	30min running	6% CHO	Overnight fast	5s	Improved (+1.7%)
Chambers et al., (2009)	8	Endurance-trained cyclist	1hr cycling TT	a) 6.4% GLU b) 6.4% MALTO	Overnight fast	10s	a) Improved (+2.0%) b) Improved (+3.1%)
Beelen et al., (2009)	14	Endurance-trained athlete	1hr cycling TT	6.4% MALTO	2hr	5s	NS
Pottier et al., (2010)	12	Endurance-trained cyclist	1hr cycling TT	6% CHO-e	3hr	5s	Improved (+3.7%)

Table 2.3 Continued

Authors	Sample size (n)	Characteristic of subject	Performance test	CHO type	Fed or fasted	Rinse Duration (s)	Performance effect (statistical improvement)
Rollo et al., (2010)	10	Endurance-trained runner	1hr running	6.4% CHO-e	13hr	5s	Improved (+211m)
Chong et al., (2011)	14	Competitive cyclist	30s max sprint	a) 6.4% MALTO b) 7.1% GLU	-	5s	NS
Fares & Kayser (2011)	13	Healthy non-athlete	Cycling TTE	6.4% MALTO	a) 3hr b) Overnight fast	5-10s	a) Improved (+3.5%) b) Improved (+10.4%)
Arnoutis et al., (2012)	10	Healthy-trained cyclist	Cycling TTE	Water	Overnight fast	5s	NS
Lane et al., (2013)	12	Competitive cyclist	1hr cycling TT	10% MALTO	a) 2hr b) Overnight fast	10s	a) Improved (+1.8%) b) Improved (+3.4%)
Sinclair et al., (2014)	11	Active recreational cyclist	30min cycling TT	6.4% MALTO	4hr	a) 5s b) 10s	a) Improved (+4.34%) b) Improved (+6.36%)

Table 2.3 Continued

Authors	**Sample size (n)**	**Characteristic of subject**	**Performance test**	**CHO type**	**Fed or fasted**	**Rinse Duration (s)**	**Performance effect (statistical improvement)**
Watson et al., (2014)	10	Healthy human	1hr cycling TT	6.4% GLU	Overnight fast	10s	NS
Che Muhamed et al., (2014)	9	Trained cyclist	10km cycling TT	6% CHO-e	+13hr	5s	NS
Ispoglou et al., (2015)	7	Trained cyclist	1hr cycling TT	a) 4% CHO-e b) 6% CHO-e c) 8% CHO-e	3hr	5s	NS
Fraga et al., (2015)	6	Well-trained runner	Running TTE	8% GLU	Overnight fast	10s	Improved (+648s)
Tromelen et al., (2015)	14	Trained cyclist	1hr cycling TT	6.4% SUC	a) 2hr b) Overnight fast	5s	NS
Cramer et al., (2015)	8	Endurance-trained cyclist	40km cycling TT	6.5% MALTO	3hr	5s	NS

Table 2.3 Continued

Authors	**Sample size (n)**	**Characteristic of subject**	**Performance test**	**CHO type**	**Fed or fasted**	**Rinse Duration (s)**	**Performance effect (statistical improvement)**
Deighton et al., (2016)	18	Healthy human	60min of treadmill walking	6.4% MALTO	Overnight fast	10s	Improved (+0.5%)

*Note: TT = time trial, TTE = time to exhaustion, hr = hour, NS = not significant, s = second, M = metre, CHO-e = carbohydrate-electrolyte, MALTO = maltodextrin, GLU = glucose, SUC = sucrose

2.4.1 Mouth rinse and endurance exercise performance

Numerous studies have shown that CHO mouth rinsing is related with improved high intensity endurance exercise performance (Carter et al., 2004b; Chambers et al., 2009; Che Muhamed et al., 2014; de Ataide e Silva et al., 2014; Fares & Kayser, 2011; Fraga et al., 2015; Gam et al., 2013; Lane et al., 2013; Pottier et al., 2010; Rollo et al., 2010; Sinclair et al., 2014; Wright & Davison, 2013).

Rollo et al., (2008) investigated on 30 minutes self-selected speeds treadmill running during perform the CHO mouth rinse. The study was the earliest to investigate the effect of CHO mouth rinsing on running exercise (Jeukendrup et al., 2013). In the study, participants were asked to run at a speed that equated to a rating of perceived exertion of 15 together with rinsing either 6% of CHO or taste-matched placebo solution. The result showed the increment of total distance covered while 30 minutes run when performed the CHO mouth rinsing compared to placebo.

In another study, Chambers et al., (2009) found a significant enhancement in time-trial cycling exercise when the cyclists do mouth rinsing with 6.4% of glucose solution compare to a placebo containing saccharin (artificial sweetener). In another study, eight different cyclists were tested on cycling performance during performing 6.4% of maltodextrin mouth rinses. The time to complete the time-trial was significantly reduced compared rinsing with artificial sweetener. The result suggested that the improvement in endurance performance with the presence of CHO orally may be due to the activation of brain parts which involved in motor control and reward. The result also suggested that there may be a class of unidentified oral receptors up till now that respond to CHO independently of those for sweetness.

Similarly, Pottier et al., (2010) were explored the effect of mouth rinse and ingestion of CHO-electrolyte solution on cycling exercise performance during 1 hour intensity time trial on 12 endurance-trained tri-athletes. The subjects rinsed the oral part, ingested 6% isotonic CHO-electrolyte solution or a placebo before and until the end of time trial exercise in which they had to accomplish a set amount of workload (975 ± 85 kJ) as fast as possible. The result was shown to have a 3.7% improvement in the trial performance with CHO mouth rinsing trial compared to an electrolyte-containing placebo.

In a latest study, Fraga et al., (2015) was investigated the time to exhaustion on treadmill exercise with CHO mouth rinsing. Six endurance-trained subjects ran at 85% of VO_2max to exhaustion in three separate trials. During each exercise trials, subjects were given either 8% of CHO or a placebo for every 15 minutes to rinse or 6% of CHO to ingest. There was an improvement in time to exhaustion when rinsing and ingesting CHO solution compared to placebo solution. Subjects ran longer in both mouth rinse (2583 ± 686 seconds) and ingestion (2625 ± 804 seconds) trials compared to placebo (1935 ± 809 seconds) trial.

2.5 Factors that influence carbohydrate mouth rinse

There are several factors that need to look at the effectiveness of CHO mouth rinse. The factors that need to be focus are the fasted and fed state of the participants, euhydrated and dehydrated state of the participants, duration of mouth rinse and environmental heat during the test.

2.5.1 Fasted and fed states

In the early study by Carter et al., (2004b), participants completed the mouth rinse trials in a fasted state (4 hours) and provided positive results. According to the result, it can be speculated that the potential effect of mouth rinsing might be considerable when the liver glycogen stores might be compromised (Beelen et al., 2009). Therefore, Beelen and his colleagues came out with a study on CHO mouth rinsing in the fed state. The idea of the study was to investigate the impact of CHO mouth rinse on exercise performance in postprandial condition. Fourteen male endurance-trained athletes were recruited to finish a two exercise test in the morning after having a standardised breakfast. They needed to perform a 1 hour time trial while rinsing using either a water or 6.4% maltodextrin solution after every 12.5% of the set amount of work. The result of the tests suggested that CHO mouth rinsing did not improve time-trial performance exercise during postprandial state.

The finding of improvement in performance related with CHO mouth rinsing from the earliest investigation by Carter et al., (2004b) is consistent with the following studies by Chambers et al., (2009), Fares & Kayser (2011), Rollo et al., (2010) where the participants had to perform the exercise in fasted state. Lane et al., (2013) investigated the 1 hour simulated cycling time-trial while in a fasted or fed condition during performing CHO mouth rinsing. Twelve male cyclists completed four exercise trials with designed as double-blind. Two trials were performed after consuming 2.5 $g.kg^{-1}$ meal and the other two trials were performed after an overnight fast. After every 12.5% of the total time during an exercise trial, they needed to do 10 seconds rinse using either 10% of maltodextrin solution or taste-matched placebo solution as placebo. The CHO trial improved the mean power output (3.4%) after an overnight fast compared to the fed state (1.8%). The result suggested that a CHO mouth rinses improved the performance to a greater extent in fasted state. However, optimal performance was achieved in fed state with CHO mouth rinsing.

In another study by Fares and Kayser (2011), thirteen non-athletic male participants were asked to perform four cycle tests at 60% Wattmax until exhaustion with rinsing using either water or 6.4% maltodextrin solution at every 5 minutes interval in fed state (trial after a CHO-rich breakfast) and fasted state (after an overnight fast). The result showed a greater improvement in endurance performance in fasted state (10.4%) compared toa fed state (3.5%).

In hot humid environment, CHO mouth rinse was shown to provide ergogenic effects compared to no rinse on 10 kilometres (km) time-trial test during Ramadhan fasting (Che Muhamed et al., 2014). Nine male cyclists completed three cycling time trials while performing randomly assigned that to a CHO mouth rinse, a placebo mouth rinse and no rinse. Each trial consisted of 65% of peak rate of oxygen consumption preloading for 30 minutes followed by 10 km time-trial under hot humid environment. During the rinse trials, participants rinsed their mouth with 25 mL of the assigned solutions after 5, 15 and 25 minutes interval at the preloading exercise, and 15 seconds before the 10 km time-trial. The main finding of this study was that mouth rinsing either with CHO or placebo solution provided an ergogenic effects on the time-trial performance compared with to no rinse trial.

The presence of sucrose solution in the oral part has been shown to stimulate cortical activation (Haase et al., 2009). There is only a study investigated the effect of sucrose mouth rinse on exercise performance during fasted or fed state (Trommelen et al., 2015). Fourteen trained cyclists were recruited to perform four 1 hour cycling time-trials with rinsing using 6.4% sucrose solution or artificial