Ketone bodies and acute energy compensation in women following exercise

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Thesis submitted to the University of Ottawa in partial Fulfillment of the requirements for the Degree of MSc in Human Kinetics

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Thesis Abstract

Acute EC (energy compensation) can occur following an exercise session in women. In recent years, the popularity of ketogenic diets or exogenous ketone bodies has drastically increased, namely due to their appetite sensation suppressive effect. The objective of this thesis is to explore the proposed effects of ketogenic diets and exogenous ketone bodies on acute EC in women following a session of exercise. Over a short period, the EC in women following exercise is partially compensated and seems to be the results of many individual factors. LCKD (Low-carbohydrate Ketogenic Diet) results in a decrease in appetite and EI (energy intake) for a short time, but this effect does not appear to be efficient to modulate EI for a duration over 12 months. EKE (Exogenous ketone esters) are a novel product that can allow a rapid increase in blood BHB (β-3-hydroxybutyrate) levels. Their effects on appetite are still elusive, as EKE decrease acute appetite sensations, but this does not translate into a decrease in EI. To date, the impact of EKE on EC in women following exercise remains unknown. Further studies are needed to better understand the regulatory roles of ketone bodies on exercise-induced energy compensation.

Abrégé de recherche

Une certaine forme de compensation énergétique semble survenir à la suite d'une session d'exercice chez la femme. Dans les dernières années, il y a eu une recrudescence de la popularité des diètes cétogènes ainsi que de corps cétoniques exogènes, notamment due à l'effet de satiété qui semble accompagner ces diètes. L'objectif de cette thèse est d'explorer les effets suggérés des diètes cétogènes et des corps cétoniques exogènes sur la compensation énergétique en période aiguë suivant l'exercice chez la femme. Sur une courte période de temps, la compensation énergétique chez la femme suivant l'exercice n'est pas univoque. Il y a une compensation partielle qui semble être causée par de multiples facteurs individuels. Les diètes cétogènes faibles en glucides ont des effets réducteurs sur les sensations subjectives d'appétit et l'apport énergétique pour une courte période de temps, mais ces effets ne se traduisent pas par une diminution de l'apport énergétique lors de période au-delà de douze mois. Les corps cétoniques exogènes sont de nouveaux produits sur le marché qui permettent d'augmenter rapidement les niveaux sanguins de β-3-hydroxybutyrate. Les effets de ces produits sur l'appétit sont encore mal compris du fait qu'ils diminuent les sensations subjectives d'appétit en période aiguë sans toutefois entraîner de diminution de l'apport énergétique. À ce jour, l'impact des corps cétoniques exogènes sur la compensation énergétique chez la femme suivant l'exercice demeure inconnu. Combler cette lacune pourrait fournir une meilleure compréhension des rôles des corps cétoniques dans la régulation de la compensation énergétique induite par l'exercice.

Acknowledgements

À la suite de cet accomplissement qu'est le passage aux études graduées, des remerciements s'imposent.

Au printemps 2018, j'ai fait la connaissance du Professeur Pascal Imbeault aux Journées Montfort. J'étais loin de me douter que cette rencontre aller prédestiner les années suivantes et mon aventure dans le monde de la recherche. Pascal, pour tes mots si justes, ton support, tes connaissances et tout simplement la personne que tu es, merci. N'oublie pas que je voudrai entendre un jour ton appel à l'orignal.

À l'été 2016, j'ai fait la rencontre du Professeure Isabelle Giroux, pour y plaider ma cause pour un crédit de cours non reconnu. Je crois qu'Isabelle a su saisir le moment opportun pour me niveler vers ce qui a été ma toute première expérience en recherche. Isabelle, pour tout ton support, pour toutes les opportunités offertes, je t'en serai éternellement reconnaissante. Merci.

Ren, je me souviendrai toujours du moment où nous avons fait connaissance à cette même Journée Montfort afin que je te ramène à l'université. Ce court trajet de voiture était le début d'une belle amitié. Ton support, tes encouragements et ton attitude exceptionnelle ont fait de mon passage à la maîtrise un moment inoubliable. Alex, merci pour ton esprit critique et ta compréhension envers le monde des nutritionnistes qui ont été pour moi un bel exemple. Également, merci de m'avoir fait écouter la meilleure télésérie. Merci à Caro, pour la relecture des documents et les séances de course (qui n'ont pu se poursuivre, faute d'une pandémie mondiale!). Je tiens à remercier Alexandra Bodnaruc, pour toutes les opportunités offertes qui ont été déterminantes dans ma décision de poursuivre en recherche. Merci également à tous les autres membres de l'équipe de recherche qui ont été de précieux alliés.

Merci aux membres de mon comité. Bénédicte, merci d'avoir accepté de te joindre à nous à mi-chemin, c'est très apprécié. Éric, merci pour tes commentaires toujours si pertinents et ta grande expertise ainsi que d'avoir compris ma grande admiration pour Kevin Hall.

Mon amour, thank you for being the biggest entertainment and support in my life. You were there for the ups and downs of this process and always having my back when I had meltdowns and always cheering me up when I had good news. You are simply the best and I love you. (Your English literacy is also priceless).

Merci à ma famille que j'adore et qui m'a toujours encouragée lors de mes nombreux appels vidéo. Maman, papa, vous avez été mes tous premiers modèles de vie et vous le serez toujours.

À maman, qui m'a transmis l'amour des mots

Preface

The intended project for this thesis was to perform an original study aiming at determining the acute effects of exogenous ketone ester drinks ingestion on energy intake and subjective appetite sensations following a high-intensity exercise session in women.

Due to Covid-19, amendments to the project have been made, which resulted in a literature review on ketogenic diet, exogenous ketone bodies and acute energy compensation in women following exercise, as presented in Chapter 3 of the thesis.

Another complementary contribution has been published during this master's degree as a lay-language article, which is presented in Appendix A of this thesis.

« Malheureusement jusqu'ici, dans les expériences des physiologistes divers, comme dans mes propres expériences, c'est toujours le poids qui a été pris comme mesure, et non la surface. C'est après coup seulement que je me suis avisé que la donnée surface était plus intéressante que la donnée poids. »

Charles Rivet (1889). *La chaleur animale*.

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List of abbreviations

AcAc	Acetoacetate
Acetyl CoA	Acetyl Coenzyme A
AEE	Activity energy expenditure
AgRP	Agouti-related Protein
AMPK	AMP-activated protein kinase
ARC	Acuate Nuclei
BHB	β-3-hydroxybutyrate
BMR	Basal Metabolic Rate
BMI	Body Mass Index
CART	Cocaine-and amphetamine-regulated transcript
CCK	Cholecystokinin
CHO	Carbohydrate
CNS	Central Nervous System
Ctl	Control
d	day
EC	Energy compensation
EE	Energy expenditure
EI	Energy intake
EKE	Exogenous Ketone Esters
Ex	Exercise
FA	Fatty Acids
GABA	Gamma aminobutyric acid
GLP-1	Glucagon-like Peptide 1
HF/LC	High-fat-Low-carbohydrate
HI	High-intensity
HMGCoa reductase	3-hydroxy-3-methyl-glutaryl-coenzyme A
HR	Heart rate
KB	Ketone Bodies
Kcal	Kilocalories
kJ	Kilojoules
LCKD	Low-carbohydrate Ketogenic Diet
LF/HC	Low-fat-High-carbohydrate
LI	Low-intensity
mM	Millimoles
NADH	Nicotinamide adenine dinucleotide-Hydrogen
NEAT	Non-Exercise Activity Thermogenesis
Nex	Rest
NPY	Neuropeptide Y
NTS	Nucleus of the Solitary Tract
POMC	Agouti-gene-related protein
PRO	Protein
PYY	Peptide YY

RCT	Randomized Control Trials
REE	Resting energy expenditure
Res	Restrained
ROS	Reactive Oxygen Species
SAS	Subjective Appetite Sensations
TEE	Total energy expenditure
TEF	Thermic effect of food
TFEQ	Three-Factor Eating Questionnaire
Unr	Unrestrained
VAS	Visual Analog Scale
VO_2	Maximal oxygen consumption

Chapter 1: Introduction

A common method used to increase EE (energy expenditure) is through increased exercise (or physical activity) levels (Wingfield et al., 2015). However, the impact of exercise on the energetic balance seems to be less than estimated (Miller et al., 1997). This is due to a variable degree of EC (energy compensation) observed following exercise (Doucet et al., 2018; Riou et al., 2015, 2019). EC from dietary intake can be defined as the difference between EI (energy intake) following a session of exercise and a session of rest, as a function of the exercise cost of exercise above resting EE (Pomerleau et al., 2004).

Some factors could impact EC following exercise interventions in a female population. In fact, a higher proportion of women are living with class 2 and 3 obesity when compared to men (Public Health Agency of Canada, 2011). It has been also shown that women have a higher "drive for thinness" (Anderson & Bulik, 2004) and experience more "body dissatisfaction" than men (Lewinsohn et al., 2002). As a result, they are more likely to apply dietary restrictions with the intent to control their body weight (Anderson & Bulik, 2004; Lewinsohn et al., 2002; Udo et al., 2013). Women are more likely to falsely report lower EI in dietary interventions when compared to men (Schoeller, 1995). This population has also been reported to seek more consultation to treat a disorder related to food than men (Bohrer et al., 2017; Ja et al., 2019; Lewinsohn et al., 2002; Thapliyal et al., 2020). However, it has been reported that the sex of an individual does not influence EC as long as EE is comparable between groups (Donnelly et al., 2003; Donnelly & Smith, 2005; Riou et al., 2015; Thackray et al., 2016). Given this information, we examined the degree of EC in women following an acute period of exercise and summarized which factors could influence it.

We also explored one of the potential nutritional strategies that has been studied to decrease EI. More precisely, a focus has been put on LCKD (low-carbohydrate ketogenic diet). Considering the difficulty of maintaining a low carbohydrate intake, we focused our attention on recent drinks made of EKE (exogenous ketone esters) that are used to increase blood ketone levels above normal physiological levels of around 0.2-0.5 mM (millimoles) to ~3 mM in a time frame of ~30 min (Clarke, Tchabanenko, Pawlosky, Carter, Todd King, et al., 2012; Stubbs et al., 2018).

Accordingly, the first section of this review article is outlining and elucidating the factors that impact and/or influence acute EC following a session of exercise in women.

The second section of this review article is presenting general information regarding the physiology of KB (ketone bodies) and nutritionally induced ketonemia. To facilitate the understanding of the complexity of feeding behavior, an overview of appetite control is presented as well as the influence of LCKD on short-term SAS (subjective appetite sensations). Moreover, to fully cover how LCKD impact EI, a non-exhaustive list of long-term studies on LCKD and their effects on weight loss is summarized. Considering the novelty of EKE, a figure and a section related to their effects on ketosis is presented. The potential mechanisms by which they could impact EI and SAS is also summarized. Finally, a section on the latest evidence in the literature concerning studies on EKE and their effects on EI, SAS and EC is presented.

Thus, this thesis project is taking the form of a literature review on acute EC following exercise and EKE consumption on EI and SAS in women. The final section of the review article is summarizing the findings found in the literature and highlighting the research gaps to help orient future studies that should be conducted.

Specific problem:

Some factors specific to women show that they could demonstrate acute EC following a high-intensity exercise session. LCKD are popular diets that are aimed at managing EI and body weight. EKE are novel products that could potentially decrease SAS and EI. However, it is unsure how EKE could impact acute EC following a session of exercise in women.

Objective:

To examine the effects of EKE consumption following a session of exercise on acute EC in women.

Hypothesis:

The consumption of EKE drinks will decrease acute EC following exercise in women.

Chapter 2: Methodology

Considering the narrative nature of the review article of this thesis, no strict protocol in terms of methodology was used. However, a focus on the methodology related to the main objective of the review article is presented in this section. Therefore, a description of the methods used to search the literature about EC in women following an acute session of exercise and EKE intake on appetite sensations and/or energy intake is included in this section.

Articles were searched in the following databases: Pubmed, Medline (Ovid), and Embase. Studies were included if they were written in French or English. Studies were included if published in peer-review journals. Articles were selected if they were meeting the inclusion criteria after reading abstract and full article (see Tables 1 and 2 below).

EC in women following an acute session of exercise

Search terms were: energy compensation; food compensation; energy intake; energy expenditure; exercise intervention; physical activity; exercise intensity; women, female, acute, short-term.

Table 1. *Inclusion and exclusion criteria for the literature search about EC in women following an acute session of exercise*

Inclusion criteria	**Exclusion criteria**
• No history of chronic disease • No limits to body weight • Non-smoking • No physical limitations that could impact ability to exercise • Acute exercise protocol and monitoring ad libitum EI, buffet-style or standardized meal • No limits of type or intensity of exercise • Randomized controlled trial	• EI not collected in laboratory • Exceeding one exercise session • Not in a human population • Not in women only • No control condition

EC: Energy Compensation; EI (Energy Intake).

EKE intake on appetite and/or EI

Search terms were: ketone*, exogenous ketone ester*, R- 1,3-butanediol, ketone monoester*, ketone diester*, ketone supplement; energy intake, subjective appetite sensation*.

Table 2. *Inclusion and exclusion criteria for the literature search about EKE intake on appetite and/or EI*

Inclusion criteria	**Exclusion criteria**
• No restrictions to: dose of EKE, sex of individuals, age or body weight • Exogenous ketone esters comprised of either: ketone monoesters, ketone diesters, ketone. • Duration: acute period (with an exception made for Poffé et al., 2019).	• Protocol using ketone salts • No measurements of either EI or SAS • Ketosis obtained with ketogenic diets

EI (Energy Intake); EKE (Exogenous Ketone Esters); SAS (Subjective Appetite Sensations).

Chapter 3: review article

Title

Ketogenic diet, ketone bodies and acute energy compensation in women following exercise

Abstract

Acute EC (energy compensation) can occur following an exercise session in women. In recent years, the popularity of ketogenic diets or intake of exogenous ketone bodies has drastically increased, namely due to their appetite sensation suppressive effect. The objective of this review is to explore the potential effects of ketogenic diets and intake of EKE (exogenous ketone esters) on acute EC in women following a session of exercise. Over a short period, the EC in women following exercise is partially compensated and seems to be the results of many individual factors. LCKD (Low-carbohydrate Ketogenic Diet) results in a decrease in appetite and EI (energy intake) for a short time, but this effect does not appear to be efficient to modulate EI for a duration over 12 months. EKE are a novel product that can allow a rapid increase in blood BHB (β-3-hydroxybutyrate) levels. The mechanisms through which they may affect appetite are still for the most part unknown, as EKE decrease acute appetite sensations, but this does not translate into a decrease in EI. To date, the impact of EKE on EC in women following exercise remains unknown. Filling this gap could provide further understanding of the regulatory roles of ketone bodies on exercise-induced energy compensation.

Keywords: Appetite, energy compensation, women, low-carbohydrate ketogenic diet, exogenous ketone esters

Introduction

TEE (Total Energy Expenditure) is the amount of energy that a human body expends over 24 h (Blasco Redondo, 2015). It is composed of three major components: BMR (Basal Metabolic Rate), TEF (Thermic Effect of Food) and AEE (Activity-induced Energy Expenditure).

BMR is the amount of energy a person is spending at rest, after waking up from a night of sleep and in a fasting state (Blasco Redondo, 2015). It represents around 60%-70% of the TEE for a sedentary person and around 50% for more physically active people (Pinheiro Volp et al., 2011). Another component, the TEF, is the energy cost of digesting food, as well as using and storing nutrients, which will vary accordingly to the type of macronutrients that a person eats and represents ~10% of TEE. The last component, the AEE, is the most variable one. It does vary in accordance with a person's daily activity and can represent 30%-40% of TEE (Westerterp, 2017). It can be partitioned into three components: spontaneous physical activity, activities of daily living and planned exercise. The latter is planned training, and the EE (Energy Expenditure) related to it will vary depending on the type of exercise and some individual characteristics (*i.e.*, body weight and composition). Spontaneous physical activity is the EE related to the unplanned moving of a human being (*e.g.*, fidgeting or shivering), generally a result of the cost of muscles' contraction. The activities of daily living, known as NEAT (Non-Exercise Activity Thermogenesis) are a part of the daily moving tasks an individual will accomplish (*e.g.*, cooking, driving, etc.).

Despite AEE being the most variable component of TEE, there is often little variability between TEE of an active vs sedentary individual (Pontzer, 2015). This could be related to the EC (energy compensation) that seems to occur following energy restriction from a diet or exercise. In fact, energy can be compensated by increasing energy intake or by reducing the energy expenditure following a deficit. Here, the focus will be put on energy intake compensation. EC in this article will be defined as the subtraction of EI (energy intake) following a session of exercise and a session of rest, as a function of the exercise cost of exercise above resting EE (Pomerleau et al., 2004). Nonetheless, the act of food consumption is more complex than ingesting energy to compensate for the exercise-induced EE. The EC following exercise is suggested to be influenced by several variables, including social, environmental, and cognitive factors, which are specific to each individual (Blundell & King, 1998, 1999; King, 1999). For example, women are more likely than men to present severe obesity (class 2 and 3) (Public Health Agency of Canada, 2011). Women are also more prone to be unsatisfied with their body (Lewinsohn et al., 2002) and to diet to control their body weight than men (Anderson & Bulik, 2004; Lewinsohn et al., 2002; Udo et al., 2013). They will consult more to treat an unhealthy relationship with food when compared to men (Bohrer et al., 2017; Ja et al., 2019; Lewinsohn et al., 2002; Thapliyal et al., 2020). However, it has been noticed that the sex of the individual is not a factor in differentiating the compensation response between men and women when the exercise EE is the same between individuals (Donnelly et al., 2003; Donnelly & Smith, 2005; Riou et al., 2015; Thackray et al., 2016). Hence, it is of interest to look at the degree of acute EC following exercise in women.

Considering women are more likely than men to have a detrimental relationship with their body and food, it is relevant to equip health professionals with the right information about the marketed dieting products. Growing interest has been observed regarding the satiating impact of the LCKD (low-carbohydrate ketogenic diet), namely because of the purported advantages of KB (ketone bodies) on appetite (Paoli et al., 2015). Increase in KB production is known to be generated predominantly in the liver from an increase in fat oxidation-derived acetyl CoA (acetyl coenzyme A) following a carbohydrate-restricted diet, short or prolonged fasting, or during pregnancy and neonatal period (Puchalska & Crawford, 2021). However, there are novel products, EKE (exogenous ketone esters) drinks, that are known for rapidly increasing blood KB levels (within ~30 min) (Clarke, Tchabanenko, Pawlosky, Carter, Todd King, et al., 2012; Stubbs et al., 2018). Of interest, EKE drinks were recently shown to acutely decrease SAS (Subjective Appetite Sensations) in human subjects in resting condition (Stubbs et al., 2018). To our knowledge, it is unknown whether the suppressive effect of EKE drinks would impact EC regulation in women following exercise. Accordingly, the purpose of this review is to summarize the current evidence about the potential effect of ketogenic diets and ketone bodies on appetite and EI on EC in women following a session of exercise. This report will be composed of three sections summarizing the evidence on: acute EC following exercise in women; the physiology of ketosis, EKE and their influence on appetite and EI; and the effects of EKE on EC following exercise.

Acute energy compensation in women following an exercise session

Methodological considerations

Relevant articles including adult female population that reported EI following a session of exercise and a session of rest (control) and EE from exercise were selected. After selection of relevant studies regarding EI following exercise, data were extracted from the articles to calculate the EC following exercise. More precisely, REE (resting energy expenditure) was calculated at first with mean value of subject characteristics with the Harris-Benedict formula (Harris & Benedict, 1918):

$$\text{REE} = 655 + (9{,}563 * \text{weight (kg)}) + (1{,}85 * \text{height (cm)}) – (4{,}676 * \text{age (years)})$$

Following that, the Ex (exercise) cost of exercise above REE was calculated with the REE, the exercise time and EE from exercise:

$$\text{Ex cost of Ex above REE} = \text{EE Ex} – (\text{Ex time} * \text{REE})$$

The EC was calculated with the following formula:

$$\text{Compensation} = [(\text{EI after exercise session - energy intake after control session}) / \text{exercise cost of exercise above REE}) \times 100]$$

Compensation could not be calculated if articles were not providing participants characteristics to calculate REE.

Articles that provided data in kilojoules were transferred in kilocalories (1 kcal = 4.1868 kJ). Compensation percentage was rounded to nearest tenth.

Results

Overall, the energy compensation calculated from the *ad libitum* test meal after exercise condition ranged from -27.9% to 93.5% (see Table 1). These results reinforce the evidence brought up by other studies indicating that the response to EI following exercise can vary among individuals (Blundell et al., 2015; Hopkins et al., 2014; Unick et al., 2010). It has been reported that predisposition to compensate may arise from an enhanced implicit wanting for food following exercise (Finlayson et al., 2009), an alteration of appetite-related hormones (like ghrelin, GLP-1 (Glucagon-like Peptide 1), PYY (Peptide YY)), an episodic satiety signal coming from a greater carbohydrate oxidation during exercise (Blundell et al., 2015; Hopkins et al., 2014), stomach related events (*e.g.*, gastric emptying rate) or skeletal muscle activity (Blundell et al., 2015). The discrepancies of results obtained from studies make it more difficult to have a clear picture of the women's energy intake following an acute bout of exercise, especially when considering the biological differences from an individual to another. Main findings have been divided into the following three sections: intensity of exercise, subject's body weight, and post exercise meal composition and cognitive restrictions.

Acute EC in women following exercise sessions at various intensities

Only individuals living without obesity were included in this section. Positive EC (27.6% – 93.5%) was observed following exercise sessions at high-intensity ($VO_{2\ peak}$ (Maximal oxygen consumption > 70%)) (Larson-Meyer et al., 2012; Panissa et al., 2016; Pomerleau et al., 2004), while no EC was observed following exercise sessions at ~ 65% of $VO_{2\ peak}$ (Kissileff et al., 1990; Melby et al., 2002; Panissa et al., 2016). Hagobian et al. (2013) showed no EC (0.15%) with at an intensity of 70% VO_2 peak. As for low-moderate intensity (20-40% $VO_{2\ max/peak}$), a 24% – 65.3% partial positive EC was observed (Kissilef et al., 1990; Pomerleau et al., 2004). Overall, these results indicate that the acute effect of exercise intensity on EC in women is quite variable. There seems to be an acute partial positive EC following exercise session as intensity increases, but caution should be taken to the fact that there were only three studies included in this section.

TABLE 3. ***ACUTE ENERGY COMPENSATION AFTER EXERCISE SESSION IN WOMEN.***

AUTHOR, YEAR	**Population characteristics (*n*; Age (y); BMI (kg/m^2)**	**Exercise Protocol**	**Energy Intake**	**Compensation (%)**
HAGOBIAN ET AL.,2013	10; 21 ± 2; 24 ± 2	1)Cycle ergometer: 70% VO_2 peak; 84 min; ~713 kcal/session 2)NEx : ctl; 60 min	*Al* buffet type meal after condition	0,15
KING ET AL.,1996	13; 22.6 ±2.3; 21.9 ±1.6	1)Cycling: 70% VO2max; ~348 kcal/session; 50 min 2)NEx: ctl; 45 min	1)HF/LC *Al* 2)LF/HC *Al* Test lunch varying in macronutrients after condition	LF/HC: 21,5 HF/LC: 32,1
LARSON-MEYER ET AL.,2012	19 in two groups: Runners: 9; 23.7 ± 2.4; 19.8 ± 1.0 Walkers:10; 24.6 ± 6.9; 22.1 ± 3.4	1) Run/walk: 70% VO2max; 60 min 2)NEx: ctl; 60 min	*Al* meal after condition	Runners:1,3 Walkers: 27,6
LLUCH ET AL., 1998 + LLUCH ET AL., 2000	Restrained eaters 12; 21.7 ± 2.2; 22.6 ± 1.9	1)Cycling: 70% VO2max; 50 min 2)NEx: ctl; 50 min	1) HF/LC *Al* 2) LF/HC *Al* Test lunch varying in macronutrients after condition	LF: -18,9 HF: 3,2

PANISSA ET AL., 2016	9; 27±3; --	1)HII-A Ex: 75% VO_2 peak; ~650±65 kJ/session; 20 min 2)HII Ex: 64% VO_2 peak; 100% maximal load; ~469 ± 56kJ/session; 17 min 3)Ss Ex: 63% VO_2 peak; 60% maximal load; 19 min ~470±57 kJ/session 4)NEx: ctl	*Al* lunch served 4 h after breakfast	HII-A: 37,7 HII: 93,5 SS: -27,9
POMERLEAU ET AL., 2004	13; 22.2 ± 2.0; 22.2 ± 2.4	1) Walk HI: 70% VO_2 peak; ~350 kcal/session; 37 min 2)Walk LI: 40% VO_2 peak; ~350 kcal/session; 65 min 3)NEx: ctl	Lunch after condition: *Al* buffet type meal	HI: 41 LI: 24
KISSILEF ET AL., 1990	1)LO: (9; 24.33±4.85; 27.72±0.9) 2)NLO: (9; 22.67±4.92; 22.14±1.78)	1)Cycle ergometer: 90W/~65% VO_2 max; 40 min (NLO: ~247 and LO: ~237) kcal/session 2)Moderate (30 W/~20% VO_2 max; 40 min) (NLO: ~114, LO: ~143 kcal/session) 3)NEx: Rest; 40 min	*Al* standardized snack after condition (Yogurt shake)	LO 1): -54,1 LO 2): -52 NLO 1): -43,5 NLO 2): 65,3
TSOFLIOU ET AL., 2003	LO: 10; 50.0±8.5; 37.2±6.5	1)Walk: 20 min; ~502 kJ 2)Snack 3)Ctl: rest; 20 min	*Al* buffet style dinner after condition	-42,2
UNICK ET AL., 2010	LO: 19; 28.5±8.3;	1)Walk: 70-75% of aged-predicted HRA; 40 min; ~354 kcal	*Al* EI after condition	0,9

	32.5±4.3	2)NEx: Rest		
MELBY ET AL., 2002	13; 23.0±0.8; 21.6±0.2	1)Bicycle ergometer: 65% VO_2 peak; 75 min; ~500 kcal 2)NEx: ctl	*Al* lunch buffet after trials	1,6
VISONA & GEORGE, 2002	D-HR: 12; 31±8; 28±3 ND-HR: 12; 23±3; 27±2 ND-LR: 12; 25±8; 30±3	1)Walking: 60-70% max HRA; 60 min; ~219 kcal 2) NEx: ctl	*Al* lunch buffet after trials	D-HR: 105 ND-HR: -81,7 ND-LR: 132,7

Note: This table represents energy compensation results from articles measuring acute energy intake after a session of exercise.
Al (*Ad libitum*); BMI (Body Mass Index; unit measures: Kg: kilograms / M^2: square meters); Ctl (Control); D-HR (Dieting high restraint); Ex (Exercise); h (hours); HC-LF (High-carbohydrate-low-fat); HI (High-intensity); HII (High-intensity intermittent); HII-A (High-intensity intermittent all-out); HRA (Heart rate); Kcal (Kilocalories); kJ (Kilojoules); LF-HC (Low-fat-high-carbohydrate); LI (Low-intensity); LO (Living with obesity); max (maximum); min (minutes); *n* (number); ND-HR (Nondieting high restraint); ND-LR (Nondieting low restraint); NEx (Rest); NLO (Non-living with obesity); Ss (Steady-state); VO_2 (Maximal oxygen consumption); W (Watts); y (years).

Acute EC following exercise sessions in women living with overweight/obesity

Three studies testing the effects of acute exercise on energy intake were considered to explore whether adiposity levels influence EC in women (Kissileff et al., 1990; Tsofliou et al., 2003; Unick et al., 2010). Participants in these studies were women with a BMI (Body Mass Index) ranging from 27.7±0.9 to 37.2±6.5 kg/m^2. Exercise conditions were cycling or walking for a duration of 20 to 40 minutes. Our calculation revealed that women living with overweight/obesity do not compensate after an acute session of exercise when compared to a control (rest) session, with EC ranging from -54.1% to 0.9% (Kissileff et al., 1990; Tsofliou et al., 2003; Unick et al., 2010). This is in accordance with previous studies (Martins et al., 2015; Sim et al., 2014; Ueda et al., 2009) reporting that individuals (mixed groups with men and women or men only) living with overweight/obesity seem to not increase EI following an acute exercise session. The hypothesis reported in these studies is that it might be linked with reduced levels of appetite stimulating-related hormones following exercise sessions (Holmstrup et al., 2013; Martins et al., 2015; Sim et al., 2014; Ueda et al., 2009).

Acute EC following exercise with various meal compositions and/or cognitive restrictions

The level of cognitive restraint can be determined with the TFEQ (Three-factor Eating Questionnaire), a test undertaken by participants to evaluate different measures of eating behavior (Stunkard & Messick, 1985). A person who restricts food intake to maintain or to lower body weight is defined as a restrained eater. Conversely, someone who restricts food intake exclusively to lose weight is a dieter (Herman & Mack, 1975; Herman & Polivy, 1975). Studies grouped in this section included women with restrictive cognition, who were dieting or not. Exercise conditions were either cycling or walking compared to a rest session, with a duration of 50 to 60 minutes. Out of the three cross-over studies evaluating cognitive restriction, the non-dieting restrained women showed no compensatory eating response in studies evaluating the *ad libitum* EI at a test lunch following a session of exercise (Lluch et al., 1998, 2000; Visona & George, 2002). The EC was ranging from -81.7% to 3.2 %. Visona and George (2002) observed a compensation of 132.7 % for a group of participants with low restraint and who were not dieting. Another group of women dieting with high restraint had a compensatory response of 105%. The authors based their explanation on the model presented by Lowe (Lowe, 1993), who suggested that individuals with high restraint and who are dieting, but having difficulty losing weight, are people who can experience episodes of overeating. This group showed an increase in EI following a bout of exercise when compared to the control session (increase of 165±284 kcal). On the contrary, individuals with high restraint, but that were not dieting, may have dieted in the past and were successful at maintaining their body weight stable, which can be why they are not compensating.

Three studies have tested the effect of acute exercise and diet composition on food intake (King et al., 1996; Lluch et al., 1998, 2000). This was done following a session of cycling or rest of 45 to 50 minutes, followed either with *ad libitum* lunch composed of HF/LC (High-fat-Low-carbohydrate) or a LF/HC (Low-fat-High-carbohydrate) food items. The main observation was that eating compensation increased with a HF/LC lunch (3.2% to 32.1%) when compared to a LF/HC lunch (-18.9% to. 21.5%) (King et al., 1996; Lluch et al., 1998, 2000). This is in line with the "passive overconsumption" of high-fat food commonly observed with the "fat paradox" (Blundell et al., 1995).

Ketone bodies vs ketone esters: what is the difference?

What is a ketone body?

The LCKD has increased in popularity in the past years, especially because of its potential reducing effect on appetite sensations (Gibson et al., 2015; Paoli et al., 2015). The particularity with this diet is that there is an increase in KB production derived from a drastic decrease in CHO (carbohydrate) intake that accounts for less than 10% of total energy intake (Feinman et al., 2015). As shown in Figure 1, KB can be an alternative fuel substrates when CHO intake is low when on a LCKD, during pregnancy and neonatal period, and while fasting for a short period or long-term starvation (Puchalska & Crawford, 2021). The KB are formed from partial oxidation of FA (Fatty Acids) in the liver. More precisely, when FA enter the hepatic mitochondria, the ß-oxidation process transforms them into acetyl-CoA molecules. Two molecules of acetyl-CoA are needed to be transformed into acetoacetyl CoA by acetoacetyl CoA thiolase. Another molecule of acetyl-CoA is paired with acetoacetyl CoA, and they are transformed in HMGCoA (3-hydroxy-3-methyl-glutaryl-coenzyme A reductase) by HMGCoA synthase. There is then the production of AcAc (Acetoacetate) and acetyl-CoA by HMGCoA-lyase. AcAc can be transformed into acetone, by decarboxylation, and is expired by the lungs. AcAc can also be reduced by β-3-hydroxybutyrate dehydrogenase into BHB (β-3-hydroxybutyrate) with the help of a molecule of NADH (Nicotinamide adenine dinucleotide, Hydrogen), previously produced by the ß-oxidation. Therefore, acetone, AcAc and BHB are main KB produced from ketogenesis, which can serve as energy fuels and by tissues such as skeletal muscles, heart and brain.

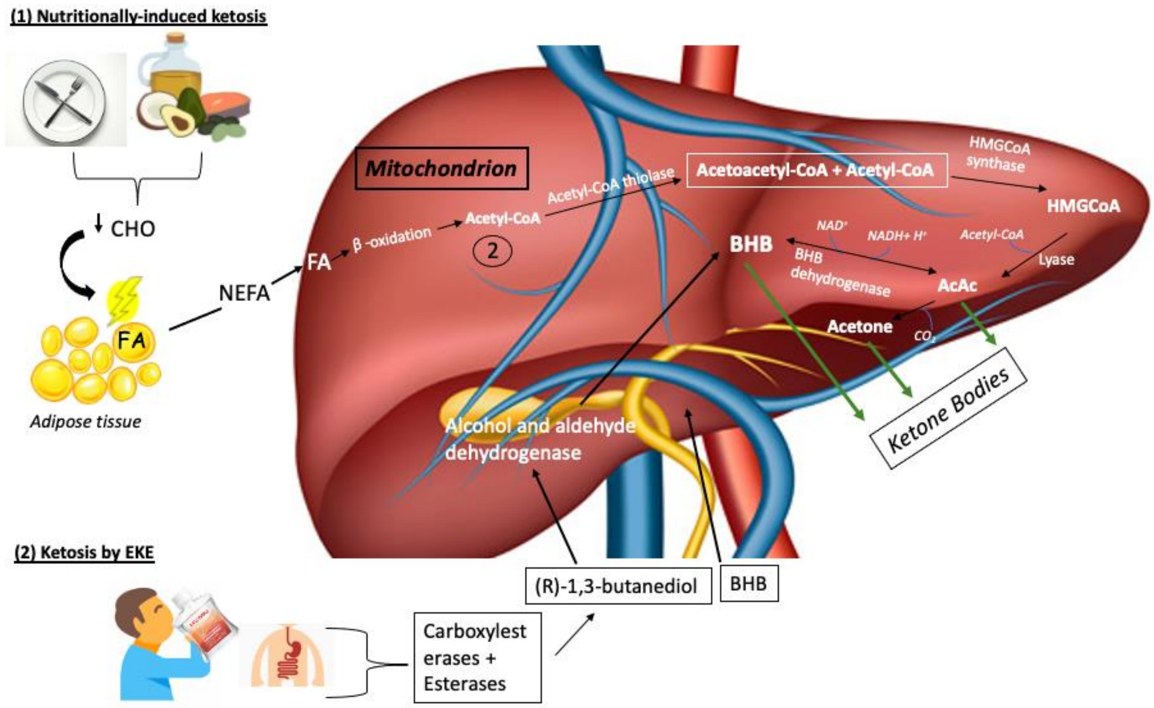

Figure 1. *Schematic illustrating metabolism of (1) ketone bodies and (2) ketone esters*

(1) Following a severe restriction in CHO, a fast period, during pregnancy and neonatal period, FA are used as an alternative fuel substrate. FA are circulating in the blood in the form of NEFA. When FA enter into the liver mitochondria, the ß-oxidation process transforms them into acetyl-CoA molecules. Two molecules of acetyl-CoA are needed to be transformed into acetoacetyl CoA by acetoacetyl CoA thiolase. Another molecule of acetyl-CoA is paired with acetoacetyl CoA and they are transformed in HMGCoA by HMGCoA synthase. There is then the production of AcAc and acetyl-CoA by HMGCoA-lyase. AcAc can be transformed into acetone, by decarboxylation, and is expired by the lungs. AcAc can also be reduced by BHB dehydrogenase into BHB with the help of a molecule of NADH, previously produced by the ß -oxidation. Therefore, three main KB are produced from ketogenesis: acetone, AcAc and BHB.

(2) Once the EKE are ingested, they undergo hydrolyzation by the enzymes carboxylesterases and esterases located in the gastrointestinal tract, in the liver and in the blood. This breakdown of EKE results in R-1,3-butanediol and BHB. In order to be used as a source of energy, R-1,3-butanediol enters into the portal circulation and is metabolized by the liver via alcohol and aldehyde dehydrogenase to form KB BHB and AcAc. Consequently, BHB and AcAc are used as a source of energy by extra-hepatic tissues.

AcAc (Acetoacetate); Acetyl-CoA (acetyl coenzyme A); BHB (Beta-Hydroxybutyrate); CO_2 (Carbon dioxide);CHO (Carbohydrate); EKE (Exogenous Ketone Esters); FA (Fatty Acids); KB (Ketone Bodies); H (hydrogen); HMGCoa (3-hydroxy-3-methyl-glutaryl-coenzyme A reductase); NAD (Nicotinamide adenine dinucleotide); NEFA (Non-esterified Fatty Acids).

Nutritionally induced ketonemia

Nutritional ketosis is believed to be attained at a threshold of 0.3 mM/L of BHB (Gibson et al., 2015). As mentioned above, one way to achieve this significant level of blood BHB is by strictly limiting CHO intake to around less than 10% of the daily energy requirements or ~20-50 g of CHO daily (Bueno et al., 2013; Kuchkuntla et al., 2019; Masood & Uppaluri, 2019; McDonald & Cervenka, 2019; Paoli et al., 2015). Although it used to be coined as Atkins diet, this eating pattern is nowadays better known as LCKD and it has regained popularity in the past few years for its purported effects favoring weight loss (Bueno et al., 2013). Moreover, the sensation of hunger often accompanying a weight loss regimen seems to be reduced with a LCKD (Gibson et al., 2015). However, maintaining a low quantity of CHO intake daily can be quite a burden for individuals, considering how restrictive it is compared to daily recommended carbohydrate intake (Trumbo et al., 2002). It has also been reported that the lack of food diversity in the LCKD calls into question the long-term health effects of such a diet. Eliminating much of the grain products and fruit in a diet contradicts health recommendations since these food groups are associated with low incidences of chronic diseases, such as type 2 diabetes and heart disease (Aune et al., 2016; Muscogiuri et al., 2019). In addition, the large amount of fat, especially saturated fat, consumed with the LCKD could raise serum low-density lipoprotein cholesterol concentrations (Muscogiuri et al., 2019; Volek & Westman, 2002; Westman, 1999). In the shorter term, discomforts related to the LCKD have been noted. Indeed, part of the production of KB is eliminated in the form of a gas, acetone, by the lungs and can give bad breath, also known as halitosis (Muscogiuri et al., 2019). Other symptoms, such as dehydration, constipation or diarrhea, nausea or vomiting, erythema, headache and fatigue are reported by people who indulge in this dietary pattern (Masood & Uppaluri, 2019; Muscogiuri et al., 2019; Yancy et al., 2004). All of these symptoms would, however, be temporary, as the body adapts to the LCKD.

An overview of the feeding behavior

The act of dieting is interrelated with a highly complex process that is appetite. Appetite is referred to as "the physiological and psychological regulatory processes underpinning feeding" (Blundell et al., 2015, p.2). EI is the act of food consumption (King et al., 1997). As for hunger, it is defined as "a conscious sensation reflecting a mental urge to eat" (Blundell et al., 2015, p.2). Appetite is assessed in a subjective manner and is self-reported on a VAS (visual analog scale). Among others, subjective appetite sensations can be qualified namely with feelings of fullness, desire to eat, satisfaction or prospective food consumption (("anticipated quantity that would or could be eaten") (Blundell et al., 2010, p.12).

The act of consuming food implies multiple interactions between body systems. The CNS (central nervous system) is the control center of the food ingestion act (Blundell, 2006). It processes internal stimuli and external stimuli. External stimuli are associated with the sight or the smell of food (Cameron & Doucet, 2007). Internal stimuli are related to the signals from gastrointestinal tract and are also divided into two subsections: direct information from circulating hormones or metabolic state that can be seen as the homeostatic pathway, or indirect information, which is more related to the affective response of feeding and can be seen as the non-homeostatic (or hedonic) pathway (Cameron & Doucet, 2007).

The hypothalamus is at the center of homeostatic food regulation. It contains important nuclei, such as the ARC (arcuate nucleus) (Dhillo, 2007). Peripheral signals mediate via the vagus nerve and bring information to the central control of food intake, in the brainstem. The latter has reciprocal connections to the hypothalamus and the nuclei ARC (Dhillo, 2007). ARC, the major nuclei implicated in appetite regulation, contains two subpopulations. NPY (Neuropeptide Y) and AgRP (agouti-gene-related protein) are recognized as orexigenic peptides, which are satiety-inhibitor. POMC (Pro-opiomelanocortins) and CART (cocaine-and amphetamine-regulated transcript) are known as anorexigenic peptides, which are satiety-stimulators (Cameron & Doucet, 2007).

Peripheral signals are influencing areas of the brain, more specifically on the ARC and the feeding circuits mentioned above. They are also bloodborne signals that connect to the first order neurons where the blood-brain barrier is absent. Neurons that can connect from the bloodstream to the blood-brain barrier are known as first order neurons (Cameron & Doucet, 2007). These peripheral signals are modulated by long- and short-term signals (or tonic and episodic signals, respectively) (Blundell, 2006). They are working concomitantly, albeit independently, and the regulation of body mass is closely linked to these signals (Cameron & Doucet, 2007). Long-term signals are regulated in function of the adiposity status and two hormones are known to impact these signals. Leptin, which is adipocyte-derived, is impacting food intake by acting on the hypothalamus. Its blood concentration is in function of fat mass (Dhillo, 2007) and is decreasing food intake. In addition, insulin, produced by the *B* cells of the pancreas, is known to have anorexigenic effects in the CNS (Badman & Flier, 2005).

Short-term signals are related to the episodic meal consumption *per se* (Cameron & Doucet, 2007). Short-term signals also influence molecules or peptides present along the gastrointestinal tract that also impact appetite. Among others, ghrelin, found mainly in the stomach, is acylated under its activated form (Kojima et al., 1999), and is the only known hormone that has been associated with meal initiation (Cameron & Doucet, 2007). CCK (Cholecystokinin), found in the small intestine, is secreted following the presence of food and known as a satiety hormone (Badman & Flier, 2005). PYY released from cells located in the ileum and the colon after the consumption of food, has anorectic effects by inhibiting NPY neurons in the ARC (Badman & Flier, 2005). Furthermore, GLP-1, an incretin hormone released from the intestinal cells, is stimulated by glucose, and is thought to have a decreasing effect on food intake (Badman & Flier, 2005).

The homeostatic system, namely the “bottom-up”, has been mostly known as the one in charge of food intake (Cameron & Doucet, 2007). In an elegant review, Cameron and Doucet (Cameron & Doucet, 2007) presented a “two-tier” system explaining feeding behavior. The feeding behavior, in all its complexity, is thought to be influenced by indirect stimuli, that could even have a stronger effect on food intake than the homeostatic system (Blundell, 2006; Cameron & Doucet, 2007). This non-homeostatic system, namely the “top-down” regulation or hedonic system, is acting from cortical and limbic centers of the brain. Considering the factors that are influencing each individual’s life (e.g., social influences, reward associated with food, cognitive restrictions), the presence of this “top-down” regulation takes all its sense into the complex system that is appetite (Cameron & Doucet, 2007).

Short-term effects of LCKD on SAS

In light of this “two-tier” feeding model, one could wonder what the effect of a LCKD on SAS is. For this section, articles with men were included to better capture how LCKD could influence SAS, without influence of the sex of the individual. Gibson and colleagues (2015) conducted a systematic review and meta-analysis on SAS before and during a LCKD. Results from this review included three studies that assessed appetite levels while undergoing a LCKD (Johnstone et al., 2008; Martin et al., 2011; Ratliff et al., 2009). In men living with obesity, a 4-week *ad libitum* high-PRO (protein) LCKD (30% of EI as PRO and 4% as CHO) induced a significant decrease (-4,6 on VAS; p =0,014) in SAS measured by a VAS in comparison to a high-PRO medium-CHO diet (30% EI as PRO and 35% as CHO) (Johnstone et al., 2008). Another study by Ratliff and colleagues (2009) showed that during a 12-week LCKD, a group of healthy men living with excess weight or obesity had a significant increase in subjective sensation of satisfaction and fullness ($p<0.05$) and a significant decrease in the desire to eat ($p<0.001$), as compared to baseline values. There was no information provided relative to energy restriction. Furthermore, hunger sensation in adults living with obesity was assessed using VAS during a LCKD with unlimited intake of fat and PRO and showed that there was a significant decrease in hunger sensation after three months ($p<0.05$) (Martin et al., 2011).

A study reported that after a 6-week period, premenopausal women who had an excess of weight and were following a LCKD with *ad libitum* PRO and fat intake reported a significant decrease in their hunger perception ($p<0.03$) in comparison to baseline values (Nickols-Richardson et al., 2005). Furthermore, a well-controlled study conducted in a respiratory chamber for 36 h showed that healthy normal-weight men and women that were following a LCKD vs a non-LCKD had a significant decrease in hunger sensation ($p<0.01$) (Veldhorst et al., 2010). However, it is important to note that in most of the studies mentioned above, the PRO intakes were not standardized. This nutrient, which is known for having a high satiating effect (Soenen & Westerterp-Plantenga, 2008) and a high TEF (thermic effect of this macronutrient is ~20% to 30%) (Tappy, 1996), may have contributed to allegedly decreased hunger. Nonetheless, in two studies, PRO intake was equivalent between both ketogenic and non-ketogenic diets, which suggests that there might be a link between ketosis and appetite suppression (Johnstone et al., 2008; Veldhorst et al., 2010). Moreover, in all those studies, EI was not monitored making it difficult to evaluate whether EI is decreased while undergoing the LCKD. Therefore, it seems that LCKD decreases SAS on a short period, but the weaknesses observed in the articles included here decrease the strength of the conclusion that can be made about their effects on SAS.

Is LCKD more beneficial for a sustained weight loss? A summary of the evidence about longer intervention.

The efficacy of a LCKD eating pattern as a proficient method to lose weight has been questioned. For study duration of 6 months or less, there are some significant results suggesting that a LCKD is more efficient in terms of weight loss when compared to a LF/HC diet (Kirkpatrick et al., 2019). Although it has been hypothesized that the drastic decrease in CHO consumption associated with a LCKD lowers food variety, which can decrease overall food intake (Hall et al., 2016), this decrease does not seem to remain for study duration of more than 6 months (Kirkpatrick et al., 2019). Even if LCKD influences SAS over the short-term, the long-term effect of this eating regimen on EI seems to show different results. To verify this, studies of a duration of more than 6 months prescribing a LCKD with 10% or less of daily energy from carbohydrate intake were compared to other diets (Table 4). It should be noted that one exception was made by including a study with 14% of daily energy intake from carbohydrates. No other restrictions have been added for population characteristics. Diets with and without energy restrictions were included. As reported in Table 4, two RCT (Randomized Control Trials) comparing LCKD to a LF/HC diet showed no significant difference in weight loss at the end of the 12-month interventions. Both diets were isocaloric and energy restricted (Brinkworth et al., 2009, 2016; Wycherley et al., 2010, 2016). Other RCT comparing *ad libitum* LCKD and energy restricted LF/HC diets for 12 to 24 months showed no significant weight loss difference at the end of the trials (Iqbal et al., 2010; Stern et al., 2004). However, one study had a significant decrease in body weight for the LCKD when compared to the LF/HC diet group (Bazzano et al., 2014).

A RCT comparing the Atkins diet (20-50 g of CHO/d), the Zone (macronutrient balance), Weight Watchers (energy intake restriction) and Ornish (fat restriction) found no significant difference in body weight loss between diets after one year (Dansinger et al., 2005). Another similar study but with LEARN diet (high-carbohydrate, saturated fat restriction) instead of Weight Watchers, and compared to Atkins, Zone and Ornish diets, showed no significant difference in weight loss between Atkins and LEARN or Ornish (Gardner et al., 2007). Other RCT comparing LCKD with other diets (LF, high-unsaturated fat, control or American Diabetes Association recommendations) found no significant difference for weight loss between diets after 11 to 15 months (Goldstein et al., 2011; Lim et al., 2010). Conversely, a meta-analysis by Bueno et al (Bueno et al., 2013) including 13 studies comparing LCKD and LF/HC diet over a period of 12 months or more concluded that the weight loss was -0.91 kg greater for the LCKD. Four studies out of the 13 also did not report carbohydrate intake per day and were not included in Table 4. This result seems to be questionable in terms of clinical significance even if it resulted in a significant difference when compared to the low-fat diet.

It should be noted that all studies mentioned above reported a higher CHO intake than what was prescribed. Moreover, dietary intake was collected outside of a laboratory setting, which can lead to a misreporting of dietary intake (Poslusna et al., 2009). This can impact the veracity of LCKD effects on weight loss and the difficulty of compliance with such restrictive diets over a longer period.

In fact, as a weight loss strategy, these results show that the LCKD seems to be no more and no less efficient over a long period of time. Despite this fact, one could question by which mechanisms ketosis brings a weight loss on a short period of time accompanied with a reduction in SAS.

TABLE 4. ***IMPACT OF LOW-CARBOHYDRATE KETOGENIC DIET VS OTHER DIETS ON WEIGHT LOSS FOR A PERIOD OVER 6 MONTHS.***

AUTHOR, YEAR	Population characteristics (*n*/age (y)/ BMI (kg/m^2))	Duration (months)	Diet prescription (cho/pro/fat) %	Energy restriction	Weight loss (kg)*	Results (time x diet on weight loss)
BAZZANO ET AL., 2014	1)Low-cho: 75/45.8±9.9/35.2±3.8 2)Low-fat: 73/47.8±10.4/35.6±4.5	12	1)Low-cho: <40g/d /--/-- 2)Low-fat: 55/15/30	No	1)-6.5 (CI -9.0 to -4.0) 2)-2.6 (CI -5.1 to -0.1)	S; low-cho >low-fat (p=0.032; -3.9 kg)
BRINKWORTH ET AL., 2016	115/ 58.5 ±7.1/34.6±4.3	12	1)Low-cho: 14/28/58 2)High-cho: 53/17/30	Both; isokcal	1) 101.8 ±2.0 to 92.6 ±2.0 2)101.1±2.0 to 91.0±2.0	NS (p=0.91)
BRINKWORTH ET AL., 2009	1)Low-cho: 33/51.5±7.7/33.6±4.0 2)Low-fat: 36/51.4±6.5/33.3±3.9	12	1)Low-cho: 4/35/61 2)Low-fat: 46/24/30	Both; isokcal	1)-14.5 ± 1.7 2)-11.5±1.2	NS (p=0.14)
DANSINGER ET AL., 2005	160/49±11/35±3.9	12	1)Atkins: 20-50/--/-- 2)Zone: 40/30/30 3)WW: 1 point = 50 kcal; aim of 24-32 points/d 4)Ornish: vegetarian; --/--/10	WW	1)2.1±4.8 2)3.2±6.0 3)3.0±4.9 4)3.3±7.3	NS (p =0,40)
GARDNER ET AL., 2007	1)Low-cho: 77/42±5/32±4 2)Zone: 79/40±6/31±3 3)LEARN: 79/40±7/31±4 4)Ornish: 76/42±6/32±3	12	1)Low-cho: ≤20 g/d 2−3 mo, up to ≤50 g/d 2)Zone: 40/30/30 3)LEARN: 55-60/<10 saturated fats 4)Ornish: --/--/<10	LEARN	1)-4.7 (CI -6.3 to -3.1) 2)-1.6 (CI -2.8 to -0.4) 3)-2.6 (CI -3.8 to -1.3 4)−2.2 (CI −3.6 to −0.8	NS Atkins and Ornish at 12 mo S Atkins vs Zone (p<0.05) NS Zone, LEARN, Ornish

GOLDSTEIN ET AL., 2011	1)Low-cho: 26/57±9/33.1±3.6 2)ADA: 26/55±8/33.3±3	11	1)Low-cho: 25g cho for 6 wks; up to 40g/d 2)ADA: 35-40/10-20/35-40	ADA	1)-3.4±4.0 2)-5.4±5.7	NS (p=0.25)
IQBAL ET AL., 2018	1)Low-cho: 70/60±8.9/38.1±5.5 2)Low-fat: 74/60±9.5/36.9±5.3	24	1)Low-cho: 30g/--/-- 2)Low-fat: --/--/30	Low-fat	1)-1.5 2)-0.2	NS (p=0.29)
LIM ET AL., 2009	113/47±10/32±6	15	1)Very low-cho: 4/36/60 2)Very low-fat: 70/20/10 3)High-unsaturated fat: 50/20/30 4)Ctl; no intervention	All; isokcal	1)-3.0±0.2 2)-2.0±0.1 3)-3.7±.01 4)0.8±0.5	NS (p=0.065) Diet groups > ctl group (p=0.012)
STERN ET AL., 2004	1)Low-cho: 64/53±9/42.9±6.6 2)Low-fat: 68/54±9/42.9±7.7	12	1)Low-cho: cho intake <30g/d 2)Low-fat: --/--/<30	Conventional	1)-5.1±8.7 2)-3.1±8.4	NS (p>0.2)
WYCHERLEY ET AL., 2010	1)Low-cho: 26/49.9±1.7/33.5±0.8 2)Low-fat: 23/50.2±1.4/33.9±0.8	12	1)Low-cho: 4(<20g/d for 8 wks, up to <40g/d) /35/6 2)Low-fat: 46/24/30(<10g/d saturated fats)	Both isokcal	1)-14.9±2.1 2)-11.5±1.5	NS (p=0.2)
WYCHERLEY ET AL., 2016	1)Low-cho: 58/58.5±1/-- 2)High-cho: 57/58.4±0.9/--	12	1)Low-cho: 14/28/58 2)High-cho: 53/17/30	Both (isokcal)	1)100.8 ±1.8 to 90.4 ±1.9 2)102.0±1.8 to 91.1±2.0	NS (p=0.70)

Note: This table represents results on weight loss between LCKD and other conventional diet used to lose weight. Data indicate non-significant differences between the diet approaches for a period over 6 months. /d (per day); > (Over); < (Under); ADA (American Diabetes Association); BMI (Body Mass Index); Cho (carbohydrate); Ctl (control); g (gram); Kcal (kilocalories); kg (kilograms); *n* (number); NS (non-significant); mo (months); Pro (protein); S (Significant); wks (weeks); WW (Weight Watchers); y (years). * order is same as diet prescription

Underlying mechanisms by which ketosis could modulate food intake

The mechanisms underlying the potential effect of ketogenic diet on appetite remains vague. It seems that the effect on hunger and appetite sensations observed under a LCKD would be related to the presence of KB, namely BHB (Sumithran et al., 2013). Nonetheless, it is interesting to notice that BHB has been reported to have both anorexigenic (hunger suppressing) and orexigenic (hunger inducing) effects (Paoli et al., 2015). See Figure 2 for a visual representation. It should be noted that articles investigating the physiological mechanisms of LCKD on appetite are from studies made on rodents. This decreases the extent to which they can be applicable to human beings and their non-homeostatic appetite process. Therefore, the term "appetite" should be interpreted with caution for this section.

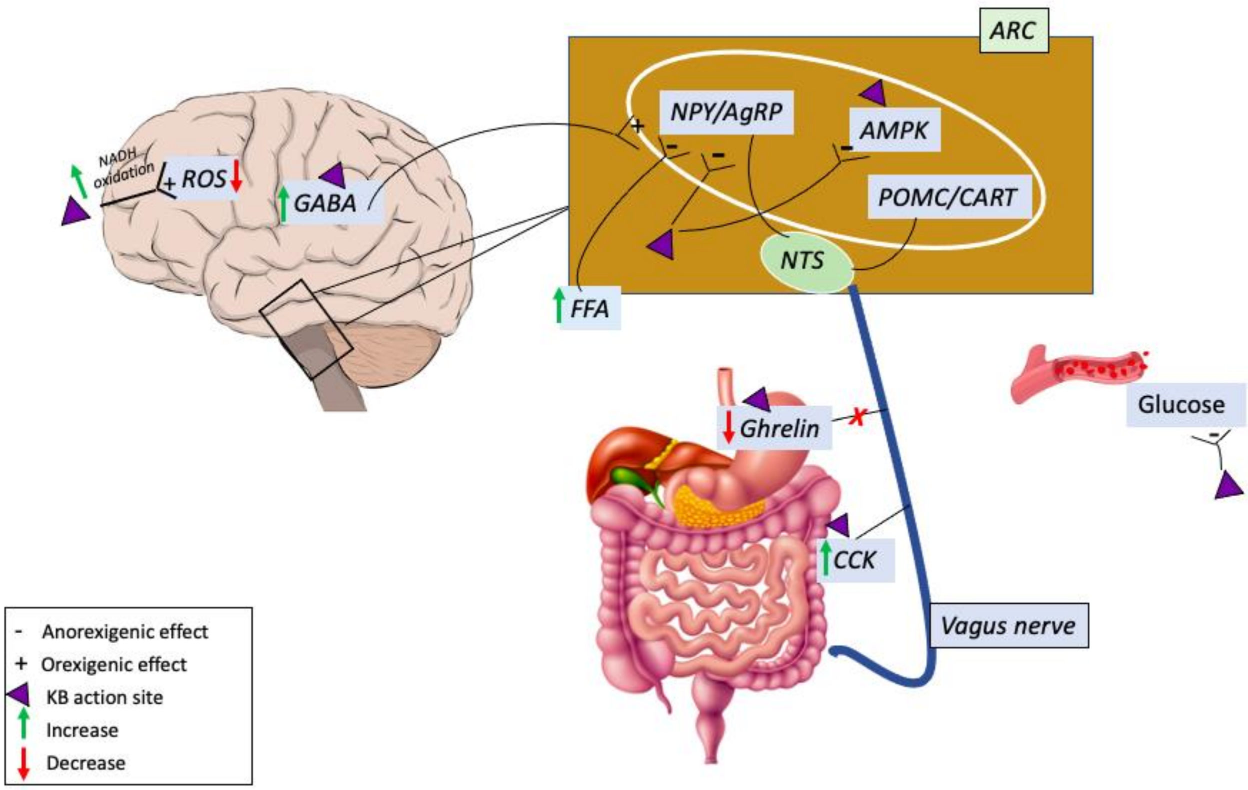

Figure 2. *Schematic illustrating potential mechanisms of ketosis on food intake*

Anorexigenic effects reported in response to ketosis: increased FFA acts on ARC and inhibits orexigenic NPY peptide; reduced increase in orexigenic peptide ghrelin; sustained CCK postprandial levels, which are sensed by the vagus nerve to the NTS; decreased orexigenic AgRP and decreased AMPK, which reduces orexigenic peptide AgRP; sustained postprandial glucose levels, favoring inhibition of meal initiation. Orexigenic effects in response to ketosis: increased GABA which in turn increases orexigenic NPY/AgRP; ROS is being decrease by BHB which would increase NADH and contribute to food intake.

AMP-activated protein kinase (AMPK) ; AgRP (Agouti-related Protein) ; ARC (Acuate Nucleus); CART (cocaine-and amphetamine-regulated transcript); CCK (Cholecystokinin);FFA (Free-fatty acids); GABA (Gamma aminobutyric acid) ; KB (ketone bodies); NADH (Nicotinatimide adenine dinucleotide-Hydrogen); NPY (Neuropeptide Y); NTS (Nucleus of the Solitary Tract); POMC (Pro-opiomelanocortins); ROS (reactive oxygen species).

Anorexigenic effects

The elevation of circulating free-fatty acids while being under nutritional ketosis is a potential mechanism underlying the anorexigenic effects of LCKD. More precisely, long-chain fatty acids- CoA in the ARC of the hypothalamus, an area of the brain implicated with the energetic balance (Morton et al., 2006), would reduce the expression of the orexigenic peptide NPY (Obici et al., 2003; Paoli et al., 2015).

During energy intake restriction, secretion of ghrelin is increased, which leads to an increase in hunger sensations (Cummings et al., 2002; Hansen et al., 2002). Ketosis state seems to suppress the increase in plasma acylated ghrelin concentrations usually seen with low-energy diets (Sumithran et al., 2013). While in ketosis, the anorexigenic hormone CCK is maintained to its postprandial levels (Chearskul et al., 2008). The sustained blood levels of CCK are sensed by the vagus nerve and delivered to the NTS (Nucleus of the Solitary Tract) in the brain and this effect is associated with satiety sensation (Valassi et al., 2008). In the brain, BHB decreases the expression of the orexigenic factor AgRP in the ARC (Laeger et al., 2012). Moreover, as the BHB concentration increases, the AMPK (AMP-activated protein kinase) phosphorylation seems to decrease (Laeger et al., 2012). AMPK is known as a "sensor of nutrient insufficiency" (Morton et al., 2006). The drop observed in the latter reduces the expression of AgRP, which leads to a decreased hunger (Laeger et al., 2012).

According to the glucostatic theory proposed by Mayer (Mayer, 1955), the hypothalamus would be the control center for hunger and satiety signals, containing receptors sensitive to glucose. The drop in glucose between meals would then trigger food intake. It has been reported that LCKD is associated with elevated postprandial glucose levels, which may contribute to EI reduction (Sumithran et al., 2013).

Orexigenic effects:

However, the fact that ketone bodies act as an energy supply in times of food restriction is also an interesting avenue to explore when considering its purported appetite suppressant effects. However, there is some evidence that they could increase food intake.

In the brain, ketonemia increases the availability of glutamate which in turn increases GABA (Gamma aminobutyric acid) levels (Yudkoff et al., 2008). GABA is known to increase feelings of hunger, by having an orexigenic effect by signaling NPY/AgRP neurons (Wu et al., 2009).

Furthermore, some evidence has demonstrated that ROS (reactive oxygen species) would be involved in energy homeostasis mechanisms in the hypothalamus and promote satiety (Benani et al., 2007). However, KB has been linked with a decrease in ROS, because they increase NADH oxidation in the mitochondrial respiratory chain (Maalouf et al., 2007), which would contribute to food intake.

Inducing ketosis by exogenous ketone esters

What are EKE and how do they induce ketosis?

When considering the potential effects of ketosis on food intake, the development of new strategies to obtain similar physiological results as a nutritional ketosis without getting into the burden of dieting is then an interesting avenue to explore. Accordingly, the new EKE products are helping to rapidly raise levels of blood BHB without dietary manipulation. Indeed, the consumption of EKE, has been shown to increase blood ketone levels to approximately 3 mM in a timeframe of 30 minutes (Cox et al., 2016; Stubbs et al., 2018; Vandoorne et al., 2017) with a return to baseline values (<1 mM) within ~ 3-4 hours after ingestion (Stubbs et al., 2017). One of the main commercially available products, ketone monoester, is in the form of drink (HVMN ®; deltaG ®) made of (R)-3-hydroxybutyl (R)-3-hydroxybutyrate (TΔS ® Ltd). Moreover, a study by Clarke and colleagues (Clarke, Tchabanenko, Pawlosky, Carter, Todd King, et al., 2012) confirmed the safety and tolerability of EKE. Participants drank 25 mL of EKE three times a day for 28 days and minimal complaints were reported by participants regarding gastrointestinal side effects (Clarke, Tchabanenko, Pawlosky, Carter, Knight, et al., 2012).

Once the EKE are ingested, they undergo hydrolyzation by the enzymes carboxylesterases and esterases located in the gastrointestinal tract, in the liver and in the blood (Anders, 1989). This breakdown of EKE results in R-1,3-butanediol and BHB (Clarke, Tchabanenko, Pawlosky, Carter, Todd King, et al., 2012). In order to be used as a source of energy, R-1,3-butanediol enters into the portal circulation and is metabolized by the liver via the alcohol and aldehyde dehydrogenase to form the KB BHB and AcAc (Desrochers et al., 1995; Tate et al., 1971). Consequently, BHB and AcAc transformed in the liver are used as a source of energy by extra-hepatic tissues, as mentioned above (Owen, 2005). Nonetheless, there is a limit to ketone body oxidation, and they seem to contribute to 5 to 20% of total energy expenditure (Puchalska et Crawford, 2017). See Figure 1 for a visual representation.

Reported effects of EKE on EI and appetite sensation

To date, there is a paucity of data regarding the impact of EKE on EI. Stubbs et al. (2018) have shown that subjective hunger and desire to eat sensations were lowered by 50% for 1.5-4 h after the consumption of 1,9 kcal/kg of body weight of EKE, compared to a control dextrose drink in healthy individuals. No data on EI was reported in this randomized crossover study. In this study, total plasma ghrelin was significantly decreased 2 to 4 hours after consumption of EKE, compared with the control group who received an energy-matched dextrose drink ($p<0.05$). Another study, with a duration of 3 weeks, with training load increasing progressively between week 1 and week 3, tested the ingestion of 25 g of

EKE compared with a control drink. They demonstrated that EKE, given following exercise and before bedtime, increased total average weekly EI (from week 1 to week 3), while no significant difference in subjective sensation of hunger was observed when compared to control group. It should be noted that these measures were not taken immediately after EKE consumption and during an intense exercise program that was increasing in intensity, and EI was self-reported (Poffé et al., 2019). However, a recent crossover study by the same group reported that consumption of 20-25 g of EKE during exercise suppressed hunger perception and the desire to eat immediately after exercise when compared to a control group. Total serum ghrelin levels decreased by about 17% for the EKE group compared to the control group (Poffé et al., 2020). The same researchers recently published another crossover study, in which they gave to participants 75 g EKE before and during an exhausting cycling race when compared to three other conditions: bicarbonate, EKE and bicarbonate, and a dextrose control drink. SAS at the end of the race showed a decrease in perception of hunger ($p=0.012$) and an increase in fullness ($p=0.026$) for EKE condition. Desire to eat was decreased in EKE group when compared to a control group ($p=0.024$) (Poffé et al., 2021). Vestergaard et al. (2021) studied 10 healthy men on a placebo-controlled crossover study within three conditions: 1) EKE drink, 2) glucose drink, energy, volume and taste-matched, and 3) placebo drink, volume and taste-matched. Ingestion of the drinks were done at rest and acylated-ghrelin and SAS were measured for the following 5 hours. Acylated-ghrelin was lower following EKE (-52.1 (-79.4; -24.8) and glucose drinks (-48.4 (-75.4; -21.5) ($p<0.01$) when compared with placebo drink at 60 minutes. No significant differences were found between drinks for SAS. However, BHB levels rose significantly higher after EKE consumption when compared to glucose and placebo drinks. BHB levels were significantly correlated with a decrease in SAS for hunger (p=0.02) and prospective food consumption (p=0.005) and an increase satiety (p=0.003) and fullness (p=0.02).

Consistent with Poffé and Vestergaard (Poffé et al., 2020; Vestergaard et al., 2021), a randomized crossover trial on healthy adults showed a decrease in acylated-ghrelin for the EKE group (0,5g/kg body weight pre-exercise and 0,25 g/kg of body weight post-exercise) compared to a control group who received a dextrose drink (Okada et al., 2020). A decrease in total area under the curve for acylated-ghrelin was observed in the EKE group in comparison with a control group (p=0.001). EKE and dextrose drinks were given before and after 60 min of high-intensity exercise at 70% of VO_{2peak}. An *ad libitum* lunch was served 90 min post-exercise. A significant difference was obtained for acyl-ghrelin results immediately after exercise, 30 min and 90 min post-exercise when compared with the dextrose drink. Despite this result, no significant effect was observed in the EKE group for perceived appetite sensations (hunger, satisfaction, fullness, and prospective food consumption) measured with VAS at all time points. *Ad libitum* EI was not significantly different between the two groups (Okada et al., 2020). It should be noted that this study protocol was not carried out with a non-exercise control group.

The few available data on EKE consumption on EI, SAS and ghrelin presented here show that part of the studies have a significant decrease in SAS and a significant decrease in ghrelin following their intake. No significant effects were observed on EI, although only one study measured EI after immediate EKE intake (Okada et al., 2020).

Exogenous ketone esters and energy compensation

Would EKE be involved in EC following a session of exercise in women?

To our knowledge, there is no study that directly assessed the effect of EKE on EC following exercise in women. As reviewed in this thesis, it seems that acute EC is inconsistent in women following exercise. In fact, there is either no or only partial positive acute EC following a bout exercise. However, it has been shown that the longer the exercise interventions are associated to greater EC (Riou et al., 2015). EKE has been explored as an exogenous aid to decrease EI. The intake of EKE revealed an increase in EI followed their delayed consumption (Poffé et al., 2019) or no differences when compared to a dextrose drink (Okada et al., 2020). To date, evidence suggests that EKE are not an efficient way to acutely decrease EI following a bout of exercise, even when considering that they lower SAS. Therefore, it could be expected that a supplement of EKE after exercise in women would not impact EC on a longer period of time.

Discussion and conclusion

The compensatory eating response is not always matched to exercise-induced EE acutely, mainly because of the influence of individual factors. Implicit wanting for food, variation in appetite-related hormones, acute satiety signal deriving from increase CHO oxidation during exercise, stomach-related events or skeletal muscle activity can all influence the degree to which an individual can compensate (Blundell et al., 2015; Finlayson et al., 2009; Hopkins et al., 2014). Moreover, this review article showed that there was no univocal response for EC in women following a session of exercise at various intensities (Hagobian et al., 2013; Kissileff et al., 1990; Larson-Meyer et al., 2012; Melby et al., 2002; Panissa et al., 2016; Pomerleau et al., 2004). The body weight of individuals seems to have a bigger impact on EC, with a lower eating compensatory response with a higher body weight (Kissileff et al., 1990; Tsofliou et al., 2003; Unick et al., 2010, 2012). As for cognitive restriction, either women with high or low restraint, dieting or not, had an overcompensation following exercise when compared to control group (Lluch et al., 1998, 2000; Visona & George, 2002). There was no EC resulting from exercise for women with higher restraint and who were not dieting (Visona & George, 2002). Meal composition is also another factor influencing EC, with a partial EC observed with a meal higher in fat when compared to a lower fat meal (King et al., 1996; Lluch et al., 1998, 2000).

Should a compensation occur following an acute bout of exercise, the energy balance would be more likely to become positive over time. This is in line with the notion that an exercise intervention program does not seem to have the expected effects on body weight reduction (Doucet et al., 2018; Melanson et al., 2013; Miller et al., 1997; Riou et al., 2019). Of note, in an adult population, this compensation seems to increase over time; the longer the exercise intervention, the higher the degree of compensation can be expected, with age and initial fat mass being also predictors of EC (Riou et al., 2015). Based on these findings, it would be of interest to explore strategies to mitigate the EC in response to exercise.

The ketogenic diet has increased in popularity in recent years. It has been reported that there are some significant effects on weight loss in a short period when compared to other diets high in carbohydrate and low in fat (Kirkpatrick et al., 2019). These positive properties seem to be due to the observed rise in blood BHB levels (Sumithran et al., 2013). EI and SAS, as hunger and desire to eat, seem to be reduced on a LCKD, an interesting result considering hypocaloric diets are usually known to increase feelings of hunger (Gibson et al., 2015). However, it becomes more complicated over a long-term period, where literature has demonstrated that LCKD is no more no less efficient for weight loss when compared to other diets (Kirkpatrick et al., 2019). The attrition rate of a LCKD is reported as being high on long-term studies (Bueno et al., 2013), highlighting the difficulty of maintaining a very low amount of CHO in the diet. It is of interest to find ways to induce the same physiological effects seen with LCKD, but without having the deleterious effects of dieting.

EKE have been developed in that manner, as they induced rapid ketosis state. However, the physiological impacts of EKE on appetite and food intake are not fully understood yet, as they appear to induce both orexigenic and anorexigenic effects (Paoli et al., 2015). The paucity of evidence in the current literature has shown significant effects on ghrelin and SAS after their consumption (Poffé et al., 2019, 2020, 2021; Stubbs et al., 2018). Two studies assessed the EI followed EKE consumption in men and women, but one not following their immediate consumption (Poffé et al., 2019). The other study reported no significant difference in EI between EKE and control groups (Okada et al., 2020).

It remains unclear what is the outcome of EKE on EC in women following exercise. The little evidence in the literature highlights that the effect of EKE on EC in women should be further examined.

Ketone bodies are now recognized as important metabolic and signaling mediators (Puchalska & Crawford, 2017). Although limited, the results obtained in this review article provide a better insight on the potential effects of LCKD and EKE on appetite and EI. More precisely, this review highlights that 1) ketone bodies induced through dietary manipulation (LCKD) results in appetite and EI reduction over a short period of time, but these effects fade off over 12 months and 2) exogeneous ketones can exerts an acute decrease in appetite sensations, but this effect is not translated into a reduction in EI. Further studies are warranted to provide better insights into the physiological roles of KB in the regulation of feeding behavior.

Financial support

M.D. was supported by les Fonds de recherche du Québec-Santé

Conflicts of interest

There is no conflict of interest.

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Images taken from:
Figure 1: *Schematic illustrating metabolism of (1) ketone bodies and (2) ketone esters*
Images taken from:
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Figure 2: *Schematic illustrating potential mechanisms of ketosis on food intake*
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Chapter 4: Conclusion & Perspectives

General Conclusion

The objective of this thesis was to determine the effects of EKE consumption on acute EC following exercise in women. Our review of the literature indicates that following a session of exercise, acute EC in women is inconsistent and can vary depending on multiple factors such as exercise intensity, body weight, and concomitant dieting and/or meal composition. To attenuate this possible EC following exercise, EKE have been suggested as a potential solution to reduce appetite sensations and EI (Gibson et al., 2015). However, to our knowledge, there is no study yet available in the literature concerning EKE consumption following an acute bout of exercise in women. The very few available data about EKE consumption relate that part of the studies present a decrease in appetite-related subjective sensations. However, no study has reported a reduction of EI over a short-term period (Okada et al., 2020; Poffé et al., 2019, 2020, 2021; Stubbs et al., 2018). It could be speculated that the short-term effects of EKE on appetite could be related to the short half-life of KB. Further studies on the impact of EKE on EC in women following exercise could provide a better understanding of the regulatory roles of ketone bodies on exercise-induced energy compensation.

Strengths & Weaknesses

This thesis includes strengths and weaknesses that need to be addressed. First of all, the narrative nature of this review included in this thesis can comprise some bias. In fact, there was no strict protocol in terms of the selection process and analyses of articles as it can be found in a systematic review and meta-analysis. The list of articles found for each section is consequently non-exhaustive. Moreover, the subject chosen for this thesis was intended to be a RCT (randomized controlled trial) in women about EC followed high-intensity exercise protocol with four experimental arms (EKE; exercise or rest and dextrose drink; exercise or rest). Due to restriction with Covid-19, this subject has been modified to process a narrative review article instead. The fact that the original objective could not be address did not allow us to cover in a randomized controlled trial the effects of EKE consumption following exercise and their effects on EI. Also, considering the lack of consistency for the results obtained for acute EC following exercise in women, it would have been of great interest to explore articles that were developed over a longer period. As presented in the review article, inconsistent results regarding EC following exercise in women were found, but greater evidence in the literature allows us to think that more coherent outcomes would have been found for longer exercise and EC interventions (Doucet et al., 2018; Riou et al., 2015).

The strength of this thesis is that it highlighted the gap in the literature about these novels products that are EKE. To our knowledge, no RCT in women and EC followed the consumption of EKE has been made so far. This thesis also allowed to put in perspective the fact that diets are not an efficient way to manage body weight over long-term and that potential exogenous solutions are being explored. Thus, it emphasizes the burden of people living with obesity and gives another perspective about the complexity of body weight management.

Perspectives concerning knowledge contribution for…

Target group

The information divulged in this article and the perspectives identified will contribute to helping women, more specifically those attempting to manage their body weight. Results from our review article found that, in a short period of time, EC in women is found to be influenced by many factors. This non-exhaustive list of factors that can or cannot influence EC are body weight, the intensity of exercise, and the presence of a concomitant diet prescribed with the exercise session and/or restrictive cognition. The articles presented in this thesis benefit the target population and can serve as a reference for women that are trying to understand their appetite sensation and EI following exercise. The factors mentioned above, which vary among individuals, bring a lot of inconsistency concerning EC in women. The results of this article can benefit women by proposing answers to the ones that are seeking alternative ways to manage their body weight. In fact, considering the popularity of LCKD for weight management, this review article summarizes data that shows that these diets are not necessarily more efficient than any other diets. Moreover, this information provided in the review article will guide individuals looking at managing their appetite and EI to have a better understanding concerning EKE consumption and provide evidence that EKE is likely not the magic pill that could modify behaviors that are related to such a complex mechanism that is appetite.

Dietetics practice and human kinetics

Even if women are looking for information regarding EC and EKE, it is of great importance for health care providers to be well informed concerning this thematic so that they can provide evidence-based and beneficial information to their patients. Among others, registered dietitians and kinesiologists are health care professionals that are commonly interacting with the target population and need to have an evidence-based practice establish with the most recent literature. In addition, this review article gives more knowledge and clarity to Registered Dietitians who are seeking evidence to justify a weight-inclusive approach concerning the low adherence and efficacy of diets over a longer period of time. As reported in this article, strong evidence shows that LCKD is not more efficient for weight loss over a period of 6 months compared to other diets (Kirkpatrick et al., 2019). In terms of exogenous aid that could replace the burden and the inefficacy of dieting, it needs to be considered that mechanism of appetite-related physiology of EKE are still elusive. As of now, there is no strong data that allows health care professionals to recommend EKE for EC following exercise for this target population.

For Human Kinetics professionals, it should be mentioned that even if there is presence or absence of EC, the benefits of physical activity on health go beyond their impact on EC. In fact, there is undisputable evidence that physical activity decreases the risk of premature mortality and chronic medical conditions (Warburton & Bredin, 2017) and this should be highlighted in their interactions with their patients.

Nonetheless, this review article highlights the need of further studies measuring the effect of EKE on EC in women over a longer period of time. Until then, health care providers should use a conservative approach when recommending the use of EKE to manage EI.

Population health & policies

As much as health care providers are the primary providers for individuals that are looking to manage their body weight, strong population health and policies should be advocated from the information provided in this review article. In fact, this article may allow Health Agencies to emphasize and better relay the message that weight management should not rely on diets seeing as they are not generally sustainable and have a low efficacy on weight management over time (Kirkpatrick et al., 2019). It should also be mentioned that trying to reduce body weight by either dieting or by increasing physical activity will inevitably lead to EC (Doucet et al., 2018). Even if, as demonstrated in this review article, exogenous aid like EKE seems to reduce SAS and hunger hormone ghrelin, it does not translate into a decrease in EI (Okada et al., 2020; Poffé et al., 2019, 2020, 2021; Stubbs et al., 2017). Therefore, one can wonder to which extent these external influences could have on body weight and complex mechanisms such as appetite (while taking into consideration the hedonic and non-hedonic factors that influences appetite) (Cameron & Doucet, 2007).

That being said, policies could better advertise and elucidate the downsides of dieting for weight management, and especially better relay the message on regulating weight management. In addition, policies should encourage further studies on natural health products before greater conclusions are made with EKE for EI and EC management.

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Appendix A

Capsule informations santé publiée dans l'Écho sayabécois, Janvier-Février 2020, Volume 40, Numéro 3, pages 24-27.

La diète cétogène : mets d'la crème…!

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Qui dit nouvelle année, dit nouvelles résolutions. Après un temps des fêtes rempli de festivités et de bons repas préparés avec amour pour nos proches, on se sent d'attaque pour se fixer les objectifs pour l'année à venir. Perdre du poids figure souvent dans cette liste d'objectifs. Une grande quantité de diètes sont présentes sur le marché, offrant des promesses toutes aussi miraculeuses les unes que les autres. Parmi celles-ci, la diète cétogène suscite beaucoup d'intérêt au sein de la population en raison de ses supposées vertus pour la diminution du poids corporel. Mais qu'est-ce que cette diète « céto quelque chose »? Cet article vous permettra de découvrir ses origines, son fonctionnement, ses risques ou bénéfices potentiels ainsi que l'opinion d'une nutritionniste relativement à cette diète.

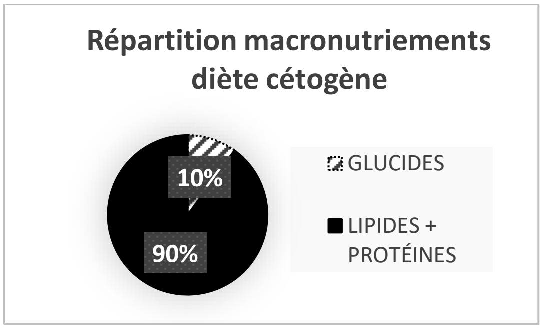
Quelques définitions

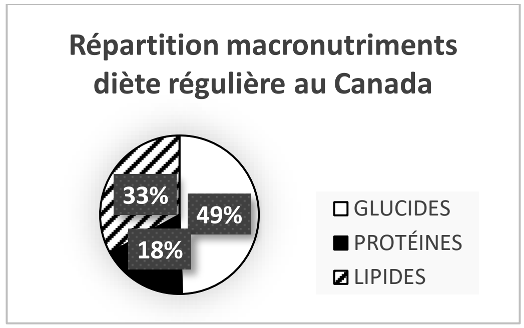
Pour débuter, une définition de termes s'impose. Les aliments contiennent de l'énergie, plus communément appelée « calorie ». Cette énergie peut être mise en réserve ou bien utilisée par le corps. Cette énergie dans les aliments peut se retrouver sous forme de macronutriments : les protéines, les glucides, les lipides. Les protéines peuvent être comparées à des matériaux de construction; elles servent à construire ou à réparer dans le corps, allant de petits bobos à la pousse des cheveux. Des exemples d'aliments qui en contiennent sont les légumineuses, la viande et les produits laitiers. Les glucides sont des sucres; c'est la principale source d'énergie utilisée par le corps pour accomplir ses fonctions quotidiennes. On peut en retrouver dans les fruits et dans les produits céréaliers. Les lipides sont des gras. Ils sont également une source d'énergie importante. Ils peuvent aussi servir, par exemple, à l'absorption de certaines vitamines. On peut penser notamment aux huiles qui font partie de cette catégorie.

Qu'est-ce que la diète 'céto'?

La diète cétogène est une diète dite riche en lipides et faible en glucides. Ses effets semblent avoir été observés il y a un moment déjà. Lors de ses expériences, Russel Wilder a reconnu, en 1921, les bénéfices de cette diète chez les enfants épileptiques[1]. Lors de cette même année, M. Woodyatt a remarqué la formation de « corps cétoniques » lorsque les glucides dans l'alimentation étaient significativement diminués[2]. Mais qu'est-ce qu'un corps cétonique? Lors d'un jeûne ou bien lorsque la consommation de glucides est minimale, le corps produit une source d'énergie alternative que sont les corps cétoniques. Plus précisément, le foie est l'usine centrale de production des corps cétoniques à partir des gras ingérés ou emmagasinés ou encore à partir de certaines protéines. Par conséquent, ce sont ces corps cétoniques qui sont utilisés à la place des glucides pour suffire aux besoins énergétiques de l'organisme.

Pourquoi une diète inventée à l'origine pour traiter l'épilepsie chez les enfants serait un moyen de perdre du poids? En 1972, un certain Dr Atkins en aurait fait la promotion en la présentant comme un moyen efficace et rapide de perdre du poids[3]. La diète cétogène n'est donc pas une nouvelle diète, mais a regagné en popularité dans les dernières années.





Pour former suffisamment de corps cétoniques, la diète cétogène implique une consommation <10% des calories quotidiennes sous forme de glucides (environ 20-50 grammes)[1,3–7]. Concrètement, cette quantité limite de glucides représente une banane moyenne et une tranche de pain, au maximum, pour toute une journée. En comparaison, les Canadiens consommeraient environ 49% de leurs besoins énergétiques quotidiens sous forme de glucides[8].
L'exemple de menu d'une diète cétogène suivant montre que les aliments riches en gras sont à l'honneur dans cette diète alors qu'il y a une absence de produits céréaliers et peu de fruits.

Tableau 1. Exemple de menu d'une diète cétogène.

Déjeuner	**2 œufs cuits dans 2 c. à table de beurre** **1 avocat moyen** **½ tasse de fromage râpé** **Café « bulletproof » : 1 tasse de café avec 2 c. à table chaque d'huile de coco et de crème 35%**
Dîner	½ poitrine de poulet avec sauce crémeuse : ½ tasse de crème sure 14% et 1 c. à thé de moutarde de Dijon Herbes au choix ½ tasse de brocoli
Collation	¼ tasse de bleuets frais 2 c. à table de noix mélangées, rôties dans l'huile
Souper	Hamburger sans pain : 1 galette de bœuf haché régulier Cuit dans 2 c. à table d'huile 2 c. à table de mayonnaise 1 tranche de tomate 1 feuille de laitue pour enrober

Inconvénients et avantages de la diète cétogène

Le peu de diversité alimentaire de la diète cétogène met en question les effets à long terme d'une telle diète sur la santé. Éliminer en bonne partie les produits céréaliers et les fruits mène à une alimentation pauvre en fibres, en vitamines et en minéraux. Présents en quantité suffisante, ces nutriments sont associés à de faibles incidences de maladies chroniques, telles que le diabète et les maladies du cœur[9,10]. De plus, la grande quantité de gras consommée avec la diète cétogène pourrait contribuer à élever le taux de cholestérol LDL, soit le « mauvais » cholestérol[11–13]. À plus court terme, d'autres inconforts liés à la diète cétogène ont été notés. En effet, une partie de la production de corps cétoniques est éliminée sous forme de gaz par les poumons et peut donner mauvaise haleine, aussi connue sous le nom d'halitose[11]. D'autres symptômes, comme la déshydratation, la constipation ou la diarrhée, les nausées ou les vomissements, les rougeurs sur la peau, les maux de tête et la fatigue sont rapportés par les gens qui s'adonnent à ce patron alimentaire[1,11,14]. Ces effets seraient toutefois temporaires.

Un des points positifs de la diète cétogène est qu'elle entraîne une perte de poids rapide. La perte de poids importante au début de la diète cétogène s'explique par la perte d'eau. En effet, notre corps entrepose habituellement ses réserves de glucides sous forme de « glycogène ». Ce dernier est lié à de l'eau. Lors d'une diète cétogène, les réserves de glycogène dans l'organisme s'atténuent, menant ainsi à une perte d'eau[15]. Lorsque les réserves de glycogènes sont réduites, l'organisme utilise les graisses comme substrats énergétiques, ce qui mène à la production de corps cétoniques. Les corps cétoniques semblent avoir un effet inhibiteur sur l'appétit, pouvant ainsi mener à diminuer l'apport en calories[16]. Dans cette même optique, l'apport énergétique lors de la diète cétogène pourrait être diminué via l'effet rassasiant du contenu élevé en protéines [15,17]

Points de vue de la nutritionniste

En résumé, la diète cétogène permet certainement de perdre du poids à court terme, mais selon les connaissances actuelles, elle semble présenter plus de désavantages que d'avantages. La restriction dans le choix des aliments à bonne teneur en glucides qu'elle implique risque d'en décourager certains, ce pour quoi je ne la conseillerais pas. Il est important de noter que la diminution du poids corporel n'est pas néfaste en soi. Toutefois, il faut être conscient de l'effet des régimes à répétition sur le poids corporel. Moins on mange, plus on réduit l'apport calorique, conduisant notre corps à fonctionner avec moins de calories. Avec le temps, la plupart des gens éprouvent de la difficulté à maintenir cette restriction calorique et reprennent progressivement leurs anciennes habitudes alimentaires. À cet égard, il a été démontré que seulement 10% des individus réussissent à maintenir une perte de poids de 10% pendant au moins 1 an[18] et que 5 ans après une perte de poids, plus de 79% du poids perdu est regagné[19]. Ce regain de poids en réponse à une restriction calorique s'explique par le fait que le corps est encore habitué à fonctionner avec moins de calories. La reprise des habitudes alimentaires avant la restriction calorique mène à un surplus de calories ingérées par rapport aux besoins énergétiques, favorisant ainsi l'emmagasinage du surplus énergétique sous forme de graisse.

Tout compte fait, il n'existe pas de diète miracle pour la perte de poids. La seule règle qui s'applique est celle de la balance énergétique. Encore faut-il être capable de maintenir à long terme une diète restrictive, ce qui nuit au plaisir hédonique qu'est de manger. Ce faisant, peut-être que la solution réside dans la perception que nous avons par rapport à la perte de poids. On devrait plutôt se concentrer à améliorer nos habitudes de vie en général. Consommez une grande variété de fruits et de légumes, des produits céréaliers à grains entiers, des sources de protéines maigres (ex. : volaille ou légumineuses) et des aliments peu transformés sont des stratégies à adopter pour avoir une saine alimentation. Enfin, en tant que nutritionniste, n'hésitez pas à consulter un professionnel de la santé qualifié pour vous guider et vous outiller si vous êtes prêts à faire de tels changements dans vos habitudes de vie.

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Pour trouver une nutritionniste certifiée, vous pouvez visiter le site web de l'Ordre professionnel des diététistes du Québec au https://opdq.org/

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