



**Studies Investigating the Influence of  
Macronutrient Intake on Sleep**

By

**Ahmad Afaghi**

**A thesis submitted in partial fulfillment  
of the requirements for the degree of  
Doctorate of Philosophy**

**The University of Sydney**

**2008**

As the doctoral thesis supervisor of Ahmad Afaghi, I certify that I consider his thesis '**Studies investigating the influence of macronutrient intake on sleep**' to be suitable for examination.

Signed .....

Date .....

Dr. Chin Moi Chow

Discipline of Exercise and Sport Science

The University of Sydney

## TABLE OF CONTENTS

List of abbreviations	1
Introduction	3
<b>Chapter 1</b>	
<b>LITERATURE REVIEW</b>	6
1. Sleep	6
2. Dreaming	9
3. Neurochemical regulation of sleep	11
• Growth hormone	13
• Cortisol	13
• Melatonin	14
4. Sleep difficulties	17
5. Effect of macronutrient on sleep and behavior	22
• High carbohydrate meals and sleep	22
• Glycemic index and glycemic load of carbohydrate	26
• Glycemic index and insulin response	26
• Tryptophan and glycemic index	28
• Carbohydrate, mood and behavior	29

• High fat meals, mood and sleepiness	33
• High protein meals, mood and behavior	36
6. The Atkins' diet	37
7. Summary and discussions	39
8. Hypotheses	40
• Study 1 (Chapter 3)	40
• Study 2 (Chapter 4 and 5)	41

## **Chapter 2**

<b>METHODOLOGY</b>	42
--------------------	----

### **Research design and methods**

• Study design	43
• Estimation of daily energy requirement: 3-day Food diary	43
• The recruitment process	44
• Inclusion criteria	44
• Exclusion criteria	45
• General protocol	45

### **Liker scales**

• Pleasantness of the meal	46
• Hunger and fullness	46

- Sleepiness 47

### **Polysomnography**

- Sleep scoring 47
- Electrode placement 51
- Respiratory and leg movement signals 52
- Sleep recording and monitoring 52

## **Chapter 3**

### **HIGH-GLYCEMIC-INDEX CARBOHYDRATE MEALS SHORTEN SLEEP ONSET** 54

- Abstract 55
- Introduction 55
- Subjects and methods 56
- Results 57
- Discussion 58
- References 59

## **Chapter 4**

### **ACUTE EFFECTS OF THE ATKINS' DIET ON SLEEP INDICES** 60

- Abstract 61

• Introduction	62
• Subjects and methods	65
• Results	71
• Discussion	76
• References	88
<b>Chapter 5</b>	
<b>INFLUENCE OF THE ATKINS' DIET ON BEHAVIORAL RESPONSES</b>	98
• Abstract	99
• Introduction	100
• Subjects and methods	104
• Results	111
• Discussion	116
• References	124
<b>Chapter 6</b>	130
<b>SUMMARY AND GENERAL DISCUSSION</b>	131
<b>REFERENCES</b>	138
<b>APPENDIX</b>	158

## LIST OF TABLES

### Chapter 1

Table 1.	Effect of diets on SWS and REM sleep in healthy subjects	25
----------	--	----

### Chapter 3

Table 1.	Effect of the glycemic index (GI) and timing of meals on sleep	57
----------	--	----

### Chapter 4

Table 1.	Study meal plan	66
Table 2.	Effect of diets on SWS and REM sleep in healthy subjects	73

### Chapter 5

Table 1.	Study meal plan	110
Table 2.	Urine ketone, subjective ratings of mood, fatigue, and dream recall	111

# LIST OF FIGURES

## Chapter 1

- Figure 1. Comparison of melatonin, cortisol and GH release during night  
13

## Chapter 2

- Figure 1.1 10%-20% electrode placement system 53  
Figure 1.2 EOG and EMG electrode placement 53

## Chapter 3

- Figure 1. Comparison of sleep onset latency (SOL) between the high glycemic-index (GI) meal ingested 1 h or 4 h before bedtime and the low-GI ingested 4 h before bedtime  
57  
Figure 2. Blood glucose response to meals with a high and low GI given 4 h before bedtime  
58

## **Chapter 4**

Figure 1. Blood glucose response following the Control and Atkins' test meals (Acute and Ketosis) given 4 h before bedtime

76

## **Chapter 5**

Figure 1. Comparison of the sleepiness score using the Epworth sleepiness scale (ESS) between the 3 test meals (Control mixed, Atkins Acute and Atkins Ketosis)

113

Figure 2. The time course of subjective sleepiness scores over a 4 h period post-test meals to bedtime.

114

Figure 3. Comparison of the proportion of subjects experiencing the Atkins diet-related symptoms between Control and Atkins Ketosis

116

## **Abstract**

Several studies have documented the direct effect of macronutrient intake on sleep. A general picture that has emerged indicates that a low carbohydrate diet with a total energy between 13-47% and high fat content with a total energy between 47-77% shows increases in slow wave sleep and may decrease rapid-eye movement sleep. However, previous studies investigating the association between carbohydrate meals and sleep have not explored the effects of the glycemic index (GI) of carbohydrate on sleep. This thesis investigated the affect of GI on the sleep pattern. In a cross-over, repeated measures design, we explored both the effect of GI and the timing of these meals on sleep in good sleepers. The effects of high and low GI carbohydrate-based meals given 4 h before the subjects' usual bedtime on their sleep quality were examined in Chapter 3. Also evaluated was the effect of high GI meal timing (4 h vs. 1 h) on sleep. Twelve healthy men (18-35y, BMI 18.5-25 kgm<sup>-2</sup>) were administered a standard, isocaloric meal of low GI = 50 or high GI=109 in a cross-over and counter balanced manner, 4 h before their usual bedtime. On another occasion, the high GI meal was given 1 h before bedtime. Following the high or the low GI meal, participants underwent a familiarization sleep night followed by three polysomnographic test nights. The subjects' blood and urine were collected for glucose and 6-sulfatoxymelatonin analysis respectively. Significant differences were found between the area under

the curve (AUC) for blood glucose responses following the high GI meal compared to the responses for the low GI meal. It was shown that a carbohydrate-based high GI meal resulted in a significant shortening of sleep onset latency (SOL) in normal sleepers compared to a low GI meal ( $P = 0.009$ ), and was most effective when consumed 4 h before bedtime ( $P = 0.01$ ). There were no significant changes in other sleep indices.

The Atkins' Diet is a popular dietary therapy that promotes weight loss. This restricted carbohydrate diet with high fat and high protein content has not been evaluated for its effects on sleep, or systematically documented for its effects on mood, fatigue or sleepiness. The short term effect of the Atkins' diet over 48 h on the sleep quality of healthy, non-obese males to a Control mixed diet was compared in Chapter 4. This study employed a repeated measure design where fourteen healthy, non-obese, good sleepers were given isocaloric diets and matching evening test meals (4 h before usual bedtime), which were either mixed (15% protein, 25% fat, 60% carbohydrate) or Atkins' (38% protein, 61% fat, <1% carbohydrate). After a familiarization night with polysomnography, further polysomnographic testing was then performed on the Control night, 4 h after the first Atkins' test meal (Atkins Acute) and 48 h (Atkins Ketosis) following commencement of the Atkins' diet. Objective sleep was recorded using Compumedics S-series Sleep system; Compumedics Ltd, Melbourne, Australia. Urine ketone level was monitored before the evening test meals and at bedtime on

the Control night, during the Atkins Acute and Ketosis phase. Blood glucose level was measured before the evening test meal until 120 min following the meal. Significant differences were found for the AUC for the blood glucose between the Control night and the Atkins Acute and Atkins Ketosis phase ( $P < 0.001$ ). Participants developed mild hypoglycemia and ketosis 48 h following the Atkins' diet. A significant reduction in the proportion of rapid eye movement (%REM) sleep to total sleep time (TST) was observed following the Atkins' Acute and Atkins' Ketosis phase compared to the Control ( $P = 0.006$  and  $0.05$  respectively). The percentage of slow wave sleep (%SWS) to TST significantly increased for both the Atkins' Acute and Ketosis phase compared to the Control meal ( $P = 0.02$  for both phases). The sleep changes may be linked to the energy metabolism of fat of the Atkins' diet.

The effects of the Atkins' diet compared to a Control mixed diet on sleepiness, mood, fatigue and dream recall were also investigated (Chapter 5). Participants' overall daytime mood, fatigue intensity, sleepiness and other symptoms were assessed using a visual analogue scale before the evening test meals. The number of subjects with dream recalls was recorded on awakening after each polysomnographic night. The daytime symptoms of fatigue, sleepiness and depressed mood were significantly increased following the Atkins' diet compared to the Control diet. A greater proportion of subjects reported dreams 48 h after the Atkins' diet compared to either the Atkins' Acute phase or the Control condition.

Our findings suggest that mild hypoglycemia resulting from the diet may mediate the subjective responses of daytime sleepiness, depressed mood and intense fatigue. The increased proportion of subjects with dream recall may be related to an increased transient arousals from sleep during which dreams are usually consolidated into memory.

The finding that “high-glycemic-index carbohydrate meals shorten sleep onset” may be relevant to persons with sleep disturbance. These meals may facilitate sleep transition for those with sleep initiation problems. The effect of the Atkins’ diet in SWS promotion and increasing feelings of fatigue and suppressing mood in the short-term may be relevant for patients with sleep apnoea (obesity), who experience low proportion of SWS and significant somnolence. Further studies to explore these effects on a longer term in this group would be worthwhile.

## **STATEMENT OF THE AUTHOR**

I, Ahmad Afaghi, hereby declare that this thesis is my own work and that it contains no material previously published or written by another person except where acknowledged in the text. Nor does it contain material which has been accepted for the award of another degree.

Name: Ahmad Afaghi

Signed:

Date:

## **PUBLISHED WORKS**

Parts of this work presented in this thesis have been published in the following journals:

### **PUBLISHED PAPER**

**Afaghi A**, O'Connor H, Chow CM (2006): High-glycemic-index carbohydrate meals shorten sleep onset. *American Journal of Clinical Nutrition* 85: 426-30

### **PUBLISHED ABSTRACTS**

**Afaghi A**, O'Connor H, Chow CM (2006): Effect of the Atkins diet on sleep. *Sleep Biology Rhythm* 4 (S1): P48

**Afaghi A**, O'Connor H, Chow CM (2006): Effect of the Atkins diet on sleepiness, dreams and mood following the Atkins diet. *Sleep Biology Rhythm* 4 (S1): P49

### **PAPERS SUBMITTED FOR PUBLICATION**

**Afaghi A**, O'Connor H, Chow CM. Acute effects of the Atkins' diet on sleep indices. *Nutrition*.

**Afaghi A**, O'Connor H, Chow CM. Influence of the Atkins' diet on behavioral responses. *Nutritional Neuroscience*.

## ACKNOWLEDGEMENTS

I would like to extend my appreciation to Dr. Chin Moi Chow who supervised and assisted me in editing and completing this project. I thank Chin Moi for her professional approach to teaching and for sharing her extensive knowledge of sleep research with me. Her willingness to discuss matters concerning this project at any time assisted me enormously.

I would also like to thank Dr. Helen O'Connor, my associate supervisor, who gave me outstanding feedback and has been supportive throughout. Helen helped me so much with the nutritional aspects of this project, the nutrition research and the editing of my publications.

The support of my family must be mentioned. To my wife Monir, I owe special gratitude. Without her hard work and support this project would not have been possible. I thank her for giving me the free time and for her patient support over the duration of this project.

My children Vahid, Mahsa and Sara also deserve thanks for their support. During the early stages of this project, when I started learning sleep research, they were among the first group of volunteers to contribute their time to my laboratory experiment.

Special thanks to my friend Chris Turton for his generous time and advice when I was completing the writing of this thesis.

Finally, I wish to express my heartfelt thanks to all the volunteers who participated in these studies. This project could not have been done without their contribution and support.