



PREMENSTRUAL SYNDROME:
Food preferences, increasing brain serotonin
availability and mood in women

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Abstract

Premenstrual syndrome (PMS) describes a group of symptoms, psychological, behavioural and physical, which can have a marked effect on a woman's quality of life. The symptoms can range from being mild to very severe. In cases where they are severe, the woman's normal day to day functioning is significantly impaired.

In some women with PMS, there is an increase in appetite during the premenstrual or late luteal phase of the menstrual cycle. Accompanying this increased appetite, an increased desire to consume foods high in carbohydrate content has been reported. This has been called 'carbohydrate craving' in some of the literature. Very few studies have investigated food intake in women with PMS over the menstrual cycle. The studies which have been done have varied in method. Only one study has recorded the foods eaten by women with PMS premenstrually and post menstrually and this was in a controlled environment. They found an overall increase in carbohydrate and total energy intake, premenstrually in women with PMS compared to the controls.

This study investigates the food consumption of overweight women over three menstrual cycles within a randomised double blind placebo controlled design. The aims of the study are firstly to determine whether women identified as exhibiting PMS symptoms including increased appetite, have a preference for carbohydrate. Secondly, if low brain levels of serotonin are involved in contributing to increased carbohydrate intake, whether increasing the availability of serotonin by using dexfenfluramine reduce total food intake or solely

selectively reduce carbohydrate intake in women with PMS. Thirdly whether there is a link between changes in food consumption, and the severity of PMS symptoms.

Women that met the study's entry criteria were blindly allocated either to the treatment or placebo group. Women participating in the study recorded their food intake premenstrually (commencing 4 days prior onset of menses) and postmenstrually (from day 5 after commencement of menses). They also completed the Steiner self-rated questionnaire and Nottingham Health Profile both pre and post menstrually.

Eighty-eight of the 144 women that completed the screening process met the study inclusion criteria. Forty-four women were allocated to the placebo and treatment groups. The diet records were analysed for total energy and macronutrients, nutrient and energy intake according to food categories and the number of episodes of food intake per day.

Analysis of the data shows a significant treatment effect on premenstrual food consumption. The mean energy and macronutrient intake for women in both the placebo and treatment (receiving dexfenfluramine) groups was elevated premenstrually when compared to the mean postmenstrual intake. The placebo group premenstrual intake of energy and all macronutrients was significantly greater over all three menstrual cycles. For the treatment group premenstrual carbohydrate was significantly higher when compared to postmenstrual intake for

the first and third menstrual cycle. Energy and fat was significantly higher for the third menstrual cycle. Analysis of the data using the percent of energy contribution from protein, fat and carbohydrate found no consistent difference between pre and post menses for the placebo and the treatment groups.

For both the placebo and treatment groups there was a preference for foods from the *cake and dessert* and *high sugar food* categories. This was consistent over the three cycles. Analysis of the food groups in terms of the percentage of each macronutrient and energy they contribute to the total diet, found that the high sugar foods consistently provided a greater proportion premenstrually for the placebo group. The pattern in the treatment group was similar but less consistent.

A commonly proposed theory is that women with PMS and other disorders such as Seasonal Affective Disorder have a specific desire or craving for high carbohydrate foods in response to low brain serotonin levels. This theory proposes that individuals with low brain serotonin levels are attempting to self-medicate by consuming high carbohydrate foods.

The findings of this study do not support the theory that there is an overall preference for foods high in carbohydrates, but rather a preference for sweet tasting foods. Dexfenfluramine reduces overall food intake when comparing the placebo and treatment groups and reduces intake of sweet tasting foods.

Changes in the Steiner self-rated menstrual score did not significantly correlate to change in total nutrient intake over the three menstrual cycles. There was a correlation between the placebo nutrient intake from *high sugar food* category. This lack of correlation suggests that mood and other PMS symptoms are not linked directly with the observed changes in nutrient intake.

Statement of Originality

This thesis contains no material that has been accepted for the awarding of any other degree or diploma at any university or other tertiary institution. To the best of my knowledge and belief, it contains no material previously published or written by another person, except where due reference and acknowledgment is given. The research conducted and presented here is the dietary part of was part of a study that investigated the use of dexfenfluramine for the treatment of PMS and was funded by Servier laboratories (Australia) Pty Ltd. The dietary part of the study was contributed entirely by myself.

Giordana B Cross

6-1-03
Date

Statement of Ethics

All subjects participating in the study received written information explaining the study and were provided written consent to participate in this study. The University of Adelaide Committee on the Ethics of Human Experimentation approved the study.

NAME: GIORDANACROSS PROGRAM: PhD

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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Contents

Premenstrual syndrome: Food preferences, increasing brain serotonin availability and mood in women.

Abstract.....	i
Statement of originality.....	v
Statement of Ethics.....	v
Acknowledgments	vi
Publication.....	vi
Contents	vii
List of Abbreviations	xiii
List of figures	xiii
List of graphs	xiii
List of tables	xiv

Chapter 1: Literature Review

1. Introduction	2
1.1 The menstrual cycle.....	4
1.2 Premenstrual syndrome	8
1.3 PMS and reproductive hormones	13
1.4 Appetite and Premenstrual Syndrome.....	15
1.4.1 Energy and macronutrient intake over the menstrual cycle.....	15
1.4.2 Nutrient intake over the menstrual cycle in women with PMS	19
1.4.3 Food craving.....	20
1.5 Serotonin and appetite in premenstrual syndrome	23
1.5.1 Serotonin and appetite	23
1.5.2 Serotonin in the central nervous system.....	26
1.6 Oestrogen and progesterone influences on appetite.....	28
1.7 Dexfenfluramine : mode of action and influence on appetite	29
1.8 Background to rationale for thesis.	31
1.9 Research aims and Hypotheses.....	33
1.9.1 Aims.....	33

1.9.2	Hypotheses.....	34
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Chapter 2: Methods

Part 1: Screening methods

2.	Introduction	36
2.1	Subject recruitment into the screening phase	36
2.1.2	Eligibility criteria for entry into the screening process	37
2.2	The screening process	38
2.2.1	Anthropometrics and other measures.....	38
2.2.2	Administration of the Steiner self rated premenstrual syndrome	38
2.2.3	Retrospective categorisation of premenstrual symptoms	40
2.2.4	Food intake documentation.....	40
2.3	Nutritional analysis of food intake data.....	42
2.3.1	Application of Goldberg's cut off limit	44
2.3.2	Analysis of food diaries according to food categories.....	46
2.3.3	Analysis of the frequency of food consumption.....	48
2.4	Statistical analysis	49
2.4.1	Subjects included in the statistical analysis	49
2.4.2	Creation of new variables	49
2.4.2.1	Calculation of percentage change in nutrient intake.....	49
2.4.2.2	Calculation of macronutrient intake as percentage of energy	50
2.4.2.3	Calculation of the percentage that each food category Contributed to the total energy or macronutrient intake	51
2.4.3	Testing nutrient data for significance.....	51
2.4.4	Relationship between energy, macronutrient intake and the Steiner Self rated PMS score.....	52

Part 2: Randomised double blind placebo controlled study

2.5	Study design	53
2.5.1	Steiner self rated and Nottingham Health Profile questionnaires	55
2.5.2	Administration of questionnaires	55
2.5.3	Anthropometric measurements	56
2.6	Food intake data collection	56
2.6.1	Returning and checking of food intake records	57
2.6.2	Food data input.....	57

2.6.3	Creation of new variables	58
2.6.4	The frequency of food consumption.....	58
2.7	Statistical analysis	59
2.7.1	Statistical analysis of the nutrient intake data	59
2.7.2	Statistical analysis of questionnaires	62
2.7.2.1	Analysis of Steiner self rated questionnaire PMS scores	62
2.7.2.2	Nottingham Health Profile Health questionnaire.....	63
2.7.2.3	Relationship between food consumption and the Steiner self rated scores and the Nottingham health profile scores.....	63
2.7.2.4	Initial subject perception and Steiner self rated scores	64

Chapter 3: Results Part 1

Part 1: Findings from analysis of the screening data

3.	Introduction	66
3.1	Hypothesis 1	68
3.2	Subject profiles	69
3.3	Retrospective perception of the severity of premenstrual symptoms	71
3.4	Additional data collected from women meeting the entry criteria	72
3.5	Macronutrient and energy intake	73
3.5.1	Data analysis prior to application of Goldberg's cut off limit	73
3.5.2	Data analysed according to food categories.....	77
3.5.3	Energy and macronutrient analysis after applying the Goldbergs cut- off limit.....	82
3.5.4	Analysis of nutrient data according to food categories after applying the Goldberg's cut off limit	89
3.6	The number of 'episodes of eating' in women with and without PMS symptoms	94
3.7	Relationship between the Steiner self rated score and nutrient intake.....	95
3.8	Summary of the screening data results.....	97

Chapter 4: Results

Part 2: Findings of the randomised double blind placebo controlled parallel group study

4.	Introduction	106
4.1	Hypotheses addressed in randomised double blind placebo study	108
4.1.1	Hypothesis 2.....	108
4.2.2	Hypothesis 3.....	109
4.2	Participant profile and medication compliance	110
4.3	Anthropometric measures over the study period	112
4.4	Comparison of the energy and macronutrient intake between the placebo and treatment groups.....	114
4.4.1	The macronutrient contribution to total energy consumption.....	122
4.4.2	Variation of energy and macronutrient intake over the three cycles of the study.....	125
4.4.3	Analysis of data according to food categories	127
4.4.3.1	The contribution to total energy intake by food categories.....	127
4.4.3.2	The contribution of the food categories to protein intake	129
4.4.3.3	Contribution of food categories to the total fat intake	130
4.4.3.4	Contribution of food categories to the total carbohydrates intake	131
4.4.3.5	Contribution of food categories to the total simple sugars intake	133
4.4.3.6	Contribution of food categories to the total complex carbohydrate intake	135
4.4.4	Percentage of energy and macronutrients contributed by each food category	135
4.4.4.1	Percentage of energy contributed by food categories	135
4.4.4.2	Percentage of protein contributed by food categories.....	137
4.4.4.3	Percentage of fat contributed by each food group	138
4.4.4.4	Percentage of carbohydrate contributed by each food category ..	139
4.4.4.5	Percent of simple sugars contributed by each food category.....	140
4.4.4.6	Percent of complex carbohydrate contributed by food categories	140
4.5	Frequency of daily meal intake over three menstrual cycles	160

4.6	Relationship between Steiner self rated PMS questionnaire, Nottingham Health Profile and nutrient intake	161
4.6.1	Steiner self rated questionnaire	161
4.6.2	Nottingham Health Profile scores.....	163
4.6.3	Relationship between the Nottingham Health Profile and the Steiner self rated score	166
4.6.4	Relationship between PMS score and energy and macronutrient intake ...	167
4.6.5	Relationship between PMS score and the number of episodes of eating ...	171
4.7	Summary of results.....	172
4.7.1	Macronutrient and energy intake.....	172
4.7.2	Food category consumption over the menstrual cycle.....	173
4.7.2.1	Energy contribution by food categories.....	174
4.7.2.2	Macronutrients	175
4.7.3	Relationship between food intake, PMS scores and Nottingham Health Profile Scores.....	176

Chapter 5: Discussion

5.	Introduction	179
5.1	Premenstrual syndrome and food consumption	180
5.1.1	Evidence for premenstrual increase in food consumption in women with PMS.....	180
5.1.2	The effect of increasing brain serotonin availability using dexfenfluramine on food consumption	183
5.1.2.1	Dexfenfluramine influence on energy and macronutrient intake during the pre and post menstrual phases.....	183
5.1.3	The influence of dexfenfluramine on the types of food consumed over the menstrual cycle.....	186
5.1.3.1	Energy contribution by food categories.....	187
5.1.3.2	Macronutrient contribution by food categories.....	188
5.2	PMS and alleviation of symptoms by dexfenfluramine.....	195
5.3	The relationship between PMS symptoms and food consumption	195
5.4	Future work	198
	Conclusion	202
	References	203

Appendices	214
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List of Abbreviations

CHO	Carbohydrate
FSH	Follicle stimulating hormone
GnRH	Gonadotrophin-releasing hormone
hCG	Human chorionic gonadotrophin
LH	Lutenising hormone
MDQ	Menstrual Distress Questionnaire
NHP	Nottingham health profile
PMS	Premenstrual Syndrome
PMDD	Premenstrual dysphoric disorder
PRL	Prolactin

List of Figures

Figure 1:	Criteria for the diagnosis of premenstrual dysphoric disorder	10
Figure 2:	A simplified representation of the regulation of food intake, from changes occurring in the brain and peripheral systems in response to food intake	25
Figure 3:	The food categories used for analysis of food intake data.....	44
Figure 4:	Outline of study design for the screening and study periods.....	51

List of graphs

Graph 1:	The kilojoule contribution by the high sugar foods category for the treatment and placebo groups at menses 1 to 3	128
Graph 2:	The carbohydrate contribution of the high sugar foods category for the placebo and treatment groups over menses 1 to 3	132
Graph 3:	The mean number of meals consumed by women that completed all three cycles in the placebo and treatment groups	161

List of tables

Table 1:	The subject profile of women that did and did not meet the criteria for entry into the study.	70
Table 2:	Women's perceptions of the severity of their premenstrual symptoms and length of time they had experienced them.....	72
Table 3:	The mean $\pm$ SD (over 4 days) premenstrual, post menstrual energy, and macronutrient intake and percent change for women that did and did not meet the study entry criteria.....	74
Table 4:	The median alcohol consumption for women completing the screening process according to whether they met the criteria for entry into the study.....	75
Table 5:	Macronutrient intake expressed as percent of total energy intake for women meeting and not meeting the study entry criteria	76
Table 6:	The mean kilojoule and the percent of the total kilojoule intake for each food category for premenstrual and postmenstrual phases for women that met the study entry criteria	78
Table 7:	The mean protein and fat and the percentage of the total protein and fat intake for each food category for premenstrual and postmenstrual phases of women meeting the entry criteria.....	79
Table 8:	The mean carbohydrate, complex carbohydrate and simple sugars and the percent of the total intake for each food category for premenstrual and postmenstrual phases for women meeting the entry criteria.....	80
Table 9:	The subject profile of women that did and did not meet the study entry criteria, after applying the Goldberg factor.....	82
Table 10:	The mean pre and post menstrual energy, macronutrient intake and percent change for each nutrient for women that did and did not meet the study criteria after excluding subjects below Goldberg's cut-off limit.....	85
Table 11:	The median alcohol consumption for women completing the screening process according to whether they met the criteria for entry into the study after application of Goldberg's cut-off limit.....	86
Table 12:	Macronutrient intake for the seventy-seven women meeting PMS criteria expressed as percent of total energy intake and thirty-six women without PMS	87
Table 13:	The mean kilojoule and the percent of the total kilojoule intake for each food category for premenstrual and postmenstrual phases for seventy-seven women with PMS	91

Table 14:	The mean protein and fat and the percentage of the total protein and fat intake for each food category for premenstrual and postmenstrual phases of seventy-seven women with PMS.....	92
Table 15:	The mean carbohydrate, complex carbohydrate and simple sugars and the percent of the total intake for each food category for premenstrual and postmenstrual phases for seventy-seven women with PMS.....	93
Table 16:	The median Steiner self rated scores for women that completed the screening process according to whether they met the study entry criteria	96
Table 17:	The number of subjects participating through the study period	110
Table 18:	The mean ($\pm$ SD) anthropometric measures taken at the commencement of the screening process for subjects that completed menses 1 of the study.....	111
Table 19:	The mean anthropometric measures for the placebo and treatment groups over the study period.....	113
Table 20:	Study participants categorised according to their BMI range.....	114
Table 21:	The basal mean ($\pm$ SD) pre and post menstrual kilojoule and macronutrient intake according to treatment group	115
Table 22:	The mean($\pm$ SD) pre and postmenstrual kilojoule and macronutrient intake for menses 1, 2 and 3 for the placebo and treatment groups.....	116
Table 23:	The mean($\pm$ SD) pre and postmenstrual kilojoule and macronutrient intake for women that completed all three menstrual cycles.....	117
Table 24:	The mean difference in energy and macronutrient intake for menstrual cycles for all women in the placebo and treatment groups	119
Table 25:	The mean difference in energy and macronutrient intake for women that completed all the cycles.....	120
Table 26:	The mean kilojoule and macronutrient intake for the treatment and placebo groups	121
Table 27:	The median and range of alcohol consumption (g) of all women and women that completed all three cycles.....	121
Table 28:	Macronutrients intake expressed as a percentage of energy for menses 1, 2 and 3.....	123
Table 29:	Macronutrients intake expressed as a percentage of energy for women that completed all 3 cycles	124
Table 30:	The GEE treatment effect coefficients for energy and macronutrients.....	126

Table 31:	The mean ($\pm$ SD) kilojoule intake from each food category in the treatment and placebo group for menses 1 to 3.....	142
Table 32:	The mean ($\pm$ SD) protein intake for each food category for the treatment and placebo group for menses 1 to 3.....	143
Table 33:	The mean ($\pm$ SD) fat intake for each food category for the treatment and placebo group in menses 1 to 3	144
Table 34:	The mean ($\pm$ SD) carbohydrate for each food category for the treatment and placebo group menses in 1 to 3	145
Table 35:	The mean ($\pm$ SD) simple sugar for each food category for the treatment and placebo group in menses 1 to 3	146
Table 36:	The mean ($\pm$ SD) complex carbohydrate for each food category for the treatment and placebo group in menses 1 to 3.....	147
Table 37:	The mean ($\pm$ SD) kilojoule contribution from each food group for women that complete all 3 cycles.....	148
Table 38:	The mean ($\pm$ SD) protein contribution from each food group for women that have completed all 3 cycles.....	149
Table 39:	The mean ($\pm$ SD) fat contribution from each food group for women that have completed all 3 cycles.....	150
Table 40:	The mean ($\pm$ SD) carbohydrate contribution from each food for women that have completed all 3 cycles.....	151
Table 41:	The mean ($\pm$ SD) simple sugars contribution from each food for women that have completed all 3 cycles.....	152
Table 42:	The mean ($\pm$ SD) complex carbohydrate from each food for women that have completed all 3 cycles.....	153
Table 43:	The mean ($\pm$ SD) percent of kilojoules from each food category for women over 3 menstrual cycles	154
Table 44:	The mean ($\pm$ SD) percentage of protein contributed by each food category over 3 menstrual cycles.....	155
Table 45:	The mean ($\pm$ SD) percentage of fat contributed by each food category over 3 menstrual cycles	156
Table 46:	The mean ($\pm$ SD) percentage of carbohydrate from each food category over 3 menstrual cycles.....	157
Table 47:	The mean ($\pm$ SD) percentage of simple sugars from each food category over 3 menstrual cycle	158

Table 48:	The mean percentage ($\pm$ SD) of complex carbohydrate from each food category over 3 menstrual cycles	159
Table 49:	The mean number of episodes of eating over 3 menstrual cycles for women in the treatment and placebo groups.....	160
Table 50:	The median score for the Steiner self rated (PMS) questionnaire over 3 menstrual cycles.....	162
Table 51:	The median pre and postmenstrual Nottingham Health Profile scores for each subsection of the questionnaire	165
Table 52:	Correlation scores (Spearman's rho) between the pre and postmenstrual change in each sub area of the Nottingham health profile and the PMS score for the treatment and placebo groups.....	167
Table 53:	Correlation coefficient (Spearman's rho) score between the change in nutrient intake and PMS score.....	168
Table 54:	Correlation coefficient (Spearman's rho) score between the premenstrual energy or macronutrient intake and PMS score for <i>high sugar foods</i> category	169

CHAPTER 1

Literature Review

1. Introduction

Premenstrual syndrome describes a group of symptoms, which are psychological, behavioural and physical that can have a marked effect on a woman's quality of life. The symptoms range from mild to very severe. In cases where they are severe, the woman's normal day to day functioning is significantly impaired. There is also evidence that women with PMS are more prone to accidents (Dalton, 1960) commit suicide (Glass et al, 1971), and commit criminal offences (Dalton, 1961).

In women both with and without PMS, an increase in appetite during the premenstrual or late luteal phase of the menstrual cycle has been reported (Both-Orthman et al, 1988, Lissner et al, 1988). Accompanying this increased appetite is a desire to eat sweet foods or foods with higher carbohydrate content (Pliner et al, 1983; Bancroft et al, 1988; Rogers et al, 1994). This has been called 'carbohydrate craving' in some of the literature. Very few studies have investigated food intake in women with PMS over the menstrual cycle. The studies which have been done have varied in method. Only one study has recorded the foods eaten by women with PMS premenstrually and postmenstrually (Wurtman et al, 1989). This occurred in a controlled environment, where women were admitted for two days pre and two days post menstrually. The food items provided, including snacks were either high in protein or high in carbohydrate. They found an overall increase in carbohydrate and total energy intake, premenstrually in women with PMS compared to the controls.

The aim of this present study was to investigate firstly, whether in 'free living' women there is a significant increase in carbohydrate intake during the late luteal phase. Secondly if this is the case, whether this is due to increased preference for foods high in carbohydrate or solely an increased appetite for food. Thirdly, if serotonin is involved in contributing to increased appetite and carbohydrate intake, does increasing the availability of serotonin reduce total food intake or solely selectively reduce carbohydrate intake in women with PMS. This study was performed as part of a larger study that was investigating the use of dexfenfluramine for the treatment of premenstrual syndrome.

The following sections will provide some background on the stages of the menstrual cycle and hormonal and neurological influences. It will then discuss diet and the menstrual cycle, Premenstrual syndrome (PMS) and diet, neurological control of appetite, in particular serotonin and the influence of dexfenfluramine on food consumption.

1.1 The menstrual cycle

The menstrual cycle can be divided into four phases (Espey et al, 1990). These are the follicular, periovulatory, luteal and menstrual. Ovarian steroids regulate the menstrual cycle via the hypothalamus and pituitary. The average length of a cycle is 28 days and may vary from 20 to 35 days. The variation in length of the ovarian cycle is primarily determined by the length of the follicular phase. This is determined by the timing of inter cycle peak of follicle stimulating hormone (FSH). A variety of factors including stress and weight loss can alter this process and delay or prevent FSH from peaking. The reasons for this are unknown. The luteal phase is more predictable and lasts for an average of 14 days.

The following sections provide a brief overview of the menstrual cycle phases in terms of cyclical changes occurring in the ovaries, uterus and hypothalamus-pituitary axis. This overview has drawn on the three sources to describe the main events occurring over the menstrual cycle. (Bates et al, 1990; Cameron et al , 1996; Espey et al, 1990) .

Follicular stage

Hypothalamus- pituitary axis

The hypothalamus- pituitary axis plays an important role in the regulation of the menstrual cycle. The arcuate nuclei, located in the mediobasal hypothalamus are thought to play a central role in the regulation of the menstrual cycle. Gonadotrophin-releasing hormone (GnRH) is secreted in

pulses by the arcuate nuclei in the mediobasal hypothalamus. From here, it is transported to the anterior pituitary. During the follicular phase the frequency of the pulses increases. GnRH stimulates the synthesis and release of luteinising hormone (LH) and follicle stimulating hormone (FSH) into the circulatory system. The level of LH in the plasma remains at a constant level for approximately 48 hours before its mid cycle surge. FSH plasma levels rise slightly during the initial part of the cycle and then decreases on day 7, remaining at a constant level until the mid cycle surge.

Ovaries

FSH stimulates the growth of some primordial follicles. In response the granulosa cells, which surround the oocytes in the primordial follicles, secrete estradiol. The estradiol stimulates follicular growth by promoting mitotic activity. By day 7 of the follicular phase, one follicle has progressed ahead of the other growing follicles. This follicle continues to grow and reaches a size of about 20mm just before the LH surge. The remaining follicles have ceased to grow and have degenerated. This is thought to occur due to the more advanced follicle secreting larger quantities of oestradiol, which inhibit the development of the other follicles.

Uterus

At the commencement of the follicular phase, there is increasing production of oestradiol that results in the proliferation of the endometrium. During the early stages of the proliferative stage, the epithelium regains its continuity and regeneration occurs. The follicle

causes the production of increasing amounts of estradiol that result in the proliferation of the endometrium.

Periovulatory phase

This is a short phase lasting for 3 days. This consists of the day of LH surge, the day in which LH peaks, and the day after the peak. During the 48 hours prior to the LH surge a rise in serum estradiol and progesterone occurs. This rise is believed to commence the LH surge.

Luteal phase

Hypothalamus-pituitary axis

The mean length of the luteal phase is 13 days. During this phase the pulse frequency, amplitude and basal concentration of FSH, LH and serum prolactin (PRL) are low. Serum progesterone and estradiol levels are elevated resulting in the inhibition of GnRH release by the hypothalamus.

Ovaries

Lutenising hormone (LH) initiates the luteal phase. The ovarian follicle is transformed to the corpus luteum. At day+10 after the LH surge, the corpus luteum regresses. As a result, the levels of progesterone and oestradiol decrease. The reduction in progesterone levels removes its inhibitory action on prostaglandins synthesis and leads to an increase in prostaglandins. The rise in prostaglandins promotes vasoconstriction and myometrial hyperactivity resulting in the shedding of the endometrium and the commencement of the next cycle.

Uterus

During the early luteal phase, endometrial growth slows down. The number of estradiol receptors decrease while progesterone receptors remain in significant numbers.

The follicle selection and development is initiated by a rise in the concentration of the gonadotrophin, FSH. FSH and another gonadotrophin, luteinizing hormone (LH), maintain its continued development. LH stimulates the ovarian stroma to secrete androgens (androstenedione). FSH stimulates the follicles' granulosa cells to aromatize androgens to estradiol-17 *B* resulting in the gradual rise of oestrogen.

Negative feedback results in a decrease in the levels of FSH. Positive feedback occurs with LH when the concentration of oestradiol reaches a certain level and there is a rapid rise in LH. This rise of LH induces ovulation where the ovum is released from the follicle. The ruptured follicle becomes the corpus luteum, which secretes large amounts of progesterone and oestradiol. This marks the completion of the first phase.

Menstrual phase

During this phase, GnRH secretion increases from the hypothalamus and FSH and LH secretion increases in frequency.

Ovaries

The rise in FSH results in the beginning of the development of more follicles and the beginning of a new cycle.

Uterus

During this time the blood flow decreases and the functional endometrial tissue becomes necrotic and ischaemic. Tissues fragment and the functional endometrium slough off.

1.2 Premenstrual syndrome

Many women experience symptoms associated with the menstrual cycle. Retrospective studies have shown that up to 90% of women have experienced at least one symptom premenstrually. Thirty per cent of these have moderate symptoms. Premenstrual symptoms overlap with those of depression and anxiety disorders. However unlike these conditions PMS symptoms occur during the luteal phase and resolve at the onset of menses (Endicott 1993). Over the past 25 years there have been a number of publications reviewing PMS, including the pattern of food and nutrient consumption (Abraham, 1983; Abraham, 1987; Chuong et al, 1992; Freeman, 1997; Korzekwa et al, 1997; Pearlstein, 1996). However, there continues to be debate on both the nature of PMS and whether it is one entity or several different entities.

The existence of a range of symptoms, with varying degrees of severity during the luteal phase of the menstrual cycle, has led to deliberation on its

classification. One hundred and fifty symptoms have been documented in the literature (Rubinow et al, 1984). Diagnosis of the problem is unclear, as is its aetiology. Criteria proposed and used in the past to identify women with PMS range from a very narrow range to a broad range of symptoms. The symptoms included have been psychological, behavioural and physical or a combination. The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) has defined research criteria for premenstrual dysphoric disorder (PMDD) (American Psychiatric Association, 1994). As can be seen in Figure 1 diagnosis is based on symptoms that occur over two menstrual cycles.

Figure 1. Criteria for the diagnosis of premenstrual dysphoric disorder (adapted from DSM- IV, 1994)

- A. Five or more of the symptoms below must be present during the final week of the luteal phase. At least one of the symptoms must include one of the first four. The symptoms should cease to be present in the week after commencement of menses.
1. the feeling of sad, hopelessness or self-deprecating
 2. feeling tense, anxious or 'on edge'
 3. marked affective lability (eg sudden feeling of sadness or tearfulness)
 4. persistent anger, irritability or increased interpersonal conflicts
 5. decreased interest in usual activities eg work, friends , hobbies
 6. experience difficulty in concentrating
 7. feeling lethargic, easily fatigued or lack of energy
 8. marked alteration in appetite which may be associated with food craving or binge eating
 9. hypersomnia or insomnia
 10. feeling of being overwhelmed or out of control
 11. physical symptoms such as breast tenderness, swelling, headaches, weight gain, joint or muscle pain
- B. The symptoms markedly interfere with work, school or usual social activities and relationships
- C. The symptoms are not an exacerbation of the symptoms of other disorders such as a major depressive disorder or personality disorder
- D. The criteria A, B and C are confirmed by prospective daily ratings during the last two consecutive cycles

Women suffering from PMDD must also exhibit a clear on/off of symptoms. The criteria for premenstrual syndrome are defined in the ICD-10. The symptoms are less severe and for diagnosis of PMS one of the following symptoms must be present during the luteal phase and disappear on the onset of menses. The symptoms include: swelling of hands and feet, breast tenderness, mild psychological distress, change in appetite, poor concentration and feeling of bloating and weight gain.

Mitchell et al (1994) investigated women with menstrual cycle associated symptoms. They proposed a categorisation into three groups. These were premenstrual syndrome, premenstrual magnification and low symptom.

Nine variables were measured. These included social demands, socialisation, personal health practices, parity, psychological distress, personal resources and age. Women were identified as being eligible for inclusion into the study retrospectively. Eligible women participated in a 90-day prospective study. During this time they documented daily symptoms using the Washington's Women's health diary. The collated results were used to categorise the women into the three groups according to the pattern of symptoms and their severity.

Jorgensen et al (1993) using data collected in a retrospective study has argued against the existence of multiple premenstrual syndromes. They proposed that there is one underlying pathophysiological process. Using a questionnaire, which measured affective, and physical symptoms, they found that the majority of profiles measured were parallel. They suggest

that the variation in symptoms is due to differences among individual women in the way the pathophysiological process is expressed.

Other researchers have proposed that the different symptoms indicated different conditions. These have been given different names.

Bancroft (1993) based on their research findings and review of other research in this field has proposed a three factor model. The model attempts to take into account '*the complexities of menstrual cycle related complexities*'. In this model, it is proposed that these three factors taken together influence the occurrence and severity of the premenstrual symptoms. The 3 factors are:

1. Timing factor
2. Menstruation factor
3. Vulnerability factor.

The timing factor reflected the cyclical effect of the menstrual cycle hormones on the brain. The menstruation factor, involves processes before and during menstruation. They suggested these could be associated with increased sensitivity to pain and negative mood. The final factor, the vulnerability factor (eg proness to depressive illness) contributes to how a woman deals with menstrual cycle changes.

1.3 Premenstrual Syndrome and reproductive hormones

The role of reproductive hormones in contributing to PMS symptoms is unclear. Treatment of severe cases of PMS with drugs that suppress ovarian function such as danazol or ovariectomy (Casson et al, 1990) results in cessation of PMS symptoms. Hysterectomy does not relieve PMS. This implies that the ovaries play a role in PMS.

Measurement of hormonal levels has not shown consistent differences between women with and without PMS. Early studies measuring sex steroid hormonal levels found lower levels of progesterone during the luteal phase. These findings of probable deficiency of progesterone, led to its use in women with PMS. However, subsequent double blind placebo controlled studies where progesterone was given as an injection or suppository found no benefit in its use.

Progesterone antagonists have been used to investigate PMS. Schmidt et al (1991) used mifepristone, a progesterone antagonist in a prospectively blinded study. Women with PMS were given mifepristone together with human chorionic gonadotrophin (hCG) or a placebo. Human chorionic gonadotrophin was given to maintain normal levels of progesterone during the luteal phase. Seven days after the LH surge, women were given mifepristone with or without hCG. Within 48-72 hours due to the sudden drop in progesterone levels, menses occurred. Those receiving mifepristone with the placebo, although they were in the early follicular phase, experienced premenstrual changes in mood.

Dennerstein et al (1993) measured daily urinary oestrogen and pregnanediol in 65 women with PMS over one menstrual cycle. Pregnanediol is a progesterone metabolite. Women were identified to have PMS with a Menstrual Distress Questionnaire (MDQ). Levels were compared with 18 volunteers without PMS symptoms. A significant delay in the peaking of pregnanediol occurred in the PMS group. For the control group it occurred on day 19.5 ± 4.2 compared to day 21.9 ± 3.7 . There was also a greater mean difference in the number of days between oestrogen and pregnanediol peaks. The PMS group having a greater mean difference in days, 7.6 ± 2.1 for the PMS group compared to 6.1 ± 2.7 for the controls.

Facchinetti et al (1993) measured blood levels of luteal progesterone and lutenising hormone in 14 women with PMS compared to 14 controls. Measurements were made 6-11 days after the mid cycle LH surge. Blood was taken every 10 minutes over 12 hours and analysed. Mean levels of both LH and progesterone were similar in the PMS and control groups. However, for both progesterone and LH there was a higher pulse frequency with a lesser amplitude for the PMS group compared with the control group. They suggested that this was due to neuroendocrine regulation of the corpus luteum.

1.4 Appetite, food intake and PMS

Increased appetite and 'carbohydrate craving' premenstrually has been documented in the literature in women with PMS. Increased food intake in normal healthy women not experiencing PMS symptoms has also been observed. The following discussion will review separately the literature on food intake during the menstrual cycle and food intake in women with PMS.

1.4.1 Energy and macronutrient intake over the menstrual cycle

The number of studies that have investigated nutrient and energy intake over the menstrual cycle have been relatively small. The studies that have been reported in the literature vary in the dietary methodologies used as well as the how nutrient intake has been reported.

Dalvit-McPhillips (1983) used a 24-hour recall method to measure energy and macronutrient intake. Eight women, aged 18-22 years, took part in the study. They were interviewed daily for 60 days (two menstrual cycles) regarding their food intake during the previous 24 hours. Energy and macronutrient intake was averaged over 10 days premenstrually and 10 days postmenstrually. Comparison of the premenstrual and postmenstrual data showed a significant change, during the menstrual cycle, for carbohydrate content of the diet but not for protein or fat. The average postmenstrual intake was 51.6% to 56.4% of the premenstrual intake. There was no significant difference in the proportion of macronutrients when calculated per 1000 kcal between the premenstrual and postmenstrual

phases. Plinar et al (1983) also showed an increase in energy intake during the luteal phase. The methodology used was also 24-hour recall. However, the mean intake was based on only one day's recall during the mid follicular and mid luteal phases. Thirty-four women took part. A later study in a small group of women (seven, aged 24-43 years) performed by Gong et al. (1989) supported these findings. They used a better defined method for measuring food intake. Meals were prepared, served and eaten in the dormitory dining area. Prior to eating their meals, the foods selected were weighed, as was the plate wastage. For meals eaten outside this area, they recorded the quantities eaten. Daily temperature records were also kept to determine day of ovulation. Energy intake was greater during the luteal phase than the follicular or periovulatory phases. There was a mean 214 kcal difference between the luteal and follicular phases. Macronutrient intake was not reported. However sucrose intake was measured, with no significant difference being found over the menstrual cycle.

In another study a group of 11 healthy women, living in a university hostel, was followed over two cycles for a total time of 60 days (Manocha et al, 1989). Women participating in this study kept detailed diet diaries which were checked and collected at the end of each day. Subjects were asked retrospectively for their dates of menses. The mean energy intake (difference of 320kcal) was significantly greater during the 10-day premenstrual phase when compared to the 10-day postmenstrual intake. Lissner et al (1988) found in a group of 24 normal weight women a mean energy intake of 364kJ higher in the 10 days premenstrually compared

with 10 days postmenstrually. In this study, food was provided (breakfast and dinner) and eaten in the dining area or taken out (lunch and snacks). Any left over food was returned and measured. In another study 14 healthy women were followed over one year with a retrospective indication of the timings of up to 4 menstrual cycles. Tarasuk et al. (1991) found an overall increase in energy and fat intake premenstrually. In addition, there was an increase in fat/1000kcal but no significant change in total carbohydrate or protein intake.

More recent studies have supported these findings. In a balanced randomised study (Martini et al, 1994), subjects kept 3-day diet diaries over 4-7 menstrual cycles. Diaries were completed during the midfollicular and midluteal phases. Urinary LH levels and basal body temperature were used to confirm ovulation. Eighteen subjects, aged 20-34 years completed the study. Analysis of energy and macronutrient intake showed a significant increase in both, during the midluteal phase. The mean energy difference was 159 kcal and carbohydrate 15.3g. In another recent study using the diet diary method similar results have been reported (Barr et al, 1995). Forty-two women took part in this study. Twenty-nine of these were shown to have ovulated (based on basal temperature measurements). Three-day diet diaries were kept over three menstrual cycles. Diaries were completed at the beginning, middle or end of each cycle. The sequence in which they were kept was randomised. In the women who had been shown to have ovulated, there was a mean difference of 1259 kJ between the luteal and follicular phases. In the group of women that had not ovulated, no

significant difference was found. There was no difference in the macronutrient intake when expressed as a percentage of energy. Li et al. (1999) reported similar findings, where they investigated the food intake of 20 Chinese university students. They found a significantly higher kilojoule, carbohydrate (15% greater) and fat (21% greater) intake during the late luteal phase.

Other studies have failed to show any significant difference in nutrient of food intake. Tomelleri et al (1987) followed 83 young women with normal cycles for 6 weeks. A questionnaire, which measured food craving on a 7-point scale, was completed weekly and subjects were asked to code on a 5-point scale how their food consumption during the previous 24 hours differed from normal. There were no significant differences detected except for a preference for chocolate during menstruation. In another study that used diet diary methodology (Lyons et al, 1989), no difference in the mean energy intake between premenstrual (10 days) and postmenstrual (10days) phases was found. Fong et al (1993) monitored nine subjects aged 23-35years in a controlled environment, a metabolic ward. Physical activity was controlled and based on the activity recorded over 7 days prior to the subjects entering the study. The diet including fluids was ad libitum. Subjects selected food from the menu and this was pre weighed before being served. Nutrient intake was analysed according to four defined phases of the menstrual cycle. The phases were: follicular (days -24 to -17), periovulatory (days -16 to -14), luteal (days -12 to-1) and menses (4 days). The mean energy, protein and fat were highest during the luteal phase and

lowest in the periovulatory phase. However, the difference was not statistically significant. Carbohydrate intake was the highest during menses and lowest during the periovulatory phase. The reported significance was marginal ($p < 0.06$).

1.4.2 Nutrient intake over the menstrual cycle in women with PMS

In women with PMS, increased appetite during the late luteal phase is also often reported. Very few studies have included the analysis of food intake during this time. Wurtman et al (1989) investigated 19 patients with PMS and 9 controls. Each subject was admitted as an inpatient for 48 hours during day 4-7 of the follicular phase and days 3-5 of the late luteal phase. Food was available ad libitum during the study as main meals or predefined snacks between meals. Analysis of food intake showed an overall increase in energy intake during the late luteal phase. There was an increase in carbohydrate (both simple and complex) intake during this phase in subjects with PMS. The increase was 24% for meals and 43% for snacks. Protein intake remained unchanged and fat intake increased in proportion to energy. The controls did not show a significant change in energy and nutrient intake. They also showed that the consumption of a carbohydrate rich meal improved depression, tension, anger, confusion and alertness in women with PMS and had no statistically significant effect in the controls.

The majority of studies, which have reported increased appetite during the late luteal phase for women identified to be suffering with PMS, have used

questionnaires that included questions on appetite and intake of specific foods. Both-Orthman et al (1988) using a daily questionnaire to measure appetite and mood over a period of 2 to 9 months showed a significant increase in appetite in both women with PMS and controls. However the effect was greater in women with PMS and this correlated with self-rating of mood.

1.4.3 Food craving

This thesis does not directly investigate food cravings in women with PMS. However as discussed above the 'craving' of carbohydrates by women with PMS has been reported and this thesis investigates the hypothesis that there is an increased premenstrual carbohydrate intake in women with PMS which is suppressed by increasing brain serotonin levels. Therefore, a review of the literature in this area is relevant to the discussion of this study's findings.

Both the concept and the existence of 'craving' have been extensively discussed in the literature. Much of the published work relates to the 'craving' of alcohol and drugs. Theories used to explain 'cravings' in alcohol and drugs have been applied to explain cravings of food. A satisfactory definition of the term 'craving' and standardized measures to assess it has yet to be developed. Within the context of food consumption, the term craving has been related to excessive eating or an extreme desire for certain foods. Weingarten et al (1990) in an excellent review on food cravings, mainly from a psychological perspective, highlight some of the

issues and theories relating to use of the term 'craving' by the scientific community. In relation to the use of the term itself they write '*if the craving concept is to be instructive in the illumination of drug and food intake there must be additional consideration to the meaning of the construct itself and to the development of scales for measuring and quantifying the state*' and '*nearly all investigator converge on a common explanation ... that cravings are elicited by need, and therefore, cravings serve to correct bodily needs*'. Their paper continues to discuss food cravings in various conditions including 'carbohydrate craving' during the menstrual cycle.

From the nutritional point of view, the term 'carbohydrate craving' during the premenstrual phase of the menstrual cycle has been argued to be a misnomer. The majority of foods that are referred to as high carbohydrate tend to be chocolates and other sweet foods; many of these foods also contain a significant amount of fat as well as varying amounts of protein (Hill et al, 1994; Dye et al, 1995). If carbohydrate was being 'craved' then one would also expect foods such as bread and other cereal products to be 'craved' and this is not the case. It would therefore be more appropriate to term this a preference for sweet tasting foods.

Hill et al (1991) investigated food cravings using a visual analogue scale that looked at frequency and intensity of 'a strong urge to eat' among 206 women. They found a strong relationship between mood and eating for those that were defined as 'cravers'. In the second part of their study a small group of women that were identified as cravers and non-cravers

completed food diaries, mood and hunger ratings and a qualitative craving record. For 6/10 cravers that experienced negative moods and hunger prior to eating the craved foods, moods improved. In three cravers eating did not lead to mood improvement but not eating did. In this very small group of women defined as cravers all but one craved sweet foods, with the most frequently craved food being chocolate. Also of interest is that they detected no significant difference between the energy intakes of the two groups. Weingarten et al (1991) in a survey of 1138 Canadian students found that food craving was a common experience, with 97% of women and 68% men reporting having experienced it in the past. The foods craved and the related triggers differed between men and women. Women nominated chocolate to be the food most frequently craved, with boredom, stress and television commercials precipitating the craving, while for men reported chocolate craving less frequently and their food cravings were preceded by the feeling of hunger. Rozin et al (1991) in a survey of undergraduate students reported similar findings. They found that chocolate was most often 'craved' by female students and that this craving peaked during the late luteal phase.

1.5 Serotonin and appetite in premenstrual syndrome

1.5.1 Serotonin and appetite

The regulation of appetite is complex. It includes the brain, neurological, and physiological aspects. Figure 2 provides a simplified outline of the regulation of appetite. It is also modified by emotional and social influences. Within the brain several neurotransmitters have been identified to participate in appetite regulation. These include serotonin, noradrenaline, cholecystokinin, endogenous opioids and neuropeptide Y. (Wallin et al, 1994). In this section, serotonin and its influence on appetite will be discussed, as low brain levels of serotonin have been implicated in the increased premenstrual appetite reported in some women. Increased brain serotonin activity suppresses appetite.

Serotonin is thought to play an important role in the regulation and control of food intake, and mood and the regulation of circadian and seasonal rhythms (Wallin et al, 1994).

Reduced brain serotonin has been implicated as having a role in the increase in food consumption premenstrually. It has been postulated that in women with PMS, brain serotonin levels are low and 'serotonin deficiency' has been postulated as a possible cause. This has in part been based on reduced prolactin responses to fenfluramine challenges in women with PMS (Fitzgerald et al, 1997). However other work contradicts these findings (Bancroft et al, 1995). The increase in food intake, in particular foods high in carbohydrate is a response by the body to increase brain

serotonin levels. Serotonin is produced from tryptophan. Tryptophan competes with other large nucleic amino acids (LNAA) to pass across the blood brain barrier. The ratio of tryptophan to other LNAA influences brain tryptophan levels (Fernstrom et al, 1994). Tryptophan competes with other amino acids for non-selective carriers across the blood brain barriers. Insulin plays a role by increasing the uptake of most amino acids by muscle cells except for tryptophan. The consumption of foods containing carbohydrate leads to an increase in insulin production (Norton et al, 1993). This leads to a relative rise in blood tryptophan concentration and consequently an increase in brain tryptophan levels.

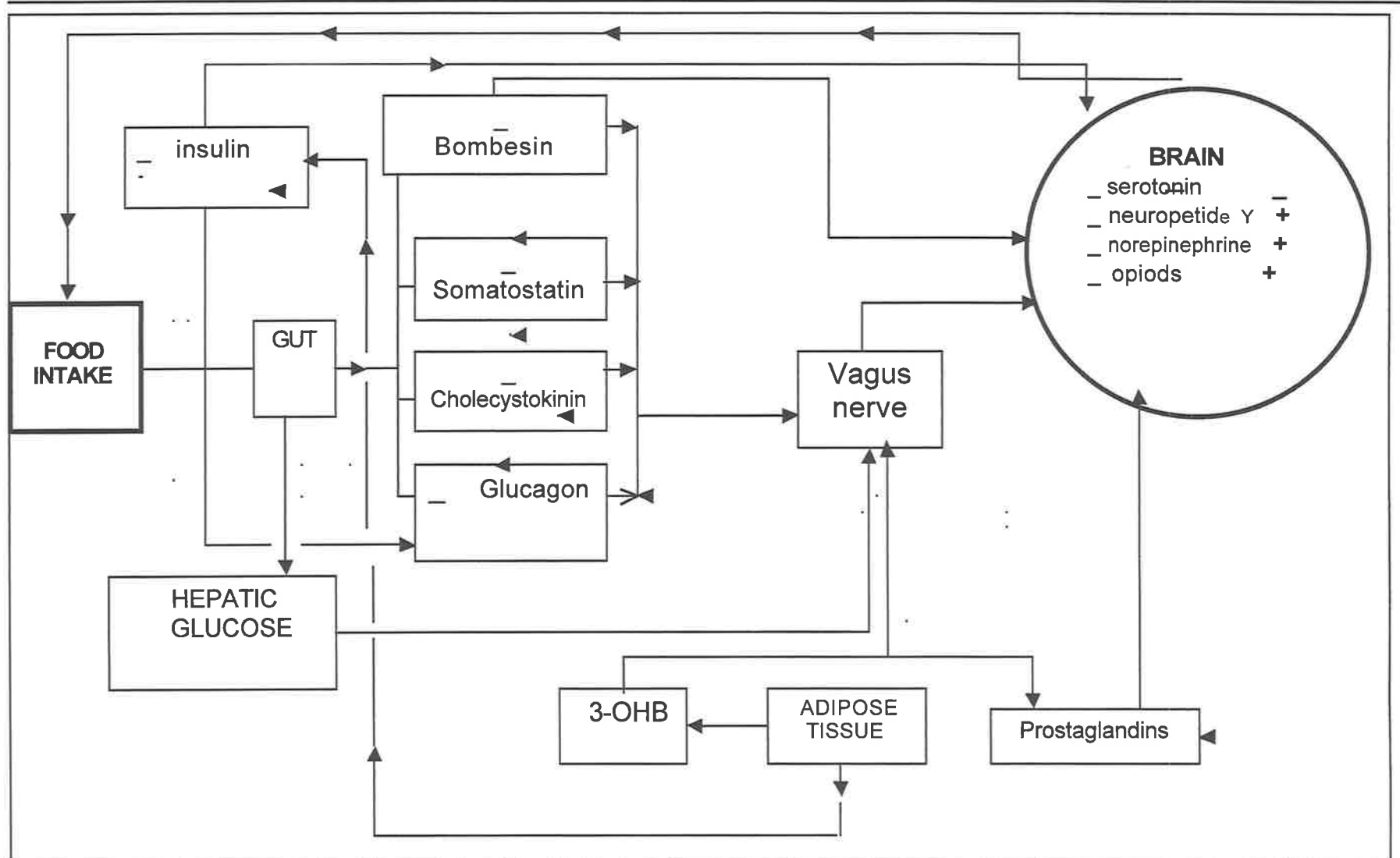


Figure 2 A simplified representation of the regulation of food intake, from changes occurring in the brain and peripheral systems in response to food intake (3-OHB is 3 hydroxybutyrate, in the brain + represents neural signals that stimulate and -ve inhibits food intake.) Modified from diagram by Norton et al, 1993.

Evidence that the nutrient content of the diet can influence tryptophan levels has come from both animal and human studies. Fasted rats fed a protein free, high carbohydrate meal exhibited increased tryptophan levels and elevated serotonin synthesis in the hypothalamus and cortex. When fed a high protein meal, serotonin synthesis and brain tryptophan levels remained unchanged or decreased if this meal was given two hours after the high carbohydrate meal (Fernstrom et al, 1995).

Blum et al (1992) investigated 5-HT levels in subjects after they had consumed a meal high in carbohydrate, fat or protein. They found that consumption of a high carbohydrate diet led to a four-fold increase in blood 5-HT. However, whether this influenced brain 5-HT and subsequently serotonin levels cannot be determined. Other work has shown that small amounts of protein in the diet can negate the influence on brain serotonin levels. In this study the high carbohydrate diet contain 12% protein.

1.5.2 Serotonin in the central nervous system

Serotonin occurs in high concentrations in the paraventricular nucleus. There are also high concentrations of norepinephrine and the opioid μ -endorphin both of which act to increase food intake. Serotonin may suppress food intake by inhibiting norepinephrine and opioid μ -endorphin.

Leibowitz et al (1998) reviewed the role of hypothalamic serotonin on the control of eating behaviour. They reported that in animal studies the administration of serotonergic agonists either peripherally or in the hypothalamus influenced the duration of individual meals or reduced their size. The commencement of meals and their frequency were unaffected. This seemed to indicate that 5-HT primarily influences when eating stops. Animal studies where 5-HT had been given indicate that 5-HT modulates appetite for specific foods (Shor-Posner et al, 1986, Blundell 1992). There appears to be feedback of carbohydrate intake on 5-HT levels in the hypothalamus and brain stem.

A relationship between brain levels of serotonin and dietary behaviour has been implied from these studies. However, such implication cannot be substantiated in human studies. For example, Fernstrom (1994) argues that if humans did crave carbohydrate as a response to low brain 5-HT levels, then any high carbohydrate food would be eaten. This is however not the case. Carbohydrate cravers tend to eat sweet foods and these foods tend to be high in fat. These foods also tend to contain protein at a level that would negate this effect.

A review of the evidence for the role of serotonin in PMS by Rubinow et al (1998) led them to suggest that serotonin did have a role. They drew on 3 lines of evidence. The first being that serotonin seems to modulate a range

of behaviours in women with PMS. These included mood, impulsivity and appetite. Secondly, measurement of platelet levels and total serotonin levels were lower in those women with PMS compared to controls in the late luteal phase. Lastly, serotonin-enhancing drugs have been shown to be effective in alleviating PMS symptoms.

1.6 Oestrogen and progesterone influences on appetite

Measurement of energy expenditure shows changes occurring over the menstrual cycle, with expenditure increasing during postovulatory or the luteal phase (Solomon et al, 1982, Meijer et al, 1992, Webb, 1986). Increases in the total energy expenditure have been found to range from 8-16% (Webb, 1986) when compared to the pre-ovulatory phase. This increase is believed to be due to increased levels of progesterone during this stage of the menstrual cycle.

Animal studies indicate that steroid hormones such as oestrogen and progesterone may influence appetite (Buffenstein et al, 1995). In terms of food intake animal studies have found that food consumption is reduced during ovulation when oestrogen is at its peak followed by an increase in intake, corresponding to the peaking of progesterone (Wade et al, 1992). Evidence from animal studies suggests that oestrogen acts directly on areas within the hypothalamus to suppress food intake (Bonavera et al, 1994). However, there does not appear to be a relationship between progesterone

and appetite as ovariectomised animals exhibited no change in food consumption when given progesterone.

1.7 Dexfenfluramine: mode of action and influence on appetite

Dexfenfluramine is the dextro isomer of dl-fenfluramine. Dexfenfluramine acts by stimulating the release of serotonin from the presynaptic axon terminals and inhibit neuronal reuptake (Garattini et al, 1975, Garattini et al, 1992). As a result there is an increase in serotonin receptor activation. Its primary effect is to enhance serotonergic transmission in the feeding centres of the ventro-medial nucleus of the hypothalamus.

Dexfenfluramine had been used until its withdrawal from use primarily as an adjunct to weight reduction in obese patients. Its effects in this context were to reduce weight by reducing food intake through its anorectic effect (Enzi et al, 1988, Finer et al, 1985). These studies were only of 3 months duration. As obesity is a chronic condition, with treatment effectiveness reducing with time a longer trial over 1 year, known as the International Dexfenfluramine Study (INDEX) was conducted. This study was a double blind randomised placebo controlled study (Guy-Grand et al, 1989). It involved 822 subjects who were greater than 120% of their ideal weight. Subjects taking dexfenfluramine had a mean weight loss of 9.8 kg over a 1-year period compared to 7.15 kg for the placebo group. Much of the weight loss occurred during the first 6 months in both the groups. However, those

on dexfenfluramine tended to maintain their weight loss while the placebo group regained some of their initial weight. The side effects experienced by the participants on dexfenfluramine included increased tiredness, diarrhoea, mouth dryness and polyuria. Dexfenfluramine has also been trialed in patients with seasonal affective disorder (O'Rourke et al, 1987) and PMS (Brzezinski et al, 1990).

The effect of dexfenfluramine has been suggested to include specific suppression of carbohydrate consumption in both obese subjects (Wurtman et al, 1985) and those experiencing PMS (Brzezinski et al, 1990). This proposed influence of dexfenfluramine has contributed to the theory that the increased appetite observed premenstrually during the late luteal phase is due to low brain serotonin levels. (See section 1.5.2) These findings have contributed towards the hypotheses developed in this thesis. Other reported work using dexfenfluramine does not support that dexfenfluramine specifically suppresses carbohydrate intake. For example, Mathus-Vliegen et al, 1993) as part of the INDEX study mentioned above looked at food intake in these women and found no change in the percentage of energy from carbohydrate containing foods.

Fitzgerald et al (1997) in a study comparing 9 women with PMS to 11 controls in a placebo controlled trial found that the prolactin response to fenfluramine in women with PMS was significantly reduced.

1.8 Background to rationale for thesis

The review of the literature indicates that the findings of the small amount of published research on the relationship between food intakes in women with PMS are inconclusive. Some researchers such as Wurtman et al (1989) have suggested that women with PMS have an increased premenstrual preference for high carbohydrate foods. They propose that this preference for carbohydrate containing foods is due to a reduced level of brain serotonin. It is argued that a high carbohydrate diet, by increasing the ratio of tryptophan to LNAA, which in turn supports the transport of tryptophan across the blood brain barrier. As tryptophan is the precursor of serotonin, this leads to increased serotonin production. Other work (Bancroft et al, 1995, Fernstrom et al, 1994) disputes these findings.

Research that has investigated food intake in women with PMS has been minimal and has looked at women's food intake for 2 days premenstrually and 2 days postmenstrually over one cycle (Wurtman et al, 1989). Women's food intake was investigated within an inpatient setting.

The work presented in this thesis resulted from the opportunity to investigate the food consumption of overweight women with PMS who were participating in a double blind randomised placebo controlled study. The study allowed for an in depth investigation of the foods being eaten by women over 3 menstrual cycles and the effect of dexfenfluramine, which enhances brain serotonin levels, on the types of foods eaten. Such an

investigation that looked at both macronutrient and types of foods being consumed in overweight women has not previously been reported in the published literature and was seen as having the potential to contribute significantly towards further understanding in this area.

1.9 Research Aims and Hypotheses

1.9.1 Aims

The aims of this thesis are:

1. To investigate macronutrient intake of overweight women who have been identified as having Premenstrual Syndrome including a premenstrual increase in carbohydrate intake by:
 - Using diet diary methodology to estimate nutrient intake during the late luteal and follicular phases of the menstrual cycle.
2. To investigate whether there is a relationship between any change occurring in macronutrient intake and total energy intake and the severity of PMS symptoms.
3. To investigate whether increasing the availability of serotonin by the use of dexfenfluramine specifically reduces carbohydrate intake and craving over 3 menstrual cycles by:
 - Comparing macronutrient intake including carbohydrate over 3 menstrual cycles between women on dexfenfluramine and placebo.
 - Comparing total energy pre and postmenstrually between women taking dexfenfluramine and placebo.
 - Comparing reported changes in appetite and craving for sweet foods as recorded by subjects in PMS Steiner self rated questionnaire.

1.9.2 Hypotheses

Hypothesis 1

There are overweight women who as part of their PMS symptoms specifically increase their premenstrual consumption of carbohydrate containing foods rather than just increasing their total food intake.

Hypothesis 2

Dexfenfluramine specifically prevents an increase in premenstrual carbohydrate intake in overweight women identified to have an increase in carbohydrate as part of their PMS symptoms.

Hypothesis 3

There is a relationship between the severity of PMS symptoms as measured by the Steiner self rated questionnaire and change food intake where:

- a) The change between pre and postmenstrual carbohydrate and total energy intake is greater in subjects with more severe symptoms.
- b) The number of 'episodes of eating' is greater in women with more severe symptoms.

CHAPTER 2

Methods

Part 1: Screening methods

2. Introduction

The following section details firstly the methods used to screen volunteers for entry into the randomised double blind placebo controlled study and secondly, the methods used to analyse the nutrient data collected during the screening process. The criteria for entry into the randomised study included a premenstrual carbohydrate intake 15% higher than postmenstrual intake. Other nutrient intake information was not directly relevant during the screening process. However, it was relevant to the aims and hypotheses presented here and are therefore included under screening methods.

2.1 Subject recruitment into the screening phase

Women were recruited into the study using posters and through the local newspapers. Initial contact was via the telephone interview and a follow up appointment was made for potential study participants if they were thought to meet the study criteria. Attendance at the appointment constituted further screening. Women, who met the initial selection criteria and provided written consent to take part, commenced the screening process.

The project nurse interviewed volunteers who met the criteria to enter the screening process. A medical practitioner also interviewed and examined

all the volunteers. The aim of the screening was to identify women who met the criteria for premenstrual syndrome.

2.1.2 Eligibility Criteria for entry into the screening process

The following criteria were used at the initial interview for selection and inclusion in the screening process. Women were required:

- to be over the age of 18 years
- to be premenopausal
- to have a regular menstrual cycle and not intend to become pregnant during the study time period
- if BMI > 25 or < 35 kg/m²
- to have had a stable weight over 3 months prior to commencing the screening process.

Women were excluded from the screening process for the following reasons:

- if they suffered from non-cyclical psychopathology, psychosis, affective disorder or alcohol or drug abuse
- had diabetes or any endocrine disorder that was predisposing to obesity
- suffered from cardiovascular, respiratory, neurological, endocrine, renal or haematological disease that contraindicated their participation
- if BMI < 25 or > 35 kg/m²
- were participating in a supervised weight loss program or attempting to lose weight

- were on any medications that could potentially interact with dexfenfluramine such as MAO inhibitors, antidepressants, anti-serotonergic drugs
- had a history of severe allergies or multiple adverse drug reactions
- were participating in any other study during the study period.

2.2 The screening process

The screening process occurred over 2 menstrual cycles. It included the use of two questionnaires; the Nottingham Health Profile (Hunt et al, 1981) and the Steiner premenstrual tension (Steiner et al, 1980) self rated questionnaire as well as the completion of food intake diaries at predetermined intervals over the menstrual cycles. The questionnaires were completed as part of the broader study. The scores from the questionnaires are used within the context of this work to investigate whether there is a link between these scores and nutrient intake.

2.2.1 Anthropometrics and other measures

For each participant entering into the screening process, height (cm), weight (kg), hip (cm) and waist (cm) measures were taken. These measures were taken by the project nurse. Other measures taken were systolic and diastolic blood pressure. These were not part of this investigation and therefore not reported here.

2.2.2 Administration of the Steiner self rated Premenstrual Syndrome and Nottingham Health Profile Questionnaires

The self rated Steiner PMS questionnaire was used to identify women who exhibited premenstrual syndrome (PMS) and the Nottingham Health Profile (NHP) questionnaire provided an indication of general well being. A copy of each questionnaire appears in the appendix. They were both self administered by the subjects. Each questionnaire was completed 2 days prior to the expected day of menses (day -2) and on day 5 after the commencement of menses (day +5).

Women were instructed on how and when to complete the questionnaires by the project nurse. This was followed up by a reminder phone call prior to the time the questionnaires (and the food diaries) were due to be completed. Screening took place over 2 menstrual cycles, with allowances for this to be extended to a third menstrual cycle. For subjects where a third cycle was included 2 of the 3 assessments were required to meet the criteria as well as exhibiting 15% higher carbohydrate intake premenstrually compared to postmenstrually.

Subjects met the criteria for participation into the randomised double blind placebo controlled study if the premenstrual score was ≥ 10 compared to the postmenstrual score for the Steiner self-rated questionnaire.

2.2.3 Retrospective categorisation of premenstrual symptoms

During the initial visit women were asked to rate how severe they perceived their symptoms to be and the length of time they had experienced these symptoms. The symptoms were scored according to whether they were mild, moderate or severe.

2.2.4 Food intake documentation

The documenting of food consumption either by recall, food frequency or diet records all have specific shortcomings (Barrett-Connor, 1991, Beaton et al 1997). In addition the reliability of all these methods varies with the population group being studied. Both under and over reporting occurs, with under reporting seeming to be more prevalent (Mertz et al, 1991). Based on the requirements of the study, which was to assess and compare the pre and post menstrual food consumption over several days, the requirement to identify the actual foods eaten by subjects the recording of food intake using the diet record method was selected as being the most appropriate.

At the initial screening appointment all the women were also interviewed by a dietitian (myself). A diet history and food frequency intake was collected from each subject. At this interview women were also provided with detailed instructions on how and when to document their food and fluid intake in their food diaries. Participants in the study were also requested to include details such as recipes for prepared dishes, brand names of any commercial products and if eating food outside the home to

provide details about where they ate. Detailed instruction on the use of household measures and the recording of food and drink consumed was provided along with a metric measuring cup to assist in the measurement of the amounts of food eaten.

The diet diaries were based on those used by the Department of Nutrition and Food Service, Clinical Dietetics at Royal Adelaide Hospital (see appendix for example). The diet diaries included an example on how to fill in a diary and a series of guidelines (eg estimating serving sizes) on how to complete the diary

Women were instructed to commence their food diaries 4 days prior to the estimated onset of menses (late luteal phase) and for 4 day postmenstrually commencing on day 5 after menstruation had begun. All food and drink eaten during this time was to be recorded. If menses did not occur on the predicted day, subjects were instructed to continue recording their food intake until it occurred. In these cases, the food intake for the four days prior to the onset of menses was analysed. In cases where menses occurred early, subjects continued with the screening process for another cycle (16 women completed a third cycle).

The number of days chosen was in part based on previous studies that compared the accuracy of food records over time (Basiotis, 1987; Potoska et al, 1990). Four days was considered optimal in terms of compliance and accuracy as well as minimising the burden on volunteers. The timings of

the diet diaries was based on studies from the literature, which showed that premenstrual symptoms worsened during the last week prior to the onset of menstruation and significantly decreased by day 5 from the commencement of menstruation (Bancroft et al, 1988, Both-Orthman et al, 1988).

One to two days prior to the estimated day that a woman would be commencing the recording of her food intake, a reminder phone call was made. Women were requested to return the diet diaries as soon as possible after their completion. On return of the diaries, they were checked and participants in the study were contacted by phone regarding any clarifications required.

2.3 Nutritional analysis of food intake data

The food diaries were analysed using Diet3 Version 4.22 (Xyris software Pty Ltd, Highgate Hill, Queensland Australia), an Australian developed nutrient analysis program. Additional nutrient data for commercial food products was obtained from some of the larger food companies and added to the database. For food products that did not have reliable nutrient content data or no data were available, comparable food products were used. Where participants provided recipes these were entered into the recipe section of Diet 3 and used when inputting that participant's food intake.

The diet diaries were analysed for the following nutrients:

- Protein (g)
- Fat (g)
- Total carbohydrate (g)
- Complex carbohydrates (g)
- Simple sugars (g)
- Alcohol (g)

Total energy intake (kilojoules) was also calculated.

For each subject the food consumed per day was entered into the Diet 3 program as soon as the diaries were returned. Daily intakes were analysed and mean over each 4 day period, pre and postmenstrually, calculated by the Diet 3 program. The initial design of the study was such that the mean postmenstrual intake at menses -2 (see Figure 4, p52) was compared to the premenstrual intake of the following cycle (menses -1). The individual's food intake was firstly analysed for total carbohydrate to assess whether the study entry criteria of an increase of fifteen percent or greater premenstrual in the intake of carbohydrate.

In the comparison between the pre and postmenstrual nutrient intake during the screening process (presented in Chapter 3), the mean pre and postmenstrual nutrient data from 2-3 menstrual cycles was used. Prior to doing this a statistical comparison of the postmenstrual data over 2 (or 3) menstrual cycles was performed using ttests. No significant differences were detected between these. A similar process was performed for the premenstrual data, with no significant difference being detected.

2.3.1 Application of Goldberg's cut-off limit

Inaccurate reporting of food intake by subjects has been widely described on and discussed in the literature. Over weight or obese subjects are particularly prone to under report the quantity of food they consume. Taking account of inaccurate reporting of food consumption in subjects in a 'free living situation' when analysing food intake data is difficult. One method of addressing inaccurate food intake reporting when analysing data has been proposed by Goldberg et al (1991).

Goldberg's cut-off limit (Goldberg et al, 1991, Black et al, 1991) has been used as an indication of the reliability and the level of possible under reporting of food consumption. Goldberg et al (1991) estimated minimum energy intake cut off limits based on the analysis of data from studies that measured energy using whole body calorimetry and doubly labelled water. They then developed tables of cut-off limits based on the number of days that intake was recorded and the sample size. These cut- off limits have been used in the literature and the 1995 Australian National Nutrition Survey to exclude food intake data that reflected intakes incompatible with actual or estimated energy requirements. The cut-off limits have been primarily used to identify under reporting. However, they can also be used to account for excessive over reporting of actual food intake and this has been discussed by Goldberg et al (1998).

To exclude energy intakes that would be incompatible with life, Goldberg's cut-off limit was applied to the 'screening' food intake data to exclude these

subjects (Black 2000). The cut-off limit was applied to exclude food intake data after the use of the following formula:

$$\frac{\text{Recorded mean energy intake (EI)}}{\text{BMR (predicted basal metabolic rate)}}$$

The predicted basal metabolic rate was calculated using Schofield's equation (Schofield et al, 1985).

Food intake data of subjects were excluded if $\text{EI: BMR} < 1.06$ (cut-off limit for individual subjects for food records kept for 4 days using 95% confidence limits). This cut-off limit assumes a sedentary lifestyle. As the reporting of physical activity levels was not included in this study it was not possible to take account of this when excluding subjects. Thus an unknown number of subjects that are included in this part of the analysis may have been excluded if the physical activity level was known.

The cut-off limit was applied separately to the mean pre and postmenstrual data as two separate sets of data to be used as comparison against one another in the study. The application of Goldberg's cut-off limit to the data resulted in a different number of exclusions depending on whether the pre or post menstrual data was used. The postmenstrual data resulted in the largest number of subjects being excluded. Another problem that arose was that a few of the subjects that would have been excluded according to their premenstrual intake would not have been excluded based on their postmenstrual energy intake.

Use of the premenstrual dietary intake data resulted in the exclusion of 31 women, 11 of these had met the PMS criteria and 20 had not. This data was analysed in the same way as for all women who had completed the screening process. The findings from this analysis are presented in Chapter 2.

2.3.2 Analysis of food diaries according to food categories

To investigate whether the differences observed between the pre and postmenstrual nutrient analyses was due to the quantities of food consumed and/ or the types of foods eaten, foods were grouped into categories.

The food categories are based on those used by Magarey et al (1995), with reference to the Australian National Nutrition survey (1995), with a number of modifications as follows: the grouping of meat, fish, poultry and eggs into one category, nuts were included under the *snack food* category rather than under vegetables, and cream included in the fat category rather than the dairy products category. The food categories used in this study appear in Figure 3 below.

Figure 3. The food categories used for analysis of food intake data

<i>Food Categories</i>	<i>Foods included within category</i>
Cereals products	Breakfast cereals, breads, crumpets, English style muffins, pasta, rice, semolina, dry biscuits
Dairy products	Milk, cheese, unsweetened plain yoghurt, Soy milks
Meat, poultry, fish and eggs	All meats including processed meats, sausages, chicken, turkey, fish and shellfish
Savoury foods	Pizza, pies, pasties, soups, casseroles and other mixed meat and vegetable dishes, vegemite and savoury spreads
Vegetables	All vegetables, fresh, dried and frozen
Fruit	All fresh, tinned, frozen and dried fruit
Fats	Oil, margarine, butter, cream
Cakes and desserts	Cakes, buns, sweet biscuits, ice-cream, custard, home made and commercial desserts, sweet yoghurt (sweetened with sugar or artificial sweetener)
High sugar foods	Confectionary, jams, honey, sugar added to cereal and drinks, sweet drink additives, non dairy iceblocks
Snack foods	Potato crisps, corn chips, extruded snacks, nuts
Beverages	Soft drinks, cordials, fruit juices, fruit juice drinks, flavoured milks, hot chocolate and related drinks, alcoholic beverages

For each subject, macronutrient and total energy intake was calculated for each of the above food categories. All foods consumed by each subject were allocated to one of the food categories using the original print out of individual foods consumed with their nutrient content. This data recorded

individual foods consumed and nutrient analysis for each day. Using Excel 97 (Microsoft Office 97), macronutrients and energy data for four days was entered into separate spreadsheets for each subject. This data was then imported into Stata 6 and used to calculate the sum and mean over four days for each nutrient in each of the food categories. The premenstrual and postmenstrual mean over two or three basal cycles was used in the statistical analysis.

2.3.3 Analysis of the frequency of food consumption

The analysis of the frequency of daily food intake was decided upon retrospectively. The decision was based on observed changes in energy and macronutrient intake over the menstrual cycle. The analysis was designed to answer the following question:

Did this change in food intake reflect solely a change in quantities being eaten or did the number of meals and snacks intake change?’

The food diaries were used to investigate whether the 'number of episodes' of eating differed premenstrually compared with postmenstrually. The documentation in the food diaries included the times at which foods were eaten. This allowed for the number of episodes of eating a meal or a snack during the day to be counted and the mean over 4 days calculated for the premenstrual and postmenstrual intervals.

The numbers of episodes of eating were not separated into meals and snacks, although this was the original intention. This was due to the

difficulty in determining the difference between a meal and snack for some of the participants. For example, one subject appeared to eat small snacks throughout the day; another appeared to have 4 moderately sized 'meals'. Intakes of fluids eg tea, coffee, soft drinks were not included.

2.4 Statistical analysis

All statistical analyses were performed using Stata 6.0. Advice, regarding the appropriate tests to be applied when analysing data was provided by a statistician, when required. If advice was obtained this is referred to in the text.

2.4.1 Subjects included in the statistical analysis

Statistical analysis was performed on the screening data from all women who completed the screening process. One hundred and forty-four completed the screening and eighty-eight women met the criteria for entry into the study.

2.4.2 Creation of new variables

2.4.2.1 *Calculation of percent change in nutrient intake*

a. Change in percent of carbohydrate intake

The percent change between pre and postmenstrual carbohydrate intake for subjects during screening was performed on a subject by subject basis using a calculator. The percent change was calculated using the following formula:

Percentage change in carbohydrate intake =

$$\frac{\text{Pre -post menstrual carbohydrate intake (g)}}{\text{Premenstrual carbohydrate intake (g)}} \times 100$$

If a subject's premenstrual carbohydrate intake was greater or equal to 15% more than postmenstrual intake, then she was eligible for entry into the study, providing all the other criteria were met.

b. Calculation of percent change of energy and macronutrient intake between pre and postmenstrual phases

The calculation of percentage change between premenstrual and postmenstrual energy and macronutrient (protein, fat and carbohydrate plus complex carbohydrate and simple sugars) intake was performed with Stata 6.0 using the following formula:

$$\frac{\text{Percentage change in nutrient intake=}}{\frac{\text{Pre -post menstrual intake}}{\text{Premenstrual intake}}} \times 100$$

The mean percent change for each nutrient was then calculated using Stata 6.0.

2.4.2.2 *Calculation of macronutrient intake as percentage of energy*

Macronutrient intake was also compared by adjusting for energy using nutrient density methodology in order to assess whether there were any changes in the proportion of energy contributed by protein, fat and carbohydrate. This method calculates the percentage of energy contributed by each macronutrient. The formula used is displayed below and was calculated using Stata 6.

$$\text{Percentage of energy from macronutrient} = \frac{(\text{Macronutrient (g)} \times \text{energy (kJ) per g nutrient})}{\text{Total energy intake}} \times 100$$

2.4.2.3 *Calculation of the percentage that each food category contributed to the total energy or macronutrient intake*

As outlined in section 2.3.2, food intake data was also analysed according to defined food categories. The data for energy and macronutrients for each food category is presented as absolute amounts and as a percentage of the total energy and macronutrient contributed by each food category. The formula used in calculating the percentage contribution by each food category using Stata 6 was:

$$\text{Percentage kilojoule or macronutrient contributed by each food category} = \frac{\text{Kilojoules or g (macronutrient) from food category}}{\text{Total kilojoule/ macronutrient intake}} \times 100$$

2.4.3 Testing nutrient data for significance

Paired t-tests were used for normally distributed variables to compare the energy and macronutrient intake between the premenstrual and postmenstrual phases. Unpaired t-tests were used when comparing data normally distributed for unrelated samples. Where data were not normally distributed the Wilcoxon sign rank test was used.

Normality of data was assessed using visual assessment of graphs for the individual variables and by performing the “*sktest*” (Hamilton, 1998). This tests for normality using skewness and kurtosis statistics. Data were judged to be non-normal when $p < 0.05$ in the joint skewness and kurtosis test. The energy (kilojoules) and macronutrient intake data, prior to modification was normally distributed. The food category data varied according to the food group.

2.4.4 Relationship between energy, macronutrient intake and the Steiner self rated PMS score

The Spearman's rank correlation coefficient was used to identify whether there was a relationship between the severity of PMS symptoms as measured by the Steiner self rated scores and the change in macronutrient and total energy intake.

Part 2: Randomised double blind placebo controlled study

2.5 Study design

A randomised, double blind placebo parallel plan was used for the study, which was conducted over 3 menstrual cycles. Women meeting the selection criteria (section 2.2.2, page 38) qualified for entry into the study and were randomly allocated to either taking dexfenfluramine (called the treatment group) or a placebo. Figure 4 outlines the study design including the timings when women completed their food intake diaries and measures such as weight were taken.

Eighty-eight women met the study criteria for randomisation. The women were blindly allocated to either the treatment (received Dexfenfluramine) or placebo group. Allocation to the treatment regime was external and was performed in a numerical order. Subjects that withdrew were replaced with additional subjects and allocated to the same treatment by an external monitor. Forty-four were allocated to each group. On commencement of the study, subjects took one capsule (15mg) per day of Dexfenfluramine or placebo for the first 5 days. This was increased to 2 (30mg) capsules per day, one in the morning and the other in the evening, for the remainder of the 12 weeks of the study.

Contact was made with the study participants monthly by phone or during their visit to the project nurse.

Figure 4. Outline of study design for the screening and study periods

Day of menstrual cycle	-2	+5	-4	-2	+5	-4	-2	+5	-4	-2	+5
Menstrual cycle	M-2		M-1		M1		M2		M3		
	Screening Period				Study period – menses 1-3						
Diet history	X										
Diet diary (4 day)	X		X	X	X	X	X	X	X	X	
*PMS quest	X	X	X	X	X	X	X	X	X	X	
†NHP Questionnaire	X	X	X	X	X	X	X	X	X	X	
Weight plus other measures (clinic)	X				X		X		X		
Weight (home)			X		X		X		X		
Clinic visit	X		X		X		X		X		
Compliance							X		X		

M= menses M-2 Day -4 = Menses 2 prior to study period on day 4 prior to the commencement of menses

* Steiner self rated questionnaire † Nottingham Health Profile

2.5.1 Steiner self-rated and Nottingham Health Profile Questionnaires

Steiner self rated questionnaire and the Nottingham Health profile were completed by each subject 2 days prior the predicted onset of menses (day-2) and on the fifth day after the commencement of menses (day +5). This data was used to investigate whether there was a relationship between the scores recorded and the food consumption data.

2.5.2 Administration of questionnaires

Participants were instructed to complete both the Steiner self rated questionnaire and the Nottingham profile on days -2 prior predicted onset of menses and day +5 after commencement of menses (see Section 2.2.2 for description of both of these questionnaires). Both questionnaires were returned together with the diet diaries as soon as practical after completion. Every participant received a reminder call the week prior menses. Participants also received a call if the questionnaires and food diaries were not returned at the estimated time post menses.

Upon receipt of the completed questionnaires, they were scored and the results were entered into the individual subjects' folder by the project nurse.

2.5.3 Anthropometric measurements

At each visit the study participants' weight (kg), hip (cm) and waist measures (cm) were taken by the project nurse. These visits occurred at approximately day 10 post menses. Women also weighed themselves at home on their own scales four days prior the predicted onset of menses. These measures were not included as part of the data analysis.

2.6 Food intake data collection

Each person in the study recorded her food intake at the same times during the menstrual cycle as was advised during the screening process. The foods and fluids consumed were recorded four days prior to menses and four days post menses, commencing from day 5. If menses occurred earlier than anticipated, food records were included in the analysis if kept for at least two days. Where women indicated that there was usually some variation (menses occurring 1-3 days earlier) in the predicted onset of menses they were requested to commence 7 days prior to predicted onset of menses. If the onset of menses was delayed, women were advised to continue to record their food intake until the onset of menses. In both these cases, the food records from the four days prior menses were used.

2.6.1 Returning and checking of food intake records

Women returned their diet diaries as soon as practical after completing their postmenstrual diary. On receipt of diaries, they were checked and subjects were contacted primarily by phone to clarify any aspects of their food records that was required.

2.6.2 Food data input

Data input from diet diaries followed the same process as described under section 2.3. Each subjects' records was printed out in full (4 day records) and checked against the original diary. The mean premenstrual and postmenstrual food intake for each subject was calculated using the Diet 3 program (Xyris). Diet diaries that contained 2-4 days of documented food intake were included in the analysis.

The mean nutrient intake was documented in each subject's case folder. Contracted data entry personnel entered these data together with other data (Steiner self-rated questionnaire and Nottingham Health Profile) into a database.

Data were also categorised into food groups as explained in Section 2.3.2. Results from the computer analysis for each subject was firstly entered into Excel 97 and then imported into Stata 6. The data were checked twice for accuracy. This was done by adding the macronutrient and energy contribution from each food category and cross checking against the original Diet 3 program data.

The Goldberg cut-off limit was not applied to the data presented. Given that the study included the use of an appetite suppressant it was thought that it was not appropriate to apply the cut-off limit.

2.6.3 Creation of new variables

New variables from the food intake data were created using Stata 6 as described under Part 1 of this chapter. A summary of the variables created appears below.

- a. Percentage of energy contributed by macronutrients (protein, fat, carbohydrate)

$$\begin{aligned} \text{Percentage of energy from macronutrient} = \\ \frac{(\text{Macronutrient (g)} \times \text{energy (kJ) per g nutrient})}{\text{Total energy intake}} \times 100 \end{aligned}$$

- b. Percentages of energy and macronutrients contributed by each food category to the total nutrient intake

$$\begin{aligned} \text{Percent of macronutrient or kJ energy contributed to by the food category} \\ \text{to total nutrient intake} = \\ \frac{(\text{g macronutrient or kJ from food category})}{\text{Total g macronutrient or kJ}} * 100 \end{aligned}$$

2.6.4 The frequency of food consumption

The 'number of episodes' of eating per day was counted for each subject as described in section 2.3.3 and entered into an Excel 97 spreadsheet. This raw data was checked against the individual subjects' food records and then imported into the statistical package Stata 6 for analysis.

2.7 Statistical analysis

2.7.1 Statistical analysis of the nutrient intake data

All the data were checked for correctness against the original raw data and analysed using Stata 6. The data was analysed in two ways. Firstly, the data from all women who commenced the study and secondly data was separately analysed for the women who completed all three cycles.

T tests were used for normally distributed data and Wilcoxon signrank tests for non-normal data distributed data. Normality of data was assessed using visual assessment of graphs for the individual variables and by performing the “*sktest*” (Hamilton, 1998) as outlines above in Section 2.4.3. Paired T tests were used when comparing pre and post menstrual intake and unpaired T tests when comparing the treatment and placebo groups.

Based on advice from the statistician, familiar with the study, Generalised Estimating Equations (GEE) analysis was used to determine whether:

- There was a treatment effect on macronutrient and kilojoule intake over the 3 menstrual cycles.
- There was a significant variation of macronutrient and kilojoule consumption over the 3 menstrual cycles.

GEE was used rather than repeated measures analysis to allow for missing data as some subjects dropped out of the study and there were occasions when subjects did not fully complete their food intake recording to enable

it to be included as part of the data. The use of GEE enabled analysis of the all the available data.

GEE analysis was performed using Stata 6. The basic program (written by a statistician) used for the GEE analysis and this was modified according to the variables being analysed. The GEE program used appears below and uses fat as an example:

The following program is testing for treatment effect, time and interaction between menstrual cycles:

```
xtgee pifat Itreat_1 Imens_32 Imens_33 Itm_1_32 Itm_1_33, i(id) family(gauss)
link(identity) corr(exc) robust

/* Treatment Main Effect */
test Itreat_1+0.3333*ItXm_1_2+0.3333*ItXm_1_3=0

/* Estimated Mean Difference Adifax vs Placebo */
lincom Itreat_1+0.3333*ItXm_1_2+0.3333*ItXm_1_3

/* menses Main Effect */
test Imense_2+0.5*ItXm_1_2=0, notest
test Imense_3+0.5*ItXm_1_3=0, accum

/* Estimated Mean Difference Menses 2 vs Menses 1 */
lincom Imense_2+0.5*ItXm_1_2

/* Estimated Mean Difference Menses 3 vs Menses 1 */
lincom Imense_3+0.5*ItXm_1_3

/* Estimated Mean Difference Menses 3 vs Menses 2 */
lincom Imense_3+0.5*ItXm_1_3-Imense_2-0.5*ItXm_1_2
```

```

/* Treatment by menses Interaction */
test ItXm_1_2 ItXm_1_3

/* Menses 1 Estimated Mean Difference Adifax vs Placebo */
lincom Itreat_1

/* Menses 2 Estimated Mean Difference Adifax vs Placebo */
lincom Itreat_1+ItXm_1_2

/* Menses 3 Estimated Mean Difference Adifax vs Placebo */
lincom Itreat_1+ItXm_1_3

```

To adjust for the screening data when testing for treatment effect, time and interaction between menstrual cycle the following program was used:

```

xtgee pifat Bpifatm Itreat_1 Imens_32 Imens_33 Itm_1_32 Itm_1_33, i(id)
family(gauss) link(identity) corr(exc) robust

/* Treatment Main Effect */
test Itreat_1+0.3333*ItXm_1_2+0.3333*ItXm_1_3=0

/* Estimated Mean Difference Adifax vs Placebo */
lincom Itreat_1+0.3333*ItXm_1_2+0.3333*ItXm_1_3

/* menses Main Effect */
test Imense_2+0.5*ItXm_1_2=0, notest
test Imense_3+0.5*ItXm_1_3=0, accum

/* Estimated Mean Difference Menses 2 vs Menses 1 */
lincom Imense_2+0.5*ItXm_1_2

/* Estimated Mean Difference Menses 3 vs Menses 1 */
lincom Imense_3+0.5*ItXm_1_3

```

/ Estimated Mean Difference Menses 3 vs Menses 2 */*

*lincom Imense_3+0.5*ItXm_1_3-Imense_2-0.5*ItXm_1_2*

/ Treatment by menses Interaction */*

test ItXm_1_2 ItXm_1_3

/ Menses 1 Estimated Mean Difference Adifax vs Placebo */*

lincom Itreat_1

/ Menses 2 Estimated Mean Difference Adifax vs Placebo */*

lincom Itreat_1+ItXm_1_2

/ Menses 3 Estimated Mean Difference Adifax vs Placebo */*

lincom Itreat_1+ItXm_1_3

2.7.2 Statistical analysis of questionnaires

2.7.2.1 Analysis of Steiner self rated questionnaire PMS scores

Data for the PMS scores was not normally distributed. For this reason, the Wilcoxon matched pairs sign rank test was used to determine whether there was a significant change between pre and post menstrual scores for the treatment and placebo groups.

To determine whether the PMS scores for the treatment and placebo groups for each cycle (menses 1 to 3) were similar or differed significantly, the Wilcoxon two sample rank-sum or Mann-Whitney test was used. This tested whether the two independent samples came from the same population.

2.7.2.2 Nottingham Health profile questionnaire

The Nottingham health profile scores were not normally distributed. As with the Steiner self rated questionnaires the Wilcoxon matched pairs sign rank test was used to determine whether there was a significant change between pre and post menstrual scores in each of the six sub areas and the life affected areas score in the Nottingham health profile for the treatment and placebo groups. The Wilcoxon two sample ranksums was used to determine whether the scores for the treatment and placebo groups were similar or differed significantly.

2.7.2.3 Relationship between food consumption and the Steiner self rated scores and the Nottingham health profile scores

The Spearman's rank correlation test was used to identify whether there was a relationship between the severity of PMS symptoms as measured by the Steiner self rated scores and food consumption. This test was used to identify whether there was a relationship between the Steiner self rated scores and the macronutrient and energy intakes (both total and according to food category), premenstrually, postmenstrually and for the difference between pre and postmenstrual intake and scores. When using the Spearman's rank correlation test the treatment and placebo groups were analysed separately.

The Spearman's rank correlation test was used in a similar way to investigate whether there was a relationship between the Nottingham

Health profile sub area scores and energy and macronutrient intakes for the treatment and placebo groups.

2.7.2.4 Initial subject perception and Steiner self rated scores

The relationship between the initial subject perception of the severity of their symptoms and the Steiner self-rated scores was also investigated using the Spearman's rank correlation test.

Data was entered from the individual subject folders into a database by contracted data entry personnel. This data was provided to myself together with the nutrient and anthropometric data as a Stata 5 file. This data was checked for correctness against the original data prior to its use in analysis.

The database was used to generate new variables using Stata 6. These variables represented the difference between the premenstrual and postmenstrual responses to both the Steiner self rated questionnaire (PMS scores) and the Nottingham profile.

CHAPTER 3

Results

Part 1 Screening data

3. Introduction

Investigations of energy and macronutrient intake of women without PMS during the menstrual cycle have been inconsistent in their findings. Some studies find an increase in total energy premenstrually, compared to postmenstrually (Barr, 1995, Martini 1994, Davitt 1981, Tarasuk 1991). Others have shown no difference in energy (Lyons 1989, Piers et al 1995, Fong et al 1993, Rock 1996). Similarly, differences in macronutrient intake between the premenstrual phase and postmenstrual phase have been shown only in some studies. Increases in carbohydrate (Dalvit-McPhillips 1983, Johnson 1995, Martini 1994) and fat (Tarasuk 1991) have been found premenstrually.

The studies that have been reported in the literature associated with food intake in women experiencing PMS symptoms can be divided into three main areas. These are studies that have investigated:

- appetite changes during the premenstrual or late luteal phase
- the types of food consumed, particularly foods higher in carbohydrate premenstrually and postmenstrually
- energy and macronutrient intake during premenstrual and postmenstrual phases.

The evidence available generally supports that there is an increase in appetite premenstrually in women with PMS. Both appetite and reported food consumption, particularly sweet foods have been observed to increase premenstrually. The majority of studies investigating appetite changes have used a rating scale (Both-Orthman et al, Bancroft et al, 1993) to detect these changes. Questionnaires have been used to identify changes in the types of foods eaten over the menstrual cycle (Bancroft et al, 1988; Rossignal et al, 1991).

There is less evidence relating to increased premenstrual energy and macronutrient intake in women with PMS. One group of researchers has performed much of the reported work surrounding nutrient consumption in PMS, particularly in relation to the preference for high carbohydrate containing foods. There has only been one study that has reported the actual energy and macronutrient intake in women with PMS. This study was performed in an 'inpatient setting' in a small group of women (Wurtman et al, 1989). Women with PMS and a control group were admitted for 48 hours premenstrually and for 48 hours postmenstrually. Women had a choice of meals and snacks with predetermined levels of protein, fat and carbohydrate. In this study there was a significant increase in carbohydrate intake premenstrually. This observed increase in carbohydrate consumption was hypothesised to be a response to reduced brain 5-HT levels and has been termed to be 'carbohydrate craving'.

The food intake and nutrient analysis of overweight women with PMS has not been reported in the literature. It is hypothesised that based on current literature there is an increase in food intake premenstrually in these women and that this increase is reflected in an increase in carbohydrate rather than an overall increase in macronutrients intake. The nutrient intake data presented in this section is from the screening phase for the randomised double blind placebo controlled parallel group study. This study investigates the effect of dexfenfluramine on PMS symptoms including carbohydrate consumption. For entry into this trial a pre and postmenstrual difference in carbohydrate intake was included as one of the criteria.

3.1 Hypothesis 1

There are overweight women who as part of their Premenstrual Syndrome symptoms specifically increase their premenstrual consumption of carbohydrate containing foods rather than just increasing their total food intake.

3.2 Subject profiles

Three hundred and thirteen women entered the screening process. One hundred and forty-four completed the screening and eighty-eight women met the criteria for entry into the study.

Table 1 outlines the subject profile data of women participating in the screening process according to whether they did or did not meet the criteria for entry into the study. The 88 women that were eligible to enter the study had a mean height of 163.5 ± 6.3 cm, mean weight of 77.7 ± 11.1 kg and had a mean BMI 29 ± 3.6 kg/m².

In the women meeting the criteria for entry into the study 52 (59%) had BMI's between $25 \leq \text{BMI} < 30$ kg/m² (range 25-28.6) and 32 (36.4%) with $\text{BMI} > 30$ kg/m² (range 30.1-36.7). Three women had $\text{BMI} < 25$ kg/m² (range 24.1-24.7) and eight a $\text{BMI} > 35$ kg/m². These women did not meet the study criteria. However, as they, all were entered into the study and their BMI and their BMIs were close to the study criteria it was decided to include them in this analysis.

Table 1. The subject profile of women that did and did not meet the criteria for entry into the study. Figures in the brackets represent the standard deviation ($\pm$ SD)

SUBJECT PROFILE	Women meeting the PMS criteria	Women not meeting the PMS criteria
Number of subjects	88	56
Mean age ($\pm$ SD)	36.9 $\pm$ 5.6	36.2 $\pm$ 6.9
Mean weight ($\pm$ SD) Kg	77.7 $\pm$ 11.1	78.4 $\pm$ 10.1
Mean height ($\pm$ SD) cm	163.5 $\pm$ 6.3	164.6 $\pm$ 6.0
Mean BMI ($\pm$ SD) Kg/m ²	29 $\pm$ 3.6	29.2 $\pm$ 3.1
Mean hip ($\pm$ SD)cm	108.9 $\pm$ 6.6	109.5 $\pm$ 5.96
Mean waist ($\pm$ SD) cm	83.5 $\pm$ 8.3	82 9 $\pm$ 8.4

The 56 women not eligible to enter the study had a mean height of 164.6 $\pm$ 6.0 cm, mean weight of 78.4 $\pm$ 10.1 kg and had a mean BMI 29.2 $\pm$ 3.1 kg/m². Categorisation of these women according to whether their BMI was within the overweight or obese range, found that 33 (58.9%) had BMI's between $\geq$ 25 to <30 kg/m² (range 25.9-29.7) and 21 (37.5%) with BMI>30 kg/m² (range 30.3-36.3). Two women had BMI<25 kg/m² (range 24.4-24.6) and one a BMI>35 kg/m² (BMI=36.3 kg/m²).

The median of the last menstrual cycle was 28 days (range 23-38days) for women meeting the entry criteria and 27 days (range 23-36 days) for women not meeting the criteria.

Statistical comparisons between women who did and did not meet the study entry criteria showed no statistically significant differences for age, height, weight, BMI, hip, or waist measurements.

3.3 Retrospective perception of the severity of premenstrual symptoms

Women's retrospective perceptions of the degree of severity of PMS they experienced was categorised as mild, moderate or severe. As can be seen in Table 2 for women meeting the PMS criteria, 59.1% categorised it as moderate, 34.1% as severe and 6.8% as mild. A similar pattern can be seen for the women not meeting the study criteria. The median number of years women reported that they had experienced PMS symptoms was 12.5years (range 2-31) for those meeting the study criteria and 11.9 years (range 2-28) for those that did not.

Table 2. Women's perceptions of the severity of their premenstrual symptoms and length of time they had experienced them.

	Women meeting the PMS criteria	Women not meeting the PMS criteria
Length (days) of menstrual cycle (range)	28 (23-38)	27 (23-36)
Perception of Premenstrual symptoms n (% total)		
Mild	6 (6.8)	9(16.1)
Moderate	52 (59.1)	31 (55.3)
Severe	30 (34.1)	16 (28.6)
Length of time (years) experiencing symptoms	12.5 (2-31)	11.9 (2-28)

3.4 Additional data collected from women meeting the entry criteria

For women who qualified for entry into the study 50% had had 3 or more pregnancies and of these 33% had 3 or more children. Only 10 women smoked and 2 reported to have smoked previously. For those that smoked, the median daily consumption was 10 cigarettes per day, with a range of 1 to 25 per day. The median number of years smoked was 14.5 (range 5-27 years).

3.5 Macronutrient and energy intake

3.5.1 Data analysis prior to application of Goldberg's cut off limit

The energy and macronutrient intakes for women who did and did not meet the PMS criteria appear in Table 3. For women that met the PMS criteria there was a mean $2620 \pm 2156\text{kJ}$ (28%) significantly greater ($p<0.001$) energy intake premenstrually when compared to postmenstrual energy intake. All assessed macronutrient intakes were statistically significantly greater premenstrually ($p<0.001$). The mean total carbohydrate intake premenstrually was $76.9\pm 58.5\text{g}$ (29.5%) greater than the mean postmenstrual intake. The mean protein intake was $13.4\pm 16.1\text{ g}$ (15.4%) and the mean fat $28.8 \pm 29.5\text{g}$ (30.5%) greater premenstrually. Analysis of total carbohydrate intake in terms of complex carbohydrates and simple sugars, showed a significantly greater premenstrual mean complex carbohydrate intake of $35.1\pm 28.9\text{g}$ (24.6%) and mean simple sugars intake of $41.9\pm 43.6\text{ g}$ (31%).

The women who completed the screening process but did not qualify for entry to the study exhibited no significant change in macronutrient and energy intake premenstrually (Table 3).

Table 3. The mean $\pm$ SD (over 4 days) premenstrual, post menstrual energy, and macronutrient intake and percent change for women who did and did not meet the study entry criteria

	Energy (kJ) $\pm$ SD	Protein (g) $\pm$ SD	Fat (g) $\pm$ SD	Carbohydrate (g) $\pm$ SD	Complex carbohydrate (g) $\pm$ SD	Simple sugars (g) $\pm$ SD
Women meeting PMS criteria (N=88)						
Premenstrual	8598 (2171) ¹	78.1 (18.8)	81 (29)	243 (59.7)	130 (32)	113 (46)
Postmenstrual	5978 (1288)	64.8 (16)	52.8 (15)	166 (37)	95 (24)	71 (24)
Mean Pre -postmenstrual intake	2620 (2156)	13.4 (16.1)	28.8 (29.5)	76.9 (58.5)	35.1 (28.9)	41.9 (43.6)
Mean Percent Change	28*	15.4*	30.5*	29.5*	24.6*	31*
Women without PMS (N=56)						
Premenstrual	7254 (1886)	70 (17.5)	67 (27.7)	200.9 (55.5)	110.5 (29.9)	89.6 (31.6)
Postmenstrual	6945 (1803)	67.7 (17.4)	62.9 (22)	196.4 (54.2)	110.2 (32.1)	86 (36.3)
Mean Pre - postmenstrual intake	309 (1716)	2.2 (17.1)	4.6 (25.9)	4.5 (48.9)	0.3 (28.9)	3.6 (31.3)
Mean Percent Change	2.05	0.2	- 1.7	0.4	-2.3	-1.2

¹ Figures appearing in brackets are standard deviations

* $p < 0.001$ (paired *t*-test)

Table 4 presents the median alcohol consumption for both groups of women. The Wilcoxon signrank test was used to compare the pre and postmenstrual consumption. There is no significant difference in alcohol intake between the pre and postmenstrual phases for either group of women. Neither was there a difference in alcohol consumption between the two groups.

Table 4. The median (range) alcohol consumption for women completing the screening process according to whether they met the criteria for entry into the study

	Women meeting PMS criteria (N=88)	Women not meeting PMS criteria (N=56)
Premenstrual alcohol (g) (range)	2.25 (0-51)	4.5 (0 - 86)
Postmenstrual Alcohol (g) (range)	2.25 (0-27)	3.5 (0 -77)
Pre -postmenstrual intake (g) (range)	0 (-18-38.5)	0 (-35 -38)
Percent change in intake (%)	42 (n=46)	41.7 (n=37)

Table 5. Macronutrient intake expressed as percent of total energy intake ($\pm$ SD) for women meeting and not meeting the study entry criteria

Macronutrient	Premenstrual % of energy ($\pm$ SD)	Postmenstrual % of energy ($\pm$ SD)	Significance
Women meeting PMS criteria (N=88)			
Carbohydrate	48.4 (5.2)	47.5 (5.6)	p=0.10
Fat	34.6 (4.8)	32.4 (4.6)	p<0.001
Protein	14.7 (2.7)	17.5 (2.98)	p< 0.001
Simple sugars	20.8 (5.7)	19.0 (5.3)	p<0.05
Complex carbohydrates	26.2 (5.4)	27.3 (4.9)	P=0.06
Women not meeting PMS criteria (N=56)			
Carbohydrate	44.6 (6.9)	45.4 (6.0)	p=0.37
Fat	33.6 (6.8)	33. (5.4)	p=0.53
Protein	16.7 (3.3)	16.8 (8)	p=0.7
Simple sugars	19.5 (4.8)	19.6 (6.6)	p=0.9
Complex carbohydrates	24.9 (6.1)	25.8 (5.8)	p=0.2

Adjustment for energy using the nutrient density method showed that when macronutrients were expressed as the percentage of the total energy they each contributed, there was no significant difference in total carbohydrate intake or complex carbohydrates (Table 5). However, there was a significant difference for simple sugars (p< 0.05).

There was a significant difference for protein and fat intakes, with protein increasing postmenstrually and fat decreasing postmenstrually.

3.5.2 Data analysed according to food categories

Tables 6-8 display the mean energy and macronutrient intake analysed according to food categories, for women who met the criteria for entry into the study. This analysis was not performed for women that did not qualify for entry into the study. The mean kilojoule contribution (Table 6) from all food categories except for the *meat based*, *fruit* and *milk* categories were statistically significantly greater premenstrually compared to the postmenstrual phase. The contribution to the total protein, fat, carbohydrate and complex carbohydrate (Tables 7 and 8) was significantly greater premenstrually than postmenstrually ($p < 0.001$) from the *cereal*, *cakes and desserts* and the *high sugar foods* categories. *Savoury foods* ($P < 0.05$), *drinks* ($p < 0.001$) *vegetables* and *savoury snacks* ($p < 0.05$) provided more towards the mean energy (kJ) and carbohydrate premenstrually (Table 8). Finally the *fat* category contributed significantly more kilojoules and fat during the premenstrual phase. The *milk* and *fruit* categories did not vary significantly between the two phases.

Table 6. The mean kilojoule and the percent of the total kilojoule intake for each food category for premenstrual and postmenstrual phases for women that met the study entry criteria

	Premenstrual kJ ($\pm$ SD)	% Total Nutrient ($\pm$ SD)	Postmenstrual kJ ($\pm$ SD)	% Total Nutrient ($\pm$ SD)
Kilojoules				
Cereal	1714 (693) **	20.5 (8.3) ††	1389 (466)	23.6 (7.2)
Milk	699 (445)	8.4 (5.1) **	646 (368)	10.9 (5.9)
Meat, fish, poultry, eggs	865 (585)	9.9 (5.7)**	794 (406)	13.3 (6.4)
Savoury foods	943 (642) †§	11.3 (8.2)	655 (422)	10.97 (6.6)
Vegetables	487 (306) ††	5.8 (3.4) ††	425 (304)	7.1 (5.1)
Fruit	214 (207)	2.7 (2.7)*§	229 (180)	4.1 (3.5)
Fat	382 (346) †§	4.3 (3.3)	265 (206)	4.4 (3.04)
Cake and desserts	1316 (919) **	14.8 (8.1)**†	626 (451)	10.2 (6.5)
High sugar foods	999 (1136) *§	11.1 (11.3)*§	317 (280)	5.2 (4.5)
Drinks	580 (542) **	6.8 (6.5)	414 (323)	6.8 (5.1)
Savoury snacks	310(393) †§	3.6 (4.3)	167 (263)	2.7 (4.0)

* $p < 0.001$, † $p < 0.05$

† paired ttest § Wilcoxon sign rank test

Table 7. The mean protein, fat and the percentage of the total protein and fat intake for each food category for premenstrual and postmenstrual phases of women meeting the entry criteria

	Premenstrual g (±SD)	% Total Nutrient (±SD)	Postmenstrua l g (±SD)	% Total Nutrient (±SD)
Protein (g)				
Cereal	13.9 (5.7) *†	18.4 (7.97)	11.5 (3.8)	18.3 (6.2)
Milk	11.9 (7.8)	15.2 (8.9)	10.80 (6.3)	16.6 (9.1)
Meat, fish, poultry, eggs	22.9 (13.3)	28.2 (13.4)††	21.8 (12.3)	32.5 (13.9)
Savoury foods	10.0 (6.8) †§	13.2 (9.7)	7.4 (5.2)	11.8 (8.3)
Vegetables	4.3 (2.8)	5.5 (3.3)	3.98 (2.7)	6.2 (4.4)
Fruit	0.79 (0.92)	1.1 (1.4)	0.8 (0.6)	1.3 (1.2)
Fat	0.2 (0.44)	0.2 (0.5)	0.1 (0.4)	0.2 (0.7)
Cake and desserts	6.2 (4.1)*†	7.9 (4.98)*†	3.4 (2.6)	5.2 (3.8)
High sugar foods	3.0 (4.2)*§	3.96 (5.8)*§	0.8 (1.0)	1.3 (1.6)
Drinks	2.5 (3.1)	3.2 (3.5)†§	2.40 (2.3)	3.8 (3.4)
Savoury snacks	1.85 (2.67) †§	2.3 (3.3)†§	1.03 (1.6)	1.6 (2.5)
Fat (g)				
Cereal	5.2 (3.8) *†	6.8 (4.7)	3.8 (1.97)	7.5 (3.95)
Milk	9.3 (6.7)	12.3 (9.2)†§	8.3 (5.5)	16.2 (10.3)
Meat, fish, poultry, eggs	11.1 (8.6)	13.6 (8.6) †§	10.1 (5.3)	19.7 (9.5)
Savoury foods	11.25 (8.1) †§	14.2 (10.5)	7.8 (5.3)	14.9 (8.9)
Vegetables	3.77 (4.6)	4.6 (4.9)	3.2 (4.5)	5.92 (7.6)
Fruit	0.02 (0.19)	0.04 (0.4)	0.03 (0.2)	0.09 (0.7)
Fat	10.2 (9.1)*§	12.0 (8.9)	7.06 (5.5)	13.25 (8.9)
Cake and desserts	13.6 (10.3)*†	16.1 (9.3)*†	6.0 (4.6)	11.35 (7.96)
High sugar foods	9.7 (13.9)*§	11.0 (13.7)*§	2.2 (2.97)	4.0 (5.3)
Drinks	0.6 (1.5)	0.7 (2.1)	0.45 (0.97)	0.84 (1.7)
Savoury snacks	5.1 (6.6)†§	6.3 (7.3)	2.97 (4.8)	4.96 (7.4)

*p<0.001, † p<0.05

‡ paired ttest

§ Wilcoxon sign rank test

Table 8. The mean carbohydrate, complex carbohydrate and simple sugars and the percent contribution to the total intake for each food category for premenstrual and postmenstrual phases for women meeting the entry criteria

	Premenstrual g (±SD)	% Total Nutrient (±SD)	Postmenstrual g (±SD)	% Total Nutrient (±SD)
Carbohydrate (g)				
Cereal	76.8 (31.1) *†	32.1 (11.9)*†	61.95 (22)	37.4 (10.7)
Milk	9.9 (8.6)	4.1 (3.3)*§	9.7 (8.1)	5.7 (4.4)
Meat, fish, poultry, eggs	3 (5.2)	1.1 (1.8) †§	2.6 (2.8)	1.5 (1.7)
Savoury foods	21.5 (15.8) *§	9.2 (7.2)	14.4 (9.7)	8.9 (5.9)
Vegetables	15.6 (8.6) ††	6.6 (3.7)*§	13.6 (7.9)	8.3 (4.9)
Fruit	11.9 (11.6)	5.1 (4.9)*§	12.9 (10.2)	8.1 (6.5)
Fat	0.2 (0.5)	0.1 (0.2)	0.2 (0.7)	0.1 (0.3)
Cake and desserts	42.95 (30.1)*†	17 (9.5)*†	20.8 (15.5)	11.99 (7.7)
High sugar foods	36.8 (38.2)*§	14.2 (12.9)*§	13.6 (11.3)	8.04 (6.5)
Drinks	19.1 (22.2)*§	7.97 (9.9)	12.0 (12.3)	7.15 (6.8)
Savoury snacks	5.6 (7.96) †§	2.4 (3.7)	2.6 (4.5)	1.9 (2.8)
Simple sugars (g)				
Cereal	6.3 (6.4) ††	5.95 (5.4)	4.8 (4.6)	6.9 (5.6)
Milk	9.6 (8.3)	9.2 (7.3)*§	9.5 (7.9)	13.5 (9.7)
Meat, fish, poultry, eggs	0.1 (0.3) †§	0.1 (0.2) †§	0.2 (0.3)	0.3 (0.6)
Savoury foods	4.4 (5.5) †§	4.2 (4.2)	3 (2.2)	4.6 (3.9)
Vegetables	3.6 (2.5)	3.6 (2.9)*§	3.7 (2.2)	5.5 (3.7)
Fruit	10.7 (10.4)	10.8 (10.6)*†	11.8 (9.3)	17.8 (13.8)
Fat	0.2 (0.5)	0.2 (0.3)	0.15 (0.2)	0.2 (0.4)
Cake and desserts	24.8 (20.5)*§	21.7 (13.8)††	12.0 (9.7)	16.6 (11.4)
High sugar foods	34 (34.1)*§	27.3 (18.3)*†	12.7 (10.6)	17.5 (13.4)
Drinks	18.3 (22.1)*§	16.5 (21.9)	11.6 (12.3)	15.2 (13.4)
Savoury snacks	0.6 (0.7)	0.5 (0.9)	0.4 (0.6)	0.5 (0.8)
Complex carbohydrates (g)				
Cereal	70.5 (27.8)*†	53.7 (15.4)††	57.2 (19.7)	59.8 (12.6)
Milk	0.3 (2.0)	0.2 (1.4)	0.19 (1.6)	0.19 (1.6)
Meat, fish, poultry, eggs	2.8 (4.9)	2.0 (3.2) †§	2.8 (2.9)	3.0 (3.2)
Savoury foods	17.0 (13.6) †§	13.2 (10.4)	11.5 (8.7)	12.3 (8.9)
Vegetables	11.9 (7.25)†	9.75 (6.7)	9.5 (6.4)	10.4 (7.4)
Fruit	1 (1.6)	0.8 (1.6)	0.9 (1.2)	1.1 (1.5)
Fat	0.009 (0.07)	0.01 (0.06)	0.003 (0.02)	0.003 (0.02)
Cake and desserts	18.2 (12.0)*	13.6 (7.6)*†	8.9 (7.4)	9.02 (6.5)
High sugar foods	2.7 (6.2)*§	2.2 (4.3)*§	0.8 (1.3)	0.8 (1.4)
Drinks	0.73 (1.57) †	0.57 (1.2)	0.48 (0.49)	0.51 (0.52)
Savoury snacks	5.01 (7.58) †§	3.87 (5.85)	2.23 (4.3)	2.38 (4.1)

*p<0.001, † p<0.05 † paired t-test § Wilcoxon sign rank test

Analysis of nutrient intake as the percentage of the total energy and macronutrients that each food category provided is also shown in Tables 6-8. The food categories *cakes and desserts* and *high sugar foods* contributed a higher percentage for all macronutrients and energy premenstrually. When grouped together, these two food categories provided 25.8% of the total kilojoules premenstrually compared with 15.4% postmenstrually. They also contributed premenstrually 27.1% of the mean total fat, 31.2 % of the total carbohydrate, 15.8% of the total complex carbohydrate and 49.04% total simple sugars compared to 15.4% total fat, 20.0% total carbohydrate, 9.8% of the total complex carbohydrate and 34.0% simple sugars postmenstrually.

Unlike the *cakes and desserts* and *high sugar foods* categories, the majority of the remaining food categories where there was a significant difference between the two phases, contributed a smaller percentage premenstrually. For example the *cereal* category provided a mean of 20.5 ± 8.3 % of the total kilojoules premenstrually compared to 23.6 ± 7.2 % postmenstrually ($p < 0.05$). The *cereal* category also contributed significantly greater percentage of carbohydrate ($p < 0.001$) postmenstrually.

3.5.3 Energy and macronutrient analysis after applying the Goldberg's cut-off limit

A total of 31 women were excluded from the calculations. Eleven were from the group that met the study entry criteria and 20 from the group that did not after applying the Goldberg exclusion factor of 1.06 to the premenstrual data. The 77 women qualifying for entry into the study had a mean age of 37.3 ± 5.1 years and a mean BMI of 28.8 ± 3.6 kg/m² (Table 9). A partitioning of the calculated BMIs according to whether they fell into the overweight or obese range found that 47 women were in the overweight ($25 \leq \text{BMI} < 30$) range and 27 were in the obese ($\text{BMI} = 30$) range. Three women had a $\text{BMI} < 25$ (range 24.1-24.7kg/m²). The median length of the menstrual cycle was 28 days with a range of 23-38 days.

Table 9. The subject profile of women that did and did not meet the study entry criteria, after applying the Goldberg factor

Subject profile	Women meeting the PMS criteria	Women not meeting the PMS criteria
Number of subjects	77	36
Race -Caucasian	77	36
Mean age (sd)	37.3 (5.1)	38.1 (6.6)
Mean weight (SD) Kg	77.0 (11.1)	76.6 (11.7)
Mean height (SD) cm	163.5 (6.4)	162.8(7.1)
Mean BMI (SD) Kg/m ²	28.8 (3.6)	28.8 (2.97)
Mean hip (SD)cm	108.4 (6.5)	108.7 (5.6)
Mean waist (SD) cm	83.2(8.5)	83.1 (8.1)

The 36 women that did not meet the criteria for entry into the study had mean age of 38.1 ± 6.6 years, a mean BMI of 28.8 ± 2.97 kg/m². Twenty-two women were overweight ($25 \leq \text{BMI} < 30$) and 12 were obese (BMI = 30). Two women were within the normal weight range with BMI < 25 (range 24.4 -24.6) and no women had a BMI > 35. The median length of the menstrual cycle was 27 days with a range of 23-36 days. There were no statistical differences between women that did and did not meet the entry criteria with respect to age, BMI, weight, height, waist or hip measures, nor length of menstrual cycle.

Table 10 presents the baseline nutritional data for the women who completed the screening process. For the group of women who met the study criteria for PMS, there was a statistically significant ($p < 0.001$) greater macronutrient intake premenstrually compared with the postmenstrual intake for each nutrient as well as for total energy intake. In comparison, women not qualifying for entry into the study showed no significant differences between the premenstrual and postmenstrual phases for all macronutrients except for fat and total energy ($p < 0.05$). This differs from the findings prior to the application of the cut-off limit where no statistically significant difference was detected for fat and energy.

A comparison of these findings to those prior to the application of Goldberg's cut-off limit shows as would be expected a higher mean intake for both the pre and postmenstrual phases for all women. The

percentage change between the pre and postmenstrual phases was also slightly greater after the application of Goldberg's cut off limit.

Table 11 presents the median alcohol intake for both groups of women. There was no significant difference between the pre and post menstrual consumption of alcohol for either group nor was there a significant difference between the groups.

Table 10. The mean pre and postmenstrual energy, macronutrient intake and percent change for each nutrient for women that did and did not meet the study criteria after excluding subjects below Goldberg's cut-off limit (1.06).

	Energy (kJ)	Carbohydrate (g)	Protein (g)	Fat (g)	Complex carbohydrate (g)	Simple sugars (g)
Women with PMS (N=77)						
Premenstrual	8947 ±2082	252.5 ± 57.2	79.7±19.2	85.6±28.8	133.9 ±32.4	118.5±45.9
Postmenstrual	6134±1264	169.9 ±36.5	66.1± 16.3	54.4 ±15	97 ±23.6	72.7±23.8
Pre - Postmenstrual	2813±2213	82.7±59.1	13.6±16.8	31.2 ±30.4	37±30	45.8±44.2
† Percent Change	29 ±16.7*‡	31 ±15.7*‡	15.1 ±19.1 **	31.8±23.4*‡	25.1 ±19.1*‡	33.7 ±23.6*‡
Women without PMS (N=36)						
Premenstrual	8281±1623†§	227±52	77.9±15.5	79.2 ±27.9† §	120.3±30.1	106±36
Postmenstrual	7544±1624	213.4±52.1	72.7±17	68.3 ±21	116.6 ±33	96.3±36.8
Pre - Postmenstrual	737±1680	13.9±49.3	5.2± 18.2	10.9±26.8	3.7±27.7	9.6±33.6
Percent Change	7.8 17.5 1‡	4.5±20.7	4.7±23.3	8.4 ±32.51‡	2.0±20.9	4.8±36.1

† Mean percentage change between premenstrual and postmenstrual nutrient analysis *p<0.001, ‡ paired *t*-test
sign rank test

Table 11. The median (range) alcohol consumption for women completing the screening process according to whether they met the criteria for entry into the study after application of Goldberg's cut-off limit

	Women meeting PMS criteria (N=77)	Women not meeting PMS criteria (N=36)
Premenstrual alcohol (g) (range)	3 (0-51)	5 (0 - 86)
Postmenstrual Alcohol (g) (range)	2.5 (0-27)	5 (0 -77)
Pre -postmenstrual intake (g) (range)	0 (-18-38.5)	0 (-35 -20)
Percent change in intake (%)	41.7 (n=42)	50 (n=24)

Table 12. Macronutrient intake for the seventy-seven women meeting PMS criteria expressed as percent of total energy intake and thirty-six women without PMS

Macronutrient	Premenstrual % of energy ($\pm$ SD)	Postmenstrual % of energy ($\pm$ SD)	Significance (<i>t</i> -test)
<i>Women meeting study entry requirements</i>			
Carbohydrate	48.25 $\pm$ 5.3	47.3 $\pm$ 5.6	P=0.08
Fat	34.9 $\pm$ 4.7	32.6 $\pm$ 4.7	P<0.001
Protein	14.4 $\pm$ 2.6	17.3 $\pm$ 3.0	p< 0.001
Simple sugars	21.1 $\pm$ 5.9	18.9 $\pm$ 5.2	P<0.001
Complex carbohydrates	25.8 $\pm$ 5.5	27.1 $\pm$ 4.9	P<0.05
<i>Women without PMS</i>			
Carbohydrate	44.1 $\pm$ 7.2	45.4 $\pm$ 6.5	P=0.26
Fat	35 $\pm$ 6.9	33.2 $\pm$ 5.7	P=0.17
Protein	16.1 $\pm$ 2.4	16.5 $\pm$ 2.9	P=0.37
Simple sugars	20.1 $\pm$ 4.9	20.4 $\pm$ 6.6	P=0.91
Complex carbohydrates	23.6 $\pm$ 6.0	24.9 $\pm$ 5.6	P=0.08

In the 77 women with PMS symptoms, adjustment of macronutrient intake as a percentage of total energy intake showed significantly greater premenstrual percentage of fat ($p<0.05$), and simple sugars

($p < 0.001$). There was a significantly reduced percentage of protein ($p < 0.001$) and complex carbohydrate ($p < 0.05$) in the premenstrual phase as compared with this group's postmenstrual data (Table 12). For carbohydrate there was also a higher percentage premenstrually but this was not significant ($p = 0.08$). In the 36 women without PMS, adjustment for energy showed no significant difference between premenstrual and postmenstrual macronutrient intakes. These findings are comparable to those found before the application of Goldberg's cut-off limit.

3.5.4 Analysis of nutrient data according to food categories after applying the Goldberg's cut-off limit

Tables 13-15 display the mean energy and macronutrient intake analysed, according to food categories, for women with PMS. All the food categories, except for the *fruit* category supplied more kilojoules during the premenstrual phase (Table 13). This contribution was significant for all food categories except for the *meat-based group*, *fruit*, *vegetable* and *milk* categories.

The contribution by the *cereal*, *cakes and desserts* and the *high sugar foods* categories to the total protein, fat, and carbohydrate (Tables 14 and 15) intake was significantly higher at the premenstrual phase compared with the postmenstrual phase ($p < 0.001$). The *cake and dessert*, and *high sugar foods* categories also contributed more premenstrually towards dietary simple sugars ($p < 0.001$) and complex carbohydrates ($p < 0.05$). *Savoury foods* contributed a significantly greater energy, carbohydrate, protein, fat and simple sugars premenstrually ($P < 0.05$). The *fat* category contributed premenstrually significantly more fat ($p < 0.001$), and protein ($p < 0.05$). However in the case of protein, it should be noted that the amount contributed by the *fat* category was extremely small. The *drinks* category contributed more carbohydrate and simple and complex carbohydrate premenstrually ($p < 0.05$) and *savoury snacks* ($p < 0.05$) contributed more carbohydrate and complex carbohydrate premenstrually (Table 15).

Analysis of the data as the mean percentage of the total energy and macronutrients that each food category provided is also shown in Tables 13-15. The food categories *cakes and desserts* and *high sugar foods* contributed a higher percentage for all macronutrients and kilojoules premenstrually. When grouped together, these two food categories provided 26.6% of the total kilojoules premenstrually compared with 15.9% postmenstrually. They also contributed premenstrually 12.5% total protein, 27.8% of the total fat, 32.2% of the total carbohydrate, 16.4% of the total complex carbohydrate and 49.9% total simple sugars compared to 15.9% total kilojoules, 6.8% total protein, 15.8% total fat, 20.6% total carbohydrate, 10.1% of the total complex carbohydrate and 34.8% simple sugars postmenstrually.

Unlike the *cakes and desserts* and *high sugar foods* categories, the majority of the remaining food categories, where there was a significant difference between the two phases of the menstrual cycle, contributed a smaller percentage premenstrually. In the case of the percentage kilojoule contribution by the *cereal, milk, meat, vegetable* and *fruit* categories For example the *cereal* category provided a mean of 20.3 ± 8.3 % of the total kilojoules premenstrually compared to 23.3 ± 7.6 % postmenstrually ($p < 0.05$). The *cereal* category also contributed significantly smaller percentage of carbohydrate ($p < 0.001$) premenstrually.

Table 13 The mean kilojoule and the percent of the total kilojoule intake for each food category (excluding alcohol) for premenstrual and postmenstrual phases for seventy-seven women with PMS

	Premenstrual Kilojoules ($\pm$ SD)	% Total Nutrient ($\pm$ SD)	Postmenstrual Kilojoules ($\pm$ SD)	% Total Nutrient ($\pm$ SD)
Kilojoules				
Cereal	1764 (704) *†	20.3 (8.3)† §	1411 (489)	23.3 (7.6)
Milk	707 (457)	8.3 (5.1)*§	669 (381)	10.9 (6.1)
Meat, fish, poultry, eggs	905 (606)	10.0 (5.9)† §	798 (421)	13.1 (6.6)
Savoury foods	936 (636) †§	10.6 (7.3)	644 (436)	10.4 (6.6)
Vegetables	492 (320)	5.5 (3.4)* §	444 (314)	7.3 (5.2)
Fruit	215 (212)	2.5 (2.6)*§	232 (180)	4.0 (3.4)
Fat	415 (356) *§	4.5 (3.3)	282 (211)	4.6 (3.1)
Cake and desserts	1391 (944)*†	15.1 (8.3)*†	657 (465)	10.5 (6.8)
High sugar foods	1071 1192)*§	11.5 (11.8)*§	332 (288)	5.4 (4.7)
Drinks	611 (550)* §	6.8 (6.3)	432 (337)	6.9 (5.1)
Savoury snacks	329 (411)†§	3.6 (4.5)	180 (277)	2.8 (4.1)

*p<0.001, † p<0.05

‡ paired ttest § Wilcoxon sign rank test

Table 14. The mean protein and fat and the percentage of the total protein and fat intake for each food category for premenstrual and postmenstrual phases of seventy- seven women with PMS

	Premenstrua I (g) (±SD)	% Total Nutrient (±SD)	Postmenstrua I (g) (±SD)	% Total Nutrient (±SD)
Protein				
Cereal	14.3 (5.8) *†	18.7 (8.2)	11.7 (3.9)	18.3 (6.5)
Milk	12.1 (8.0)	15.2 (9.0)	11.1 (6.6)	16.8 (9.45)
Meat, fish, poultry, eggs	23.3 (13.7)	28.2 (13.4) †§	22.2 (12.9)	32.5 (13.9)
Savoury foods	9.75 (6.5) †§	13.2 (9.65)	7.3 (5.4)	11.8 (8.3)
Vegetables	4.35 (2.9)	5.5 (3.4)	4.1 (2.7)	6.4 (4.5)
Fruit	0.79 (0.95)	1.1 (1.45)	0.78 (0.63)	1.3 (1.2)
Fat	0.18 ((0.46) †§	0.2 (0.56) †§	0.08 (0.29)	0.12 (0.41)
Cake and desserts	6.5 (4.2)*†	8.3 (5.1)* §	3.6 (2.7)	5.5 (3.9)
High sugar foods	3.2 (4.4)*§	4.25 (6.1)*§	0.84 (1.04)	1.3 (1.7)
Drinks	2.6 (3.1)	3.3 (3.5)†§	2.5 (2.3)	3.8 (3.3)
Savoury snacks	1.8 (2.7) †§	2.3 (3.2)	1.09 (1.7)	1.6 (2.6)
Fat				
Cereal	5.4 (4) *§	6.6 (4.7)	3.8 (2.03)	7.3 (3.7)
Milk	9.4 (6.7)	11.7 (8.4)*§	8.6 (5.6)	16.3 (10.4)
Meat, fish, poultry, eggs	11.8 (8.9)	13.9 (8.8)*†	10.1 (5.5)	19.1 (9.7)
Savoury foods	11.2 (7.9) †§	13.4 (9.8)	7.6 (5.4)	13.9 (8.3)
Vegetables	3.8 (4.7)	4.3 (4.8)†§	3.45 (3.8)	6.2 (7.9)
Fruit	0.003 (0.03)	0.003 (0.03)	0.03 (0.2)	0.1 (0.72)
Fat	11.05 (9.4)*§	12.6 (9.2)	7.6 (5.6)	13.9 (9.05)
Cake and desserts	14.2 (10.6)*§	16.2 (9.6) ††	6.3 (4.8)	11.6 (8.3)
High sugar foods	10.6 (14.6)*§	11.6 (14.3)*§	2.35 (3.1)	4.2 (5.5)
Drinks	0.67 (1.6)	0.72 (2.1)	0.44 (0.97)	0.78 (1.7)
Savoury snacks	5.49 (6.93)†§	6.4 (7.5)	3.23 (5.1)	5.2 (7.6)

*p<0.001, † p<0.05

‡ paired ttest § Wilcoxon sign rank test

Table 15. The mean carbohydrate, complex carbohydrate and simple sugars and the percent of the total intake for each food category for premenstrual and postmenstrual phases for seventy-seven women with PMS

	Premenstrual (g) (±SD)	% Total Nutrient (±SD)	Postmenstrual (g) (±SD)	% Total Nutrient (±SD)
Carbohydrate				
Cereal	79.3 (31.45)*§	32 (12) †§	62.9 (23.1)	37.1 (11.2)
Milk	9.9 (8.9)	3.9 (3.2)*§	10.0 (8.5)	5.8 (4.6)
Meat, fish, poultry, eggs	3.4 (5.4)	1.3 (1.9)	2.5 (2.8)	1.5 (1.7)
Savoury foods	21.3 (15.8) †§	8.6 (6.45)	14.2 (10.0)	8.5 (6.2)
Vegetables	15.7 (8.9)	6.4 (3.7)*§	13.66	8.5 (4.95)
Fruit	11.9 (11.8)	4.9 (4.8)*§	13.0 (10.2)	7.9 (6.3)
Fat	0.23 (0.48)	0.1 (0.2)	0.22 (0.7)	0.12 (0.3)
Cake and desserts	45.6(30.8)* §	17.5 (9.6)*†	21.9 (15.9)	12.4 (7.9)
High sugar foods	36.8 (38.2)*§	14.7 (13.5)*§	13.6 (11.3)	8.2 (6.5)
Drinks	19.4 (21.5)*§	7.7 (8.5)	12.1 (11.7)	7.1 (6.6)
Savoury snacks	5.96(8.3) †§	2.5 (3.8)	2.7 (4.8)	1.7 (2.9)
Simple sugars				
Cereal	6.6 (6.7) †§	5.96 (5.7)†§	4.95 (4.9)	6.9 (5.7)
Milk	9.6 (8.5)	8.6 (7.1) *§	9.8 (8.4)	13.4 (10.0)
Meat, fish, poultry, eggs	0.15 (0.4)	0.1 (0.3) †§	0.18 (0.36)	0.3 (0.6)
Savoury foods	4.6 (5.8) †§	4.1 (4.3)	3.1 (2.2)	4.6 (4.0)
Vegetables	3.6 (2.5)	3.5 (2.96)*§	3.8 (2.2)	5.6 (3.8)
Fruit	10.8 (10.6)	10.2 (10.4)* §	11.9 (9.3)	17.3 (13.4)
Fat	0.25 (0.46)	0.2 (0.34)	0.15 (0.24)	0.2 (0.4)
Cake and desserts	26.6 (21.1)*§	22.4 (14.1)††	12.8 (10.1)	17.2 (11.7)
High sugar foods	35.9 (35.3)*§	27.5 (18.7)*	13.3 (10.8)	17.6 (13.2)
Drinks	18.7 (21.4)*§	15.7 (17.1)	11.6 (11.7)	15.2 (13.2)
Savoury snacks	0.5 (0.7)	0.5 (0.9)	0.37 (0.57)	0.5 (0.73)
Complex carbohydrates				
Cereal	72.6 (28.1)* §	53.9 (15.3)†	58.1 (20.7)	59.3 (13.1)
Milk	0.3 (2.2)	0.2 (1.5)	0.2 (1.7)	0.2 (1.7)
Meat, fish, poultry, eggs	3.2 (5.2)	2.04 (3.2)	2.7 (2.8)	3.0 (3.2)
Savoury foods	16.6 (13.5) †§	13.2 (10.4)	11.2 (8.9)	12.3 (8.9)
Vegetables	12.1 (7.4) ††	9.6 (6.7)	9.9 (6.5)	10.7 (7.6)
Fruit	0.98 (1.6)	0.8 (1.6)	0.9 (1.3)	1.1 (1.6)
Fat	0.01 (0.07)	0.01 (0.06)	0.003 (0.2)	0.004 (0.02)
Cake and desserts	19.2 (12.4)*†	14(7.7)*§	9.2 (7.6)	9.3 (6.8)
High sugar foods	3.0 (6.5) †§	2.4 (4.6)*§	0.77 (1.2)	0.8 (1.4)
Drinks	0.6 (0.67) †§	0.49 (0.51)	0.50 (0.5)	0.6 (0.53)
Savoury snacks	5.4 (7.9) †§	4.1 (6.1)	2.3 (4.5)	2.4 (4.3)

*p<0.001, † p<0.05 † paired t-test, § Wilcoxon sign rank

3.6 The number of 'episodes of eating' in women with and without PMS symptoms

As described in Chapter 2, Methods the food intake diaries were used to count the number of 'episodes of eating' for all women that completed the screening process. This was done to investigate whether the observed higher food consumption during the premenstrual phase differed to the postmenstrual phase. For women who met the entry criteria the mean number of times per day that food was consumed was 5.5 ± 1.2 meals premenstrually compared to 4.2 ± 0.98 meals postmenstrually. Statistical analysis using paired *t-test* showed a significant difference ($p < 0.001$). Women not meeting the study entry criteria ate a mean of 4.4 ± 1.2 meals premenstrually compared with 3.98 ± 1.02 meals postmenstrually. For this group of women there was no significant difference in the number of 'episodes of eating' between the two menstrual phases.

Analysis of the data, including only those women meeting the Goldberg cut-off limit resulted in similar findings. Women meeting the study criteria had a mean premenstrual intake of 5.6 ± 1.2 meals compared to 4.2 ± 0.99 postmenstrually. Paired *t-test* showed a significant difference ($p < 0.001$). Women not meeting the study criteria showed no significant difference between pre (4.5 ± 1.1 meals) and postmenstrual (4.0 ± 1.1 meals) phases.

3.7 Relationship between the Steiner self-rated score and nutrient intake

Table 16 details the median Steiner self-rated scores for all women completing the screening process. There was a significant change in the median score between the two menstrual phases for both women that did and did not meet the criteria for entry into the randomised double placebo controlled study. This was also the case after excluding the data of subjects whose energy intake led them to be below Goldberg's cut-off limit.

Spearman's correlation coefficient was used to identify whether there was a relationship between the severity of PMS symptoms, as measured by the Steiner self rated PMS scale and the change observed in the unadjusted nutrient intake. When the Spearman's correlation coefficient was calculated for all subjects (those with and without PMS), there was a weak correlation (Spearman's rho 0.34, $p < 0.001$, 120 degrees of freedom) for carbohydrate. For complex carbohydrate, Spearman's rho 0.29, $p < 0.05$ and simple sugars Spearman's rho 0. $P < 0.05$. There was also a weak correlation between the change in fat intake and total energy intake with respect to change in PMS score. This was 0.27 ($p < 0.05$) and 0.32 ($p < 0.05$) respectively. The correlation for protein was very weak (Spearman's rho 0.19, $p < 0.05$).

Table 16. The median Steiner self rated scores for women that completed the screening process according to whether they met the study entry criteria

	Women meeting entry criteria (median scores)	Women not meeting entry criteria (median scores)
All women completing screening process		
Premenstrual score	25.25 (13 -34) ^a	20.5 (8-34) ^a
Post menstrual score	2 (0-15)	3 (0-29)
Women included after application of Goldberg's cut-off limit		
Premenstrual score	25.5 (13-34) ^a	23 (8-34) ^a
Post menstrual score	2 (0-15)	3.5 (0-20)

^a Wilcoxon signrank test $p < 0.001$ for change in score between menstrual phases

For women meeting the study's entry criteria, Spearman's correlation coefficient was weak (Spearman's rho 0.26, $p < 0.05$, 80 degrees of freedom) for carbohydrate. There was also a weak correlation between the change in fat intake and total energy intake with respect to change in PMS score. This was 0.27 ($p < 0.05$) and 0.29 ($p < 0.05$) respectively. Spearman's correlation coefficient for protein, simple sugars and complex carbohydrates were not significant. In women not meeting the entry criteria there were no significant correlations between the Steiner self rated PMS scale and energy and macronutrient intake.

3.8 Summary of the screening data results

The screening data presented in this chapter support the very small number of reports found in the literature of women with normal weight with PMS, where there are increases in both energy and carbohydrate intakes during the premenstrual phase (Wurtman et al 1989). Women, who met the criteria for entry into the randomised double blind placebo controlled study, exhibited an increase in premenstrual carbohydrate. Premenstrual carbohydrate was 29.5% higher than postmenstrual carbohydrate. For women that did not meet the study entry criteria there was only a 0.4% difference in carbohydrate intake. When the carbohydrate intake was calculated as a percent of energy, no significant change in the proportion of total carbohydrate was detected.

However, there was also a significantly greater intake of protein, fat as well as kilojoules for women that met the study entry criteria. This finding points to the likelihood that in this group of overweight and obese women there is not a specific preference for carbohydrate containing foods. In addition, adjustment of carbohydrate according to the energy contributed, revealed no significant difference between the pre and postmenstrual phases. Analysis of the two main components of carbohydrate did reveal a significant difference between their pre and postmenstrual contribution. 'Simple sugars' contributed a significantly greater proportion of energy premenstrually ($p < 0.05$)

while there was a greater proportion of energy postmenstrually ($p < 0.05$) from complex carbohydrate. After adjustment for energy there was also an increase in fat premenstrually and a decrease in protein. Analysis of the data after applying the Goldberg cut off limit showed similar findings. The percentage change in energy and macronutrient, as can be seen when comparing the data in Tables 3 and 11, shows a slightly greater percent change for women meeting the screening criteria except for protein, which was slightly less. For the women not meeting the study criteria exclusion of data that was below Goldberg's cut off limit resulted in there being a significantly higher kilojoule and total fat intake which was not the case when all data was included in the analysis.

Examination of the data in terms of food categories helps to clarify these findings. For all the food categories except for '*milk*' and '*fruit*', there was a significantly greater kilojoule intake premenstrually. However, when analysed in terms of the percentage that each group contributed to the total kilojoule intake, the *cake and dessert* and '*high sugar foods*' contributed a higher percentage premenstrually (25.8% compared to 15.4% postmenstrually), while the other groups either contributed more postmenstrually or there was little difference between the pre and postmenstrual phases. Analysis of the food groups according to the percentage of macronutrients they contributed resulted in similar findings. When combined the *cake and dessert* and

high sugar foods contributed premenstrually 31.2% of total carbohydrate (postmenstrual contribution 20.03%), 49 % simple sugars (postmenstrual 34%) and 15.8% complex carbohydrate (9.8% postmenstrual). They also contributed premenstrually 27.1% fat (15.3 % postmenstrual) and 11.9% protein (6.5% postmenstrual). The use of Goldberg's cut off limit when analyzing the data showed similar results. These findings show that in this group of women there is a preference for sweet foods that contribute a major proportion of the total carbohydrate, fat and simple sugars. They support other findings in women with and without PMS.

Previously reported studies in women, both with and without PMS have shown increases in energy and macronutrient intake during the premenstrual compared to the postmenstrual phase. However although many studies have shown increased total energy intake, there is lack of consistency when macronutrients are analysed. Lissner et al (1988) found in a group of normal weight women without PMS, that their mean daily energy intake was 364kJ higher during the 10 days premenstrually compared to 10 days postmenstrually. Tarasuk et al (1991) retrospectively demonstrated an increase in energy, fat and fat/1000kcal premenstrually but no difference in protein or carbohydrate in women without PMS.

In the few studies of women with PMS, increases in appetite and food intake, in particular foods high in carbohydrates have been reported during the late luteal phase (Both-Orthman et al. 1988). Wurtman et al (1989) monitored the food intake of 19 women with PMS and nine controls for 48 hours pre and postmenstrually in an inpatient setting. In women with PMS there was a 24% and 43% increase in carbohydrate intake at main meals and snacks respectively, during the late luteal phase. There was no change in protein intake and fat intake rose in proportion to total energy intake. No change in food intake was seen in the control group. In contrast, our study in free living women showed significant increases in energy and all macronutrients, including protein, in women with PMS. This difference may be due to our study design. In Wurtman's et al study, the main meals and snacks provided were either high in carbohydrate or protein. In this current study subjects were free living with ad libitum food choices. As many foods contain a combination of macronutrients, it is difficult to demonstrate a preference for a specific nutrient. Another reason may be that there is not a specific preference for craving for carbohydrate, but rather a desire for pleasant tasting sweet high fat foods as suggested by Hill et al (1994).

A frequently proposed hypothesis for the observed increased food intake in women with PMS is that these women premenstrually have low brain serotonin levels. Carbohydrate consumption can influence

brain serotonin levels by increasing the ratio of tryptophan: large amino acids. Tryptophan, the precursor of serotonin competes with large amino acids for entry into the brain. There are both animal and human studies that support the hypothesis that low levels of brain serotonin may play a role in PMS including increasing carbohydrate intake. Measurement of total blood serotonin, which is believed to reflect brain levels, during the last 10 days of the menstrual cycle, was found to be lower in women with PMS compared to controls (Rapkin et al. 1987). A high carbohydrate meal in comparison to a high protein meal results in elevated blood tryptophan which is a precursor of serotonin and can cross the blood brain barrier. It has been proposed that the observed increase in carbohydrate is an attempt to elevate brain serotonin levels in order to improve mood. A pilot study in women with PMS given L-tryptophan (6g/day) orally showed a reduction in PMS symptoms (Steinberg et al. 1994).

Craving of foods has been reported in women without PMS and conditions such as obesity, bulimia nervosa and seasonal affective disorder. 'Carbohydrate craving', a term used to describe a preference for carbohydrate containing foods has also been reported in some obese individuals (Lieberman et al. 1986) and those with seasonal affective disorder (Rosenthal et al. 1989). It has been proposed that carbohydrate craving in obese subjects may be related to reduced brain serotonin levels. This has been supported indirectly by the

measurement of 5-Hydroxytryptamine (5HT), a precursor of serotonin, in platelet-poor plasma (Blum et al, 1993). Obese individuals of both sexes, and lean males who craved carbohydrate containing foods had lower plasma 5-HT compared to lean individuals who were not carbohydrate cravers.

Fernstrom (1994) in a review of dietary amino acids and brain function argues that 'carbohydrate cravers' as a subtype of obese individuals are likely not to exist. These individuals tend to have a preference for high fat and high carbohydrate snacks such as chocolate bars. These snacks also have sufficient quantities of protein to prevent a rise in brain tryptophan and therefore serotonin. He suggests that if there were a drive to consume carbohydrate then all carbohydrate foods would be equally craved, which is not the case. Fernstrom theorises that it is the natural human preference for sweet high fat foods that leads to the choice of these foods.

Other work investigating 'food cravings' in women supports the likelihood that the desire for certain foods is not solely biological, but psychological factors play an important role. Also food craving seems to be fairly widespread in the general population. Weingarten et al (1991) retrospectively found that in 758 female and 380 male Canadian college undergraduate students, 97% of the female and 68% of the male students reported experiencing food cravings. Chocolate

was the most frequently craved food among women and they craved it more frequently than men. In women there also appeared to be more specific triggers (eg TV commercials, stress or boredom) compared to men, who most often craved foods as a response to hunger. Hill et al report similar findings in a group of 25 healthy women over a 5-week period. They found 49% of the reported cravings were for chocolate or chocolate containing foods, 16% for sweet foods and 12% for savoury foods. Other foods were much less frequently craved. When relating this to the menstrual cycle they found an increase in the cravings of food premenstrually. But there was no selective craving of one food over another and it was concluded, given the mixed macronutrient content of these foods that the subjects were not carbohydrate cravers.

The screening data presented here provides evidence that there is a premenstrual increase in energy and nutrient intake in overweight women with PMS symptoms. The preference for 'sweet foods' that are high in carbohydrate, fat and also contain some protein supports the available literature, that this is not specifically 'carbohydrate craving'. It also presents data, not previously documented, on the frequency of food consumption in women with PMS. This premenstrual increase has implications for women who are experiencing PMS symptoms and trying to lose weight. Increased appetite and difficulty in coping with this may decrease successful longer-term changes in dietary

behaviour.

The women that completed the screening process and met the entry criteria were randomly entered into the study. As discussed above, the screening process identified women with PMS who also showed at least a fifteen percent or greater premenstrual intake of carbohydrate when compared to their post menstrual intake. In the following chapter the macronutrient and energy intake data of women participating in the double blind randomised controlled study is presented and discussed.

CHAPTER 4

Part 2

**Findings of the randomised double blind
placebo controlled parallel group study**

4. Introduction

Increased appetite and food consumption during the premenstrual phase of the menstrual cycle has been reported in the literature for both women with and without PMS. In women with PMS the few studies that have been reported have concluded that subjects have a preference for carbohydrate containing foods. This preference has been called 'carbohydrate craving'. It has been suggested that the 'carbohydrate craving' is a response to reduced brain serotonin levels.

As discussed in Chapter 1, brain serotonin levels are influenced by the ratio of tryptophan to large amino acids within the circulating system. Tryptophan is the precursor of serotonin. Dietary carbohydrate directly influences the blood levels of tryptophan. The protein content of the meal being consumed determines the ratio of tryptophan to large amino acids. Based on this rational, it has been proposed that women with PMS exhibit a preference for foods high in carbohydrate ('carbohydrate craving') in order to increase brain serotonin level. This theory has led to research to determine whether the consumption of high carbohydrate foods or fluids ameliorates PMS symptoms. For example, Sayegh et al (1995) in a double blind placebo crossover study found that symptoms in women with PMS were significantly reduced after a high carbohydrate drink.

The evidence for the proposed low brain serotonin levels in women with PMS is indirect. It is derived from animal studies and the measurement of peripheral blood levels of serotonin in women.

Other work in this area disputes the theory that the observed increased appetite and increased premenstrual food consumption is due to low brain serotonin levels. (See Chapter 1 for a more detailed discussion on this). Firstly, it is argued that if women did 'crave carbohydrate', then any high carbohydrate containing foods would be craved. This is not the case in studies reported. Women tend to have a preference for sweet foods rather than any carbohydrate containing foods.

Secondly, high tryptophan to large amino acid ratio occurs in the blood system only if the diet is very low in protein. This is not the case in the foods reported to be preferred and therefore using this rationale the brain serotonin levels would not be affected. Also the sweet foods preferred are often high in fat, which tends to add to the pleasant taste of foods.

The first part of this chapter therefore seeks to investigate whether in free living overweight women with PMS symptoms increasing the availability of serotonin, by using dexfenfluramine, in the brain specifically reduces the consumption of high carbohydrate foods.

The relationship between premenstrual symptoms such as irritability, mood etc and food consumption is unclear. The literature both supports such a relationship and disputes it. The differing methodologies and instruments used in measuring these relationships vary widely.

No studies have examined this relationship in overweight women with PMS. A relationship between the increase in food consumption, in particular carbohydrate and the severity of PMS could indicate a link with neurological and physiological factors that contribute to PMS symptoms. If such a link exists then it would be expected that for subjects taking dexfenfluramine, increasing serotonin availability would both improve mood and reduce food intake. The second part of this chapter presents the findings addressing this question.

4.1 Hypotheses addressed in randomised double blind placebo controlled study

4.1.1 Hypothesis 2

Dexfenfluramine specifically prevents an increase in premenstrual carbohydrate intake in overweight women identified to have an increase in carbohydrate as part of their PMS symptoms.

The hypothesis will be tested by:

- Comparing carbohydrate and other macronutrient intake over 3 menstrual cycles, pre and postmenstrually between women on dexfenfluramine and placebo.
- Comparing total energy intake pre and postmenstrually between women taking dexfenfluramine and placebo.
- Comparing the types of food consumed pre and post menstrually between those on dexfenfluramine and placebo.

In addition the number of episodes of eating will be investigated to assess whether the dexfenfluramine influences frequency of food intake.

4.1.2 Hypothesis 3

There is a relationship between food intake, PMS score, and perception of well being in overweight women with PMS. Women who have a high PMS score as measured by the Steiner self-rated questionnaire tend to have a relative greater food intake premenstrually. Conversely, dexfenfluramine suppresses both food intake and score.

This hypothesis will be tested by investigating:

- The relation ship between the Steiner self-rated scores and Nottingham health profile scores.

- The relationship between change in PMS score as measured by the Steiner self rated score and change in carbohydrate, and other macronutrient and total energy intake.
- Whether there is a relationship between Nottingham Health Profile subarea scores and changes in energy and macronutrient intake.
- The relationship between the frequency of food consumption and severity of PMS score.

4.2 Participant profile and medication compliance

Eighty-three subjects completed the recording of their pre and postmenstrual food intake at menses 1. Forty-two of these received the placebo and 41 dexfenfluramine (from now on called the treatment group). Table 17 summarises the number of subjects continuing in the study over the 3-month study period.

Table 17: The number of subjects participating through the study period

Group	Menses 1	Menses 2	Menses 3
Treatment	41	38	38
Placebo	42	38	35
Total	83	76	73

The median medication compliance for the placebo and treatment groups was assessed at visit 3 and 4 during the study period as part of the whole study. Compliance was assessed by assessing the ratio of

the number of tablets returned to the total number provided. They were not calculated by myself but provided by the statistician. For the placebo, group compliance at visit 3 was 97.5% with 5% of subjects have less than 75% compliance. At visit 4 compliance was 95% with no subjects having less than 75% compliance. In the treatment, group the median compliance at visit 3 was slightly less, 95%, with 5% having less than 75% compliance. For visit 4 compliance was 95.5% and 6 % of subjects had less than 75% compliance.

Table 18 presents the age, weight, height, BMI, waist, and hip mean screening (called the basal measures) measures for the subjects that completed menses 1 according to their allocated group. Statistical analysis showed no difference between the placebo and treatment groups.

Table 18: The mean ($\pm$ SD) anthropometric measures taken at the commencement of the screening process for subjects that completed menses 1 of the study

Measure	Treatment	Placebo	Total
Number of subjects	41	42	83
Age (years)	36.3 $\pm$ 4.8	37.5 $\pm$ 6.3	36.8 $\pm$ 5.6
Weight (kg)	77.6 $\pm$ 10.9	77.5 $\pm$ 11.6	77.6 $\pm$ 11.2
Height (cm)	163.9 $\pm$ 6.7	163.5 $\pm$ 5.8	163.7 $\pm$ 6.2
BMI (Kg/m ²)	28.8 $\pm$ 3.2	28.9 $\pm$ 3.9	28.9 $\pm$ 3.5
Waist (cm)	82.4 $\pm$ 7.0	84.3 $\pm$ 9.5	83.5 $\pm$ 8.3
Hip (cm)	109.3 $\pm$ 6.6	108.2 $\pm$ 6.4	108.7 $\pm$ 6.5

4.3 Anthropometric measures over the study period

The anthropometric measurements and BMI for each of the three menstrual cycles appear in Table 19. These measures were compared to the initial screening data (Table 18). Student's *t-tests* have been used to compare all the data, except for the waist measurements that were not normally distributed. Wilcoxon signrank tests were used to compare this data.

No significant changes in weight, BMI, hip and waist measurements occurred over the study period for the placebo group (Table 19). For the treatment group, comparison between the screening data and menses 3 there was a significant reduction in weight, BMI, hip and waist measurements ($p < 0.001$). There were also significant differences between all measures at the commencement of the study (menses 1) and menses 3 ($p < 0.001$), menses 1 and 2 ($p < 0.001$) and menses 2 and 3 ($p < 0.001$) for all the above measures in the treatment group.

Table 19: The mean anthropometric measures for the placebo and treatment groups over the study period

	Treatment group	Menses 1	Menses 2	Menses 3
Number of subjects	Treatment Placebo	41 42	38 38	38 35
Weight (Kg)	Treatment Placebo	77.8 ± 10.7^3 77.5 ± 11.7	76.7 ± 10.8^4 77.6 ± 11.9	$74.42 \pm 11.2^{1\ 2}$ 78.1 ± 12.0
Height (cm)	Treatment Placebo	163.9 ± 6.7 163.5 ± 5.8	164.1 ± 6.9 163.6 ± 5.9	164.1 ± 6.9 163.8 ± 5.9
Waist measure (cm)	Treatment Placebo	82.5 ± 6.7^3 84.6 ± 8.9	81.4 ± 7.4^4 84 ± 9.3	$79.2 \pm 7.4^{1\ 2}$ 84.9 ± 9.8
Hip measure (cm)	Treatment Placebo	109.5 ± 6.5^3 108.3 ± 6.9	108.7 ± 6.3^4 108.4 ± 6.8	$107.1 \pm 7.2^{1\ 2}$ 108.3 ± 6.6
BMI (kg/m²)	Treatment Placebo	28.9 ± 3.3^3 28.99 ± 3.9	28.4 ± 3.3^4 28.98 ± 4.1^4	$27.6 \pm 3.5^{1\ 2}$ 29.1 ± 4.2

¹ Comparison between screening and menstrual cycle $p < 0.001$

² Comparison of menses 1 and 3 $p < 0.001$ ³ Comparison of menses 1 and 2 $p < 0.001$

⁴ Comparison of menses 2 and 3 $p < 0.001$

A summary of the number of subjects categorised according to BMI classification appears in Table 20. The majority of subjects were within the overweight range ($25 < \text{BMI} < 30$) at the commencement of the study.

A minority of subjects fell within the normal weight or had a BMI > 35 , which were outside the study criteria. However, as these subjects participated in the study and their BMIs were close to the inclusion criteria, it was decided they would be included in the study.

In both the treatment and placebo groups, there was a movement toward reducing BMI (Table 20). This was more marked, as would be expected, in the group receiving dexfenfluramine.

Table 20: Study participants categorised according to their BMI range

BMI *	Basal data		Menses 1		Menses 2		Menses 3	
	Treatment N=41	Placebo N=42	Treatment N=41	Placebo N=42	Treatment N=38	Placebo N=38	Treatment N=38	Placebo N=35
20<BMI<25	2	1	1	1	5	2	10	4
25 ≤BMI<30	24	26	25	26	19	22	17	17
30 ≤BMI<35	14	9	15	9	14	11	11	11
BMI≥ 35	1	6	0	6	0	3	0	3

* 20<BMI <25 is normal weight range, 25 ≤BMI<30 overweight, 30 ≤BMI<35 obese
BMI≥ 35 markedly obese

4.4 Comparison of the energy and macronutrient intake between the placebo and treatment groups

Table 21 presents the basal kilojoule and macronutrient intake of women receiving the placebo and dexfenfluramine. The intakes of the two groups did not differ significantly except for the postmenstrual protein intake ($p<0.05$).

The mean kilojoule and macronutrient intake for menses 1 to 3 appears in Table 22. In the placebo group there was significantly greater fat, carbohydrate, simple sugar and complex carbohydrate and energy

Table 21: The basal mean ($\pm$ SD) pre and postmenstrual kilojoule and macronutrient intake according to treatment group

	Energy (kJ) $\pm$ SD	Protein (g) $\pm$ SD	Fat (g) $\pm$ SD	Carbohydrate (g) $\pm$ SD	Complex carbohydrate (g) $\pm$ SD	Simple sugars (g) $\pm$ SD
Women receiving dexfenfluramine						
Premenstrual	8242 (1654) ¹	75 (14.1)	78.1 (22.4)	237 (49.1)	124.7 (32.3)	112.3 (37.6)
Postmenstrual	5793 (1156)	61.3 (13.8)	51.6 (16.4)	163.8 (34.4)	92.5 (22.1)	71 (21.4)
Women receiving the placebo						
Premenstrual	8954 (2557)	81.4 (22.2)	85 (34.5)	249 (68.7) ¹	135 (31.7)	113 (53)
Postmenstrual	6163 (1397)	68.2 [†] (17.5)	53.9 (16.4)	168.9 (40)	98 (25.5)	71 (26.4)

¹ Figures appearing in brackets are standard deviations [†]p<0.05

intake premenstrually compared to postmenstrually over the three menstrual cycles. Protein intake did not significantly alter.

In the treatment group (subjects taking dexfenfluramine), there was a significantly ($p<0.05$) higher intake of carbohydrate and complex carbohydrate in menses 1 and 3. For menses 3, the energy ($p=0.003$), protein ($p=0.007$) and fat ($p=0.006$) intake is also significantly greater. Analysis of data that included only those women that had completed all 3 cycles showed similar results (Table 22).

Table 22: The mean ($\pm$ SD) pre and postmenstrual kilojoule and macronutrient intake for menses 1, 2 and 3 for the placebo and treatment groups

Nutrient	Menses 1		¹ P-value	Menses 2		P-value	Menses 3		P-value
	Pre	Post		Pre	Post		Pre	Post	
kJ									
treatment	5467 (1246)	5045 (1260)	0.07 [‡]	5349 (1333)	4991 (1593)	0.3 [‡]	5697 (1309)	5122 (1331)	0.003 [‡]
placebo	6923 (1835)* ^{‡2}	6005 (1973) ^{†‡}	0.0001 [‡]	6973 (1926)* [‡]	5813 (1859) ^{†‡}	0.0004 [§]	6813 (1690) ^{†‡}	5930 (1533) ^{†‡}	0.003 [§]
Protein (g)									
treatment	57.8 (18.9)	54.2 (15.9)	0.16 [‡]	54.8 (13.9)	54.7 (18.5)	0.93 [‡]	59.5 (14)	54.1 (14)	0.007 [‡]
placebo	67.3 (18.8) ^{†‡}	66.2 (22) ^{†‡}	0.7 [‡]	68.5 (19.7) ^{†‡}	63.2 (18.7) ^{† §}	0.15 [‡]	69.6 (19.4) ^{†‡}	63.4 (17.3) ^{†‡}	0.3 [§]
Fat (g)									
treatment	47.5 (14.5)	43.8 (15.6)	0.24 [‡]	48.8 (15.7)	42.9 (23.5)	0.22 [‡]	51.1 (14.4)	44.5 (16)	0.006 [‡]
placebo	64.4 (22.8)* [‡]	53.1 (23) ^{†‡}	0.0008 [‡]	63.1 (21) ^{†‡}	50.5 (21.8)	0.001 [‡]	60.9 (19.4) ^{†‡}	48.3 (16.3)	0.0004 [§]
Carbohydrate (g)									
treatment	158.6 (35.4)	144.4 (37.5)	0.025 [‡]	152.1 (42.1)	143.9 (37.4)	0.31 [‡]	159.1 (38.5)	148.1 (34.8)	0.02 [‡]
placebo	191 (47.9)* [‡]	162.6 (48.8)	0.0001 [‡]	194.3 (57.1)* [‡]	161.8 (54.8)	0.000 [‡]	191.8 (55.2) ^{†‡}	166.4 (51.6)	0.001 [§]
Simple sugars (g)									
treatment	70.4 (27.6)	63.9 (25.4)	0.14 [‡]	65.7 (27)	63.3 (19)	0.6 [‡]	68.3 (25.5)	68.6 (22.3)	0.55 [‡]
placebo	85.2 (36.2) ^{†‡}	67.9 (28.9)	0.003 [‡]	84.8 (37.8) ^{†‡}	67.8 (31.5)	0.0006 [‡]	88 (42.8) ^{†‡}	70.5 (32.7)	0.006 [§]
Complex CHO(g)									
treatment	87.8 (22.2)	79.8 (24.7)	0.02 [‡]	85.8 (26.1)	80.2 (29.2)	0.3 [‡]	90.5 (23.4)	78.7 (24.9)	0.005 [‡]
placebo	105.9 (27) ^{†‡}	94.7 ^{†‡}	0.005 [‡]	109.4 (31)* [‡]	93.9 (31.2)	0.001 [‡]	103.7 (28.4) ^{†‡}	95.7 (29.6) ^{†‡}	0.1 [‡]

¹ p values when comparing pre and post menstrual intakes within the treatment and placebo groups

² the significance test between the treatment and placebo groups

[‡] paired t-test [§] Wilcoxon sign rank test * p<0.001[†] p<0.05

Table 23: The mean ($\pm$ SD) pre and postmenstrual kilojoule and macronutrient intake for women that completed all three menstrual cycles

	Menses 1		¹ P-value	Menses 2		P-value	Menses 3		P-value
Nutrient	Pre	Post		Pre	Post		Pre	Post	
kJ									
treatment	5490 (1284)	5104 (1274)	0.125 [‡]	5302 (1394)	4980 (1591)	0.3 [‡]	5688 (1314)	5115 (1326)	0.003 [‡]
placebo	6919 (1881)	6177 (2020)	0.0013 [‡]	6949 (1951)	5769 (1851)	0.0006 [§]	6804 (1693)	5921 (1540)	0.004 [§]
Protein (g)									
treatment	57.6 (19.4)	55.2 (15.9)	0.35 [‡]	54.3 (15)	54.6 (18.6)	0.93 [‡]	59.4 (14.2)	54.0 (13.9)	0.006 [‡]
placebo	69.1 (19.3)	69.7 (22.2)	0.83 [‡]	68.2 (20.1)	62.8 (18.6)	0.12 [§]	69.1 (19.1)	63.7 (17.2)	0.25 [‡]
Fat (g)									
treatment	47.8 (15)	44.2 (16.1)	0.29 [‡]	48.6 (16.1)	42.9 (23.5)	0.22 [‡]	50.9 (14.4)	44.5 (16)	0.006 [‡]
placebo	63.7 (23.4)	54.6 (23.6)	0.005 [‡]	62.7 (21.0)	50.2 (21.7)	0.002 [‡]	60.9 (19.4)	48.2 (16.3)	0.0007 [§]
Carbohydrate (g)									
treatment	160.1 (35.7)	145.8 (38.1)	0.04 [‡]	150.3 (42.4)	143.4 (37.4)	0.3 [‡]	158.9 (38.6)	147.7 (34.9)	0.02 [‡]
placebo	190.2 (47.6)	166.7 (50.2)	0.0007 [‡]	194.6 (57.4)	160.9 (54.7)	0.0001 [‡]	191.7 (55.3)	165.9 (52.2)	0.002 [§]
Simple sugars (g)									
treatment	71 (28.4)	64.0 (25.7)	0.15 [‡]	65.4 (27.2)	63.2 (19)	0.6 [‡]	68.4 (25.4)	68.3 (22.6)	0.55 [‡]
placebo	83.6 (33.4)	70.2 (31.6)	0.03 [‡]	84.4 (38.1)	67.1 (31)	0.001 [‡]	87.9 (42.8)	70.4 (32.8)	0.005 [§]
Complex CHO(g)									
treatment	88.6 (21.6)	81.1 (24.9)	0.02 [‡]	84.3 (25.9)	79.7 (29.1)	0.3 [‡]	90.3 (23.5)	78.7 (24.9)	0.005 [‡]
placebo	106.4 (27.8)	96.4 (28.4)	0.004 [‡]	110 (31)	93.7 (31.2)	0.002 [‡]	103.6 (28.5)	95.2 (30.1)	0.2 [‡]

¹ p values when comparing pre and post menstrual intakes for the treatment and placebo groups

² the significance test between the treatment and placebo groups

[‡] paired t-test [§] Wilcoxon sign rank test

* p<0.001 † p<0.05

A comparison of the energy and macronutrient intake between the placebo and treatment groups reveals a greater energy and macronutrient for the placebo group compared to the treatment group for both the premenstrual and postmenstrual phases.

Analysis, using unpaired t-test or Wilcoxon sign rank tests for non-normal data to compare the nutrient intake between the placebo and treatment groups, found a significantly greater premenstrual energy and macronutrient intake for the placebo group (Table 22). Postmenstrually there was a significantly higher intake by the placebo group for energy and protein for each of the three menstrual cycles. For the other macronutrients the intake was higher for all 3 menstrual cycles for the placebo, but only of significance for fat in menses 1 and complex carbohydrate for menses 1 and 3. Thus, women receiving dexfenfluramine were eating less than those on the placebo.

However, analysis of the data that compared the pre/postmenstrual difference in energy and macronutrient intake between the placebo and treatment groups, detected no consistently significant difference between the two groups, although the placebo exhibited the greatest difference (Table 24). The placebo group at menses 2 showed a greater change between pre and postmenstrual intake when compared to the treatment group, for kilojoules, carbohydrate, and simple sugars. It should also be noted that the standard deviations were very large reflecting a large variation between the pre and postmenstrual energy and macronutrient intake. Women who completed the whole study exhibited similar findings (Table 25).

Table 24: The mean difference ($\pm$ SD) in energy and macronutrient intake for 3 menstrual cycles for all women in the placebo and treatment groups.

Mean energy and macronutrient difference	Menses 1		Menses 2		Menses 3	
	Treatment N=41	Placebo N=42	Treatment N=38	Placebo N=38	Treatment N=38	Placebo N=35
Diff kJ	459 (1413)	924 (1430)	327 (1617)	1133 (1552) ^{†‡}	637 (1121)	882 (1502)
Diff protein (g)	3.8 (16.7)	0.94 (13.2)	0.14 (17.8)	4.73 (18.5)	6.4 (12.7)	6.1 (18.7)
Diff fat (g)	4.4 (18.2)	11.3 (19.9)	5.4 (24.5)	12.5 (18.7)	6.7 (24.5)	12.6 (18.7)
Diff carbohydrate (g)	14.5 (39.3)	29 (40.8)	7.6 (37.4)	33.1 (40.5) ^{†‡}	14.8 (35.8)	25.4 (40.7)
Diff simple sugars (g)	7.01 (30.8)	17.4 (27.0)	1.9 (21.9)	17.6 (27) ^{†‡}	2.3 (25.6)	17.5 (32.8)
Diff complex carbohydrate (g)	7.48 (18.9)	11.3 (24.4)	5.7 (24.3)	15.4 (24.3)	12.8 (24.4)	8.1 (22.9)

[†] paired t-test [‡] Wilcoxon sign rank test * p<0.001 [†] p<0.05

Table 25: The mean difference ($\pm$ SD) in energy and macronutrient intake for women that completed all three menstrual cycles (treatment group= 38 and placebo group =35)

Mean energy and macronutrient difference	Menses 1		Menses 2		Menses 3	
	Treatment	placebo	Treatment	placebo	Treatment	placebo
Diff kJ	386 (1495)	742 (1248)	291 (1667)	1133 (1535) ^{†‡}	631 (1165)	883 (1505)
Diff protein (g)	2.6 (16.9)	-0.46 (16.1)	-0.27 (18.1)	4.7 (18.3)	6.3 (13.0)	5.4 (18.9)
Diff fat (g)	3.3 (18.8)	9.2 (18.4)	5.2 (25.1)	12.3 (19.6)	6.5 (13)	12.7 (18.7)
Diff carbohydrate (g)	14.6 (40.8)	23.5 (37)	6.35 (37.8)	33.1 (40.4) ^{†‡}	14.9 (37.1)	25.8 (40.2)
Diff simple sugars (g)	7.6 (31.8)	13.35 (29.9)	1.7 (22.1)	17.9 (27.0) ^{†‡}	2.7 (26.4)	17.5 (32.8)
Diff complex carbohydrate (g)	7.2 (19.7)	10.1 (23.9)	4.6 (24.6)	15.1 (24.4)	12.7 (24.8)	8.4 (22.7)

* $p < 0.001$ # $p < 0.05$

† paired t-test § Wilcoxon sign rank test

When analysed in terms of the mean macronutrient and energy intake for menses 1, 2 and 3, (Table 26) for the placebo all were significantly greater. For the treatment group, all except protein and sugar was significantly greater.

Table 26: The mean kilojoule and macronutrient intake for the treatment and placebo groups. (P-protein, F-fat, CHO-carbohydrate, SGR-simple sugar, CPLCHO-complex carbohydrate)

Group	Menstrual phase	kJ	P	F	CHO	SGR	CPLCHO
Treatment	Pre	5496	57	48.8	156	68	87.56
	Post	5035	53.9	43.57	144	64.9	79.45
		p=0.004	p=0.43	p=0.013	p=0.008	p=0.2	p=0.0006
Placebo	Pre	6912	67	63.5	193	87	105.7
	Post	5833	62.9	50.31	160	67	93.21
		p=0.0001	p=0.03	p=0.001	p=0.00	p=0.0	p=0.0001

The median alcohol intake for women in the treatment and placebo groups appear in Table 27. For both the analysis including all women participating in the study and those that completed all 3 cycles there was no significant difference between the pre and post menstrual alcohol consumption, except for at menses 3 for the placebo group.

Table 27: The median and range of alcohol consumption (g) of all women and for women completing all three cycles

Women taking part in the study	Menses 1		Menses 2		Menses 3	
	Treatment	Placebo	Treatment	Placebo	Treatment	Placebo
All women -pre menses	0 (0-14)	0 (0-71)	0 (0-32)	2 (0-40)	0 (0-43)	0 (0-42) ^{#§}
- post menses	0 (0-43)	2 (0-73)	0 (0-14)	0 (0-46)	0 (0-18)	6 (0-45)
All 3 cycles - pre menses	0 (0-14)	0 (0-71)	0 (0-32)	2 (0-40)	0 (0-43)	0 (0-42) ^{#§}
- post menses	0 (0-43)	0 (0-73)	0 (0-14)	0 (0-46)	0 (0-18)	6 (0-45)

[#] p<0.05 [§] Wilcoxon sign rank test

There was also no significant difference between the placebo and treatment groups for the premenstrual alcohol intake. For the postmenstrual alcohol intake, this was also the case, except at menses 3, where the median placebo intake was greater than the treatment group ($p < 0.007$).

4.4.1 The macronutrient contribution to total energy consumption

Table 28 displays the percentage of energy contributed by each macronutrient for all women participating in the study. Statistical analysis revealed no significant difference between the pre and post menstrual percentage of carbohydrate, complex carbohydrate or simple sugars for both the placebo and treatment groups. The remaining macronutrients (protein and fat) displayed inconsistent findings for both the placebo and treatment groups. Given the small differences between pre and post percent contribution for fat and protein, it is unlikely that they are of significance. Analysis of both the data that included only the women that completed the study showed similar findings (Table 29). The premenstrual percentage of protein at menses 1 and 2 for the placebo group was significantly less than the postmenstrual protein; this was also the case for the treatment group at menses 2. In addition, there was a significantly greater premenstrual percentage of fat for the treatment group at menses 2 ($p = 0.03$) and the placebo group at menses 3 ($p = 0.006$).

A comparison of the percent of macronutrient intake between the placebo and treatment groups found no statistically significant difference between them for either the premenstrual and postmenstrual phases.

Table 28: Macronutrient intake expressed as the mean percentage ($\pm$ SD) of energy for menses 1, 2 and 3

Percent Nutrient	Menses 1		¹ P-value	Menses 2		P-value	Menses 3		P-value
	Pre	Post		Pre	Post		Pre	Post	
Protein (%)									
treatment	17.9 (3.3)	18.45 (4.1)	0.4	17.8 (4.5)	19.1 (4.4)	0.07	18.0 (3.5)	18.2 (3.5)	0.8 ^s
placebo	16.7 (3.0)	19.1 (3.9)	0.00	16.9 (2.8)	18.9 (3.8)	0.005 ^s	17.5 (3.3)	18.5 (3.3)	0.1
Fat (%)									
treatment	31.9 (4.9)	31.6 (5.8)	0.93 ^s	33.7 (5.6)	30.4 (7.4)	0.03	33.0 (5.3)	31.5 (5.3)	0.3
placebo	34.1 (6.0)	32.2 (5.9)	0.077	33.2 (5.2)	31.6 (7.1)	0.14	33.0 (5.6)	29.9 (6.2)	0.006
Carbohydrate (%)									
treatment	46.7 (5.2)	46.1 (6.3)	0.4 ^s	45.4 (6.5)	47.0 (6.1)	0.2	44.8 (5.1)	46.8 (5.1)	0.2
placebo	44.7 (6.2)	44.0 (6.3)	0.4	44.8 (5.2)	44.9 (7.3)	0.9	44.9 (6.5)	44.6 (6.6)	0.7 ^s
Simple sugars (%)									
treatment	20.5 (6.2)	20.3 (6.5)	0.7	19.6 (6.1)	21.0 (5.7)	0.1	19.0 (5.3)	21.7 (6.0)	0.09
placebo	19.4 (5.8)	18.1 (5.4)	0.14	19.1 (5.6)	18.6 (5.9)	0.4	20.1 (7.1)	18.6 (6.2)	0.09
Complex CHO (%)									
treatment	27.7 (6.2)	27.2 (6.7)	0.6	27.2 (5.8)	27.3 (6.0)	0.96	27.3 (5.0)	26.3 (5.5)	0.3
placebo	26.6 (6.0)	27.5 (6.2)	0.4	27.2 (5.5)	27.7 (5.7)	0.6	26.3 (5.9)	25.6 (5.8)	0.3

¹Tests are t-tests unless otherwise indicated ^s Wilcoxon sign rank test

Table 29: Macronutrient intake expressed as the mean percentage ($\pm$ SD) of energy for women that completed all 3 cycles

Percent Nutrient	Menses 1		¹ P-value	Menses 2		P-value	Menses 3		P-value
	Pre	Post		Pre	Post		Pre	Post	
Protein (%) treatment	17.8 (3.4)	18.6 (4.2)	0.21	17.8 (4.5)	19.1 (4.4)	0.042 ^s	18.0 (3.5)	18.2 (3.5)	0.77 ^s
placebo	17.2 (3.0)	19.5 (4.0)	0.0001	16.9 (2.9)	18.9 (3.8)	0.006 ^s	17.5 (3.3)	18.5 (3.3)	0.17
Fat (%) treatment	31.99 (5.1)	31.5 (6.0)	0.9 ^s	33.7 (5.6)	30.4 (7.4)	0.034	33.04 (5.3)	31.5 (5.3)	0.29
placebo	33.6 (6.3)	32.1 (6.1)	0.16	33.1 (5.2)	31.4 (7.1)	0.12	33.0 (5.6)	29.9 (6.2)	0.006
Carbohydrate(%) treatment	47.0 (5.1)	46.0 (6.6)	0.25	45.3 (6.5)	47.0 (6.1)	0.24	44.8 (5.2)	46.8 (5.1)	0.19
placebo	44.6 (6.4)	43.8 (6.6)	0.45	45.0 (5.1)	44.9 (7.3)	0.9	44.9 (6.5)	44.6 (6.6)	0.6
Simple sugars(%) treatment	20.5 (6.4)	20.1 (6.6)	0.59	19.6 (6.1)	21.0 (5.7)	0.11	19.0 (5.3)	21.7 (6.0)	0.09
placebo	19.25 (5.7)	18.0 (5.6)	0.19	19.1 (5.7)	18.6 (5.9)	0.48	20.1 (7.1)	18.5 (6.2)	0.08
Complex CHO (%) treatment	28.0 (6.2)	27.3 (6.8)	0.54	27.2 (5.8)	27.3 (6.0)	0.95	27.3 (5.0)	26.3 (5.5)	0.32
placebo	26.8 (5.9)	27.4 (6.2)	0.66	27.5 (5.4)	27.9 (5.7)	0.8	26.3 (5.9)	27.6 (5.8)	0.2

¹ Tests are t-tests unless otherwise indicated

^s Wilcoxon sign rank test

4.4.2 Variation of energy and macronutrient intake over the three cycles of the study

The Generalized Estimating Equations (GEE) was used to determine whether the energy and macronutrient intake varied significantly over the study period (menses 1-3) and whether there was a treatment effect. As explained in Chapter 2, this analysis was used as it allows for missing data that resulted from participants dropping out of the study prior to its completion.

Table 30 presents the treatment effect coefficients for energy and macronutrients. For premenstrual and postmenstrual energy and macronutrient intake there was no significant effect of time (ie, menses 1-3) or an interaction between menses and treatment. This indicates that the variation in the women's food intake over the study period was relatively stable and remained within an acceptable range.

Women taking dexfenfluramine significantly reduced premenstrual energy and macronutrient intake. Dexfenfluramine suppressed kilojoule intake premenstrually by a mean of 1455kJ (CI -2130 - -780) when compared to the placebo group. It also suppressed postmenstrual energy, but to a lesser degree.

Adjustment for basal (ie screening data) energy and macronutrient intake data lessened this effect but it was still significant. For

example, in the case of kilojoule intake, Dexfenfluramine suppressed premenstrual kilojoule intake by a mean of 1297kJ (CI -1975 - -619) when compared to the placebo group.

Table 30: The GEE treatment effect coefficients ($\pm 95\%$ confidence limit) for energy and macronutrients

Nutrient	Menstrual phase	Treatment effect coefficient (95%CI)	P value	Treatment effect coefficient (95% CI) after adjusting for basal data	P value
Kilojoule	Pre	-1455 (-2130- -780)	0.000	-1297 (-1975- -619)	0.000
	Post	-951 (-1658- -243)	0.0054	-659 (-1242- -77)	0.011
Protein	Pre	-9.54 (-17.6- -1.42)	0.0010	-7.3 (-14.9- 0.031)	0.003
	Post	-11.8 (-20.0- -3.57)	0.002	-8.2 (-15.0-1.4)	0.026
Fat	Pre	-16.9 (-25.15- -8.7)	0.000	-15.6 (-23.7- -7.5)	0.0001
	Post	-6.5 (-13.4- 0.4)	0.065	-5.5 (-10.5 - 0.50)	0.031
Carbohydrate	Pre	-32.8 (-50.9- -14.7)	0.000	-29.4 (-47.1- -11.8)	0.0001
	Post	-16.4 (-32.95- 0.21)	0.053	-10.5 (-21.5- 0.41)	0.059
Simple sugars	Pre	-14.8 (-28.7- -0.98)	0.0036	-15.2 (-28.3- -2.16)	0.0007
	Post	-4.2 (-16 -7.7)	0.49	-3.9 (-11.1 -4.3)	0.53
Complex carbohydrates	Pre	-18.03 (-28.6- -7.4)	0.0003	-14.1 (-24.3- -3.9)	0.0027
	Post	-14.7 (-26.2 - -3.2)	0.007	-10.4 (-19.1- -1.7)	0.012

Treatment with dexfenfluramine also decreased postmenstrual energy, protein, and complex carbohydrate intake. For example for postmenstrual energy there was a significant treatment effect ($p=0.0054$) with the treatment coefficient = -951kJ (95% CI -1658 - -243). Adjustment for basal data reduced this effect but it was still significant ($p=0.0112$), with the treatment effect coefficient = -659kJ (95% CI -1242 - -77).

Postmenstrual carbohydrate and fat intake was also reduced in women taking dexfenfluramine, but this was not significant. Adjusting for the basal data resulted in the treatment significantly reduced the fat intake, but not for carbohydrate.

4.4.3 Analysis of data according to food categories

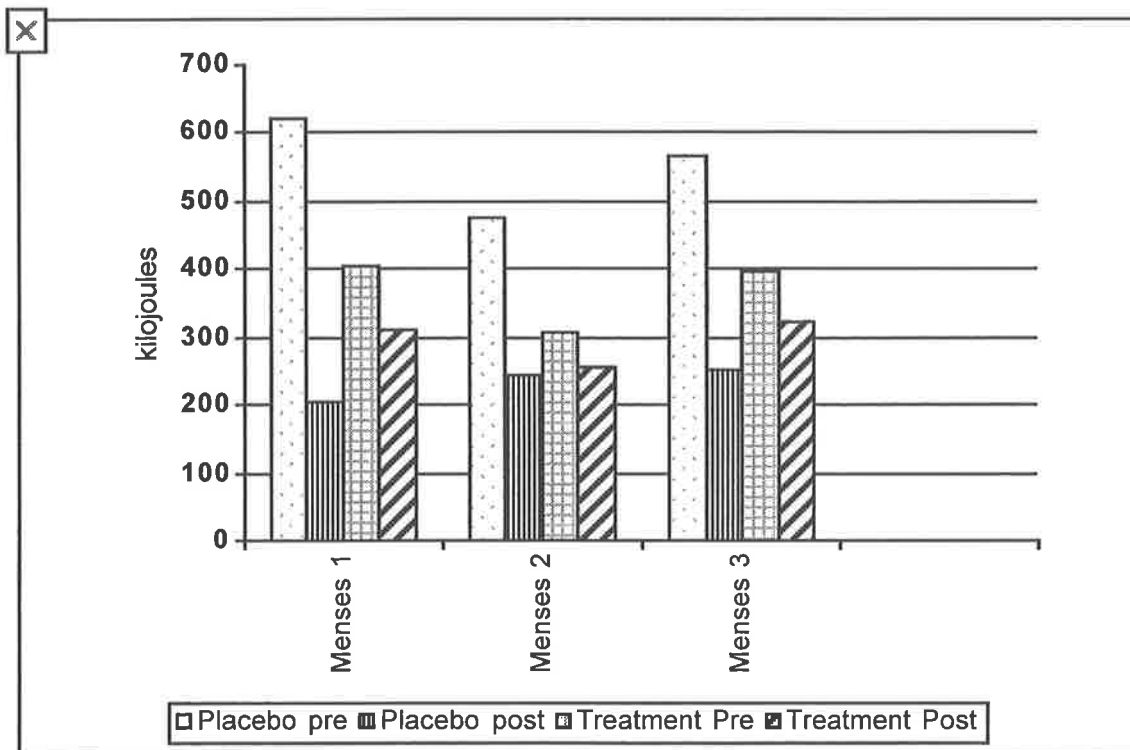
Data were analysed according to food categories to identify whether there was a preference for specific groups of food. The energy and macronutrient analysis for each food group appear in Tables 31-36 on pages 136-141 for all women who took in the study and in Tables 37-42 for women that completed the study.

4.4.3.1 *The contribution to total energy intake by food categories*

In the placebo group, the energy contribution by most of the food categories were higher premenstrually compared to postmenstrually (Table 31). The elevated premenstrual intake was consistently significantly greater across all three menstrual cycles for the *cake and desserts* ($p<0.05$) and *high sugar food* (menses1 and 2, $p<0.001$ and

menses 3 $p<0.05$) categories. Graph 1 illustrates the contribution by the high sugar food category to total energy intake. There was also a significantly greater intake from *savoury snacks* ($p<0.05$) at menses 3.

Graph 1: The mean kilojoule contribution by the *high sugar foods* category for the treatment and placebo groups at menses 1 to 3



In the treatment group, there was no consistently significant difference between pre and post menstrual intakes of any of the food categories. For the *cake and desserts* category, there was a significantly greater contribution premenstrually at menses 1 and 3 ($p<0.05$). For menses 2, the intake from the *fat* category was greater ($p<0.05$) and in menses 3 the intake from the *meat* group was greater ($p<0.05$).

The food category data was also analysed to determine whether there was a significant difference between the intakes of the placebo and

treatment groups. No consistent difference was identified for either the pre or postmenstrual intake. The differences identified were for the *fat* category at menses 1. The placebo group contributed significantly more kilojoules premenstrually ($p<0.006$) and postmenstrually ($p<0.03$).

4.4.3.2 *The contribution of the food categories to protein intake*

For the placebo group there was a significantly greater premenstrual protein contribution by the *cake and dessert* ($p<0.05$) and *high sugar foods* categories (menses 1 $p<0.001$, menses 2 and 3 $p<0.05$) for all 3 cycles (Table 32).

There was no other significant difference between the pre and postmenstrual intake except for the *fat* category in menses 3 ($p<0.05$).

In the treatment group, there was no consistent pattern. There was a significantly greater premenstrual intake for the *cake and dessert* category ($p<0.05$) during menses 1 and 3, but not menses 2. There was also a significantly reduced premenstrual protein contribution from the *fruit* category in menses 2 and 3. Lastly in menses 3 the *fat* category ($p<0.05$) contributed significantly more protein (although the quantities were very small).

4.4.3.3 Contribution of food categories to the total fat intake

In the placebo group, the *high sugar food* category contributed significantly ($p < 0.001$ for menses 1 and $p < 0.05$ for menses 2 and 3) more fat over all menstrual cycles (Table 32). The *cake and dessert* category provided significantly more fat ($p < 0.05$) in menses 2 and 3 but not menses 1. Examination of the data showed that for one subject the contribution by the *cake and dessert* category to the total fat intake was 46.6% of the total fat intake for this subject. Thus for the *cake and desserts* category, this subject had a noticeable influence on the findings. This subject was not excluded from the analysis of the data, as her total macronutrient and energy intake for menses 1 (or menses 2 and 3) was not considered to exhibit outlier features. Examination of the food category data showed that the *cake and desserts* category was a major source of postmenstrual energy and macronutrients for menses 1 (43% of the total kilojoules, 21% protein, 46% total carbohydrate, 67.8% simple sugars and 34.9% complex carbohydrate). Analysis of the data excluding this subject resulted in there being a significantly higher premenstrual compared to postmenstrual intake ($p = 0.03$)

Savoury snacks contributed a significantly greater premenstrual intake of fat ($p < 0.05$) at menses 1 and 3. There was also a significantly greater intake from the *fat* category in menses 3 ($p < 0.05$).

In the treatment group, most food categories there was a higher premenstrual fat intake compared to postmenstrual intake. However,

this was not significant except for the *fat* category in menses 2 and the *vegetables* category in menses 3.

4.4.3.4 Contribution of food categories to the total carbohydrates intake

Most food categories contributed more carbohydrate premenstrually compared to postmenstrually for both the placebo and treatment groups (Table 34). One exception of interest was the *fruit* category. For this group in the treatment group the postmenstrual carbohydrate was greater and this was significant in menses 2. This was also the case in the placebo group for menses 1 and 2, although the difference was not significant. Similar patterns occur for the *fruit* category for its contribution of kilojoules and to a lesser extent for protein.

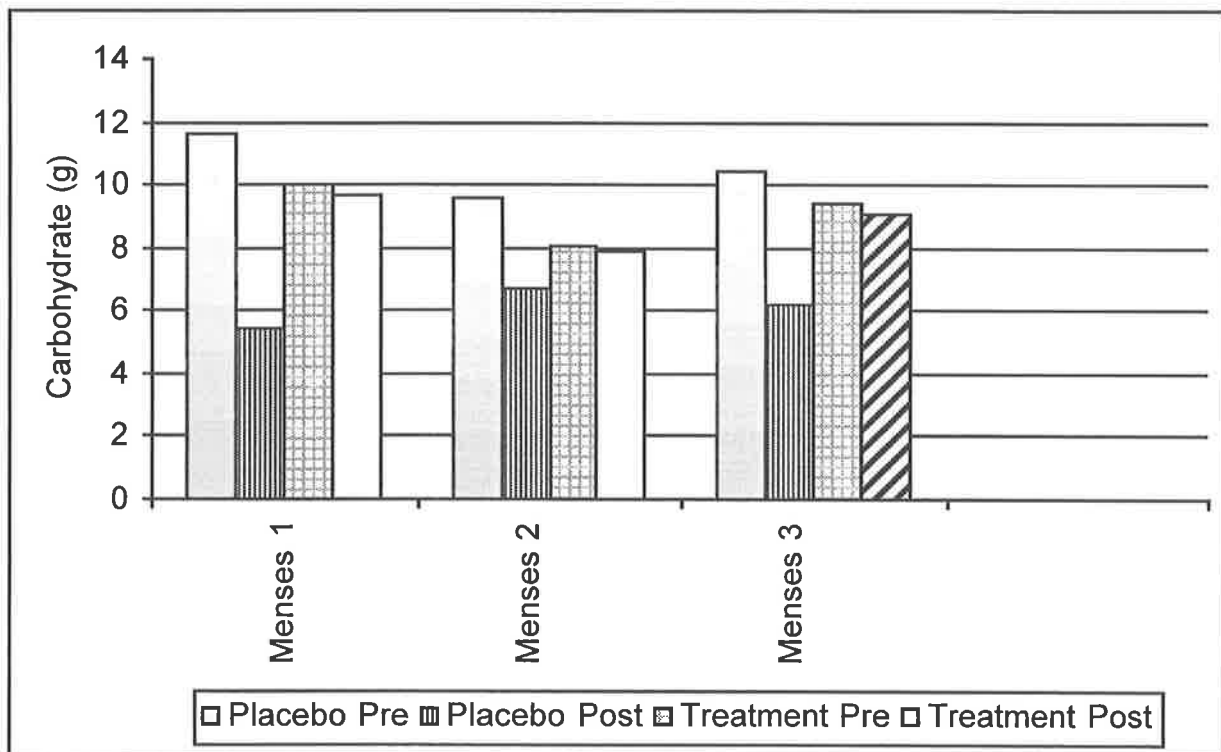
The *high sugar foods* category contributed significantly ($p < 0.001$ for menses 1 and 2 and $p < 0.05$ for menses 3) more carbohydrate premenstrually for all menstrual cycles in the placebo group (Graph 2).

In the *cake and desserts* category there was a greater contribution premenstrually in all cycles but this was only significant in menses 2 ($p < 0.05$) and 3 ($p < 0.05$). For menses 1, $p = 0.06$ indicating a border line significance. Examination of the data showed that for one subject the contribution of postmenstrual carbohydrate from *cake and desserts* category was 128g compared to a mean of 19.5 g. Exclusion of this

subject's data resulted in a significantly greater premenstrual intake ($p=0.03$).

There was also a greater intake premenstrually at menses 3 for the *savoury snacks* category.

Graph 2: The mean carbohydrate contributed by the *high sugar foods* category for the placebo and treatment groups over menses 1 to 3.



In the treatment group as stated above there was a greater premenstrual contribution to the carbohydrate intake by most food categories. These were not significant except for the *cake and desserts* category in menses 1 and 3 ($p < 0.05$), *milk* category in menses 1 ($p < 0.05$) and a greater postmenstrual contribution from the *fruit* category in menses 2 ($p < 0.05$).

4.4.3.5 Contribution of food categories to the total simple sugars intake

In the placebo group, the *high sugar foods* category contributed significantly more towards the ($p < 0.001$ for menses 1 and $p < 0.05$ for menses 2 and 3) premenstrual simple sugar intake (Table 35). Also as for total carbohydrate, in menses 2 and 3 there was a significantly greater ($p < 0.05$) premenstrual intake from the *cake and desserts* category. At menses 1, for the *cake and desserts* category, the premenstrual intake was of border line significant ($p = 0.056$). As in the analysis of carbohydrate provided by this category, there was one subject whose intake at menses 1 from this food group postmenstrually, influenced the outcome of the analysis. Exclusion of this subject resulted in a significantly greater premenstrual intake for menses 1 ($p = 0.024$).

In the placebo group there was also a greater premenstrual intake from the *cereal* category in menses 1 ($p < 0.05$).

In the treatment group there was a significantly greater premenstrual intake for *cereal* ($p < 0.05$), *milk* ($p < 0.05$) and from the *cake and desserts*

category in menses1 and 3. There was a significantly greater contribution of simple sugars postmenstrually for the *fruit* category at menses 2 and 3 ($p < 0.05$).

4.4.3.6 *Contribution of food categories to the total complex carbohydrate intake*

As for total carbohydrate and simple sugars, there was a significantly greater premenstrual contribution to the total complex carbohydrate intake by the *high sugar foods* category for all cycles (menses 1, $p < 0.001$, menses 2 and 3, $p < 0.05$) by the placebo group (Table 36). For the *cake and desserts* category there was a greater premenstrual contribution at all cycles, but this was only significant at menses 3 ($p < 0.05$). There was also a significantly greater contribution by *savoury snacks* at menses 3 ($p < 0.05$).

In the treatment group the premenstrual intake was greater for both the *cake and desserts* and the *high sugar foods* categories for all menstrual cycles. However this was not significant except for in menses 1 (*cake and desserts* category, $p < 0.05$) and in menses 2 (*high sugar foods* category, $p < 0.05$). The *vegetable* category was significantly greater premenstrually at menses 1 ($p < 0.05$) and the *fruit* category postmenstrually at menses 2 ($p < 0.05$).

4.4.4 **Percentage of energy and macronutrients contributed by each food category**

4.4.4.1 *Percentage of energy contributed by food categories*

Table 43 displays the percentage energy that each food category contributed to the total mean energy intake for both the treatment and placebo groups. It can be seen that for the majority of food

categories in the treatment and placebo groups the comparison of pre and postmenstrual percentages is non-significant or is significant for one cycle only. For example for the *cereal* category the percentage energy varied little for the treatment group with a slightly greater percentage of energy, but not significant post menstrually. In the placebo group these findings were similar and non-significant except for menses 3 where the percentage of kilojoules from the *cereal* category was significantly higher postmenstrually ($p < 0.05$).

Similarly in the *milk* category, there was little difference for the treatment group except for menses 3, where premenstrual percentage was significantly less than postmenstrual ($p < 0.05$). No significance differences were observed in the placebo group.

The food categories that were significantly different, when comparing their pre and postmenstrual kilojoule contribution, were the *cake and desserts* and *high sugar foods* categories. In the *cake and desserts* category there was a significantly greater percentage ($p < 0.05$) of energy premenstrually compared to postmenstrually for the placebo group for all cycles.

In the treatment group the percent of energy premenstrually was also greater for these two food categories, but not significant.

When the percentage of energy from these two categories (*cakes and desserts* and *high sugar foods*) are combined the premenstrual contribution for the placebo group for menses 1 to 3 were 19.3%, 18.3% and 17.6% respectively compared to the postmenstrual contribution of 12%, 13.6% and 10.2%. For the treatment group a similar pattern is observed with the premenstrual percentages being 18.4%, 16.2% and 17.4% compared to the postmenstrual contribution of 14.1%, 13.6% and 15% respectively. A comparison of the pre and postmenstrual intake for the combined categories found the premenstrual contribution of these two groups to be significantly higher ($p<0.05$) in the placebo group and not significant for the treatment group.

4.4.4.2 *Percentage of protein contributed by food categories*

In the placebo, both the premenstrual *cake and desserts* ($p<0.05$) and *high sugar foods* ($p<0.001$ for menses 1 and $p<0.05$ for menses 2 and 3) categories exhibited a significantly higher percent of protein when compared to the postmenstrual phase (Table 44). For the remaining food categories, there was no significant change between the pre and postmenstrual contribution, with exception of the *cereal* category ($p<0.05$) at menses 3.

In the treatment group, the percentage of protein from *cake and desserts* category was significantly greater ($p<0.05$) premenstrually for menses 1 only. In the treatment group, significant differences

occurred at menses 1 for the *cake and desserts* category ($p<0.05$), menses 2 for the *fruit* ($p<0.05$) and *fat* categories ($p<0.05$) and menses 3 for fruit ($p<0.05$).

4.4.4.3 *Percentage of fat contributed by each food group*

The percentage of fat contributed by all the food categories did not alter significantly between the pre and postmenstrual intakes in most cases (Table 45). The *meat* and *savoury dish* categories combined contributed the largest proportion of fat. This was between 32% and 41% of the total mean fat intake over the 3 cycles. The percentage of fat contributed by the *cakes and desserts* categories was higher premenstrually for both the placebo and treatment groups. However, this was not statistically significant.

The *high sugar food* category exhibited a significantly higher percentage of fat for the placebo group at menses 1($p<0.001$) and 3 ($p<0.05$) and for the *cereal* category at menses 3 ($p<0.05$). For the treatment group the postmenstrual percentage of fat from the *milk* category was a significantly higher ($p<0.05$) in menses 2 and for the *vegetable* category at menses 3 the percentage of fat premenstrually was significantly ($p<0.05$). For both the placebo and treatment groups, the standard deviations were large when compared to the mean percentage contribution and reflects the large variation in intake.

4.4.4.4 Percentage of carbohydrate contributed by each food category

Table 46 displays the percent of carbohydrate from each of the food categories. As would be expected the *cereal* category contributed the greatest percent of carbohydrate for both the placebo and treatment groups. In the placebo group, the postmenstrual percentage of carbohydrate was significantly at menses 2 and 3 ($p<0.05$). The combined *cake and desserts* and *high sugar foods* categories provided the second highest percent of the total mean carbohydrate. Premenstrually it ranged from 20.8-23% for the treatment group and 21-24.4% for the placebo group.

In the placebo group the premenstrual percentage of carbohydrate was significantly greater than the postmenstrual intake for the *high sugar foods* over the 3 menstrual cycles (menses 1 $p<0.001$, menses 2 and 3 $p<0.05$). The mean percent contribution for the treatment group did not alter significantly over the pre and postmenstrual phases.

For the *cake and desserts* category the percent contribution premenstrually, although higher was not consistently significant in the placebo or in the treatment groups. In the placebo group, the *cake and desserts* category was higher at menses 3 ($p<0.05$) and for the treatment group at menses 1 ($p<0.05$).

Other significant differences were isolated. For example for the placebo, the percentage of carbohydrate from the *milk* and *fruit*

categories were significantly greater postmenstrually at menses 2 ($p<0.05$).

4.4.4.5 *Percent of Simple sugars contributed by each food category*

As for total carbohydrate, in the placebo group the percentage of simple sugars (Table 47) from the *cereal* category was significantly higher postmenstrually in menses 2 and 3 ($p<0.05$). For the *high sugar food* category, the percentage of simple sugars was significantly greater premenstrually over all 3 cycles for the placebo ($p<0.001$ for menses 1 and $p<0.05$ for menses 2 and 3). This was also the case for the cake and dessert category for menses 2 and 3 ($p<0.05$) in the placebo group and for menses 3 ($p<0.05$) in the treatment group.

Also as for total carbohydrate the percentage of simple sugars from the fruit category was lower premenstrually compared to postmenstrually for both the placebo and treatment groups. This difference was significant for the treatment group in menses 2 and 3 ($p<0.05$) and menses 2 ($p<0.05$) for the placebo.

4.4.4.6 *Percent of complex carbohydrate contributed by food categories*

The *cereal* category provided the highest percentage of complex carbohydrate over all 3 cycles (Table 48). In the placebo group, this ranged from 57.3% premenstrually to 66.7% postmenstrually; and in the treatment group from 55.9% premenstrually to 64.1% postmenstrually. The difference between the pre and postmenstrual

percentage of complex carbohydrate from the *cereal* category reached significance in the placebo group for menses 2 and 3 ($p < 0.05$).

Analysis of the percentage change between pre and post menses for other food categories did not reveal any consistent pattern of significance. The *high sugar foods* category provided a significantly higher premenstrual percentage of complex carbohydrate for menses 1 and 2 ($p < 0.05$). However, it should be noted that the percentage of complex carbohydrate is very small. It is also of interest that although the percentage of complex carbohydrate is higher premenstrually for the cake and desserts category this was not significant for the placebo.

Table 31 : The mean ($\pm$ SD) kilojoule intake from each food category in the treatment and placebo group for menses 1 to 3

	Menses 1 Treatment		Menses 1 Placebo		Menses 2 Treatment		Menses 2 Placebo		Menses 3 Treatment		Menses 3 Placebo	
Kilojoules	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Cereal	1283 (510) ¹	1230 (540)	1471 (489)	1344 (501)	1254 (557)	1162 (515)	1479 (566)	1364 (494)	1208 (514)	1197 (599)	1402 (550)	1517 (593)
Milk	530 (386)	491 (355)	638 (391)	595 (367)	540 (391)	547 (470)	628 (371)	593 (296)	475 (332)	558 (355)	734 (381)	705 (393)
Meat, poultry, fish and eggs	681 (594)	645 (425)	774 (455)	797 (525)	678 (420)	658 (399)	800 (552)	750 (480)	786 (428)	586 (487)	728 (503)	737 (444)
Savoury foods	647 (431)	685 (526)	798 (613)	698 (573)	728 (536)	600 (587)	886 (586)	637 (399)	801 (597)	741 (547)	823 (671)	619 (654)
Vegetables	440 (306)	336 (251)	446 (266)	430 (287)	365 (316)	408 (309)	454 (272)	376 (226)	451 (334)	328 (275)	440 (241)	379 (270)
Fruit	220 (223)	265 (212)	202 (211)	213 (233)	239 (198)	312 (224)	162 (163)	213 (177)	201 (170)	284 (240)	198 (201)	194 (166)
Fat	174 (169)	168 (155)	368 (288)	349 (382)	245 ^{†§} (234)	160 (172)	280 (229)	257 (234)	202 (164)	221 (234)	285 (293)	226 (207)
Cake and desserts	640 ^{†§} (491)	415 (353)	782 ^{†§} (640)	592 (757)	596 (524)	425 (436)	878 ^{†§} (831)	618 (671)	623 ^{†§} (487)	474 (466)	702 ^{†§} (590)	398 (503)
High sugar foods	406 (541)	309 (363)	621 ^{*§} (757)	203 (205)	305 (354)	254 (362)	477 ^{*§} (407)	243 (274)	398 (427)	322 (447)	568 ^{†§} (745)	252 (389)
Drinks	333 (303)	356 (368)	527 (564)	512 (622)	320 (312)	309 (277)	612 (607)	447 (452)	422 (387)	335 (274)	636 (697)	693 (537)
Savoury snacks	102 (206)	128 (304)	263 (381)	114 (161)	115 (174)	144 (537)	166 (278)	123 (189)	121 (209)	59 (174)	201 ^{†§} (282)	103 (223)

¹ Figures in brackets are standard deviations

*p<0.001, † p<0.05

‡ paired t-test § Wilcoxon sign rank test

Table 32: The mean ($\pm$ SD) protein intake for each food category in the treatment and placebo groups for menses 1 to 3

Protein	Menses 1 Treatment		Menses 1 Placebo		Menses 2 Treatment		Menses 2 Placebo		Menses 3 Treatment		Menses 3 Placebo	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Cereal	10.2 (4.2) ¹	9.7 (4.4)	12 (4.2)	11.1 (3.8)	9.8 (4.2)	9.1 (4.03)	11.6 (4.1)	11.1 (3.9)	9.8 (4.4)	9.48 (4.6)	11.3 (4.2)	12.4 (4.7)
Milk	8.9 ^{s†} (6.9)	7.8 (5.8)	10.4 (6.3)	9.9 (6.2)	9 (7.2)	8.9 (8.1)	10.2 (5.9)	9.9 (5.2)	8 (6.3)	9.24 (6.8)	12.2 (6.3)	12.04 (6.95)
Meat, poultry, fish and eggs	20.1 (18.3)	18.75 (13.5)	21 (12.8)	24.1 (16.1)	17.4 (11.5)	18.3 (10.7)	21.1 (11.2)	20.9 (13.5)	20.4 (10.9)	16.5 (12.9)	21 (14.8)	20.4 (11.4)
Savoury foods	7.3 (4.9)	8.1 (7.9)	8.9 (6.9)	7.7 (7)	7.6 (5.5)	6.5 (5.8)	9.2 (6.7)	7.6 (6.4)	9.0 (6.8)	8 (5.7)	8.8 (8)	6.5 (7.3)
Vegetables	3.4 (2.5)	2.8 (2)	3.8 (1.96)	4.1 (2.8)	3.2 (2.6)	3.7 (2.5)	4.1 (2.7)	4 (2.3)	3.7 (2.1)	2.99 (2.1)	4.1 (2.14)	3.5 (2.8)
Fruit	0.75 (0.9)	0.8 (0.82)	0.8 (0.94)	0.8 (0.83)	0.75 ^{s†} (0.8)	1.04 (0.95)	0.7 (0.96)	0.72 (0.67)	0.65 ^{s†} (0.62)	1.02 (1.1)	0.8 (1.03)	0.74 (0.7)
Fat	0.03 (0.9)	0.01 (0.08)	0.08 (0.26)	0.1 (0.4)	0.1 ^{s†} (0.4)	0.01 (0.04)	0.01 (0.06)	0.02 (0.09)	0.05 (0.12)	0.07 (0.2)	0.04 ^{s†} (0.1)	0.01 (0.04)
Cake and desserts	3.3 ^{s†} (3)	2.1 (1.9)	4.65 ^{s†} (4.6)	2.8 (3.1)	3.6 (3.1)	2.56 (2.8)	4.5 ^{s†} (4.3)	3.03 (3.3)	3.4 ^{s†} (2.8)	2.65 (2.9)	3.73 ^{s†} (3.3)	1.95 (2.35)
High sugar foods	0.9 (1.7)	0.7 (1.1)	1.8 ^{s*} (2.7)	0.45 (0.7)	0.78 (1.3)	0.6 (1.3)	1.2 ^{s†} (1.4)	0.47 (0.75)	1.01 (1.5)	0.77 (1.7)	1.6 ^{s†} (2.4)	0.6 (1.5)
Drinks	2.1 (2)	2.2 (3.3)	2.7 (3)	2.6 (3.1)	2.2 (2.1)	2.5 (3.1)	3.1 (3.8)	3 (2.5)	2.5 (3)	2.4 (3)	3.7 (3.8)	3.5 (3.3)
Savoury snacks	0.5 (0.9)	0.9 (2.9)	1.2 (1.7)	0.67 (1.1)	0.71 (1.6)	1.3 (5.7)	1.1 (2.1)	0.99 (2.1)	0.7 (1.6)	0.6 (1.8)	1.04 (1.6)	0.6 (1.56)

¹ Figures in brackets are standard deviations*p<0.001, † p<0.05 ‡paired t-test ^sWilcoxon sign rank test

Table 33: The mean ($\pm$ SD) fat intake from each food category in the treatment and placebo groups for menses 1 to 3

	Menses 1 Treatment		Menses 1 Placebo		Menses 2 Treatment		Menses 2 Placebo		Menses 3 Treatment		Menses 3 Placebo	
Fat	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Cereal	3.9 (2.7) ¹	3.8 (2.6)	4.6 (2.6)	4 (2.1)	3.4 (3)	3.1 (1.7)	4.5 (2.9)	3.67 (1.9)	2.9 (1.9)	3.3 (3.3)	3.7 (2.3)	4.55 (2.8)
Milk	6.6 (5.2)	6.7 (5.3)	8.2 (5.9)	7.5 (5.2)	7.2 (5.6)	7.2 (7.3)	7.4 (5.6)	7.1 (4.8)	5.7 (3.8)	7.2 (4.9)	8.9 (5.5)	7.98 (5.3)
Meat, poultry, fish and eggs	8.3 (7.4)	8.2 (6.0)	10.4 (6.7)	9.3 (6.8)	9.3 (6.5)	8.1 (5.4)	10.6 (9.1)	9.5 (7.1)	10.4 (6.4)	7.5 (6.8)	9.1 (7.5)	9.7 (6.8)
Savoury foods	7.9 (5.7)	8.4 (7.4)	9.5 (7.9)	8.5 (7.5)	8.7 (6.6)	7.6 (8.3)	10.9 (8.2)	7.9 (7.7)	9.9 (7.1)	9.5 (7.9)	10.3 (8.6)	7.4 (8.4)
Vegetables	4.15 (4.6)	3.05 (3.9)	3.4 (3.3)	2.7 (3.2)	3 (4.5)	3.2 (4.5)	3.05 (3.2)	2.16 (2.4)	3.8 ^{†§} (5.4)	2.1 (3.8)	2.9 (2.9)	2.35 (2.7)
Fruit	0	0	0.03 (0.12)	0.03 (0.12)	0	0	0.03 (0.1)	0.02 (0.1)	0.03 (0.2)	0	0	0
Fat	4.7 (4.5)	4.4 (3.9)	9.85 (7.7)	9.3 (10.1)	6.5 ^{†§} (6.3)	4.3 (4.6)	7 (6.5)	6.93 (6.3)	5.4 (4.3)	5.9 (6.2)	7.7 ^{†§} (7.9)	5.9 (5.3)
Cake and desserts	6.4 (5.4)	4.4 (4)	7.5 (7.4)	6 (8.9)	6 (6.2)	4.2 (5.2)	9.16 ^{†§} (9.8)	6.3 (7.3)	6.14 (5.8)	4.7 (5.1)	7 ^{†§} (7.0)	3.74 (5.2)
High sugar foods	3.04 (5.3)	2.1 (3.4)	5.7 ^{*§} (8.7)	1.3 (2.1)	2.5 (4.1)	1.7 (3.3)	3.8 ^{†§} (3.9)	1.8 (2.75)	3.7 (5.1)	2.2 (4.5)	5.2 ^{†§} (8.3)	2.04 (4.9)
Drinks	0.4 (0.96)	0.42 (1.3)	0.4 (1.3)	0.56 (1.4)	0.34 (0.8)	0.45 (1.1)	0.72 (1.9)	0.56 (1.1)	0.6 (1.3)	0.49 (1.1)	0.9 (1.8)	0.79 (1.63)
Savoury snacks	1.8 (3.5)	2.5 (6.3)	4.1 ^{†§} (5.9)	1.98 (2.9)	2.04 (3.3)	2.8 (10.7)	3 (5.0)	2.1 (3.3)	2.03 (3.7)	1.17 (3.5)	3.3 ^{†§} (4.6)	1.9 (4.4)

¹ Figures in brackets are standard deviations

*p<0.001, † p<0.05

‡ paired t-test § Wilcoxon sign rank test

Table 34: The mean ($\pm$ SD) carbohydrate intake in the treatment and placebo groups from each food category for menses 1 to 3

	Menses 1 Treatment		Menses 1 Placebo		Menses 2 Treatment		Menses 2 Placebo		Menses 3 Treatment		Menses 3 Placebo	
Carbohydrate	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Cereal	57.3 (23.5) ¹	54.8 (24.3)	64.9 (23)	59.8 (23.5)	56.6 (25.3)	53 (24.8)	65.6 (25.2)	61.4 (22.4)	55.2 (23.5)	53.7 (26.9)	63.3 (25.2)	67.1 (27.1)
Milk	8.4 ^{†§} (7.6)	7.1 (5.7)	9.8 (8)	9.3 (8.8)	7.7 (6.1)	8.0 (6.4)	11.2 (8.5)	10 (7.7)	8 (7.6)	8.6 (8.3)	12.2 (9.1)	12 (9.2)
Meat, poultry, fish and eggs	1.9 (3.2)	2.2 (2.8)	1.7 (2.5)	1.8 (2.7)	2 (3.1)	2.6 (3.8)	2.5 (4.2)	2.6 (4.2)	3.1 (4.1)	1.7 (2.6)	1.9 (2.8)	1.94 (2.7)
Savoury foods	13.7 (9.7)	16.7 (17)	17.6 (13.7)	15.2 (13.2)	16.5 (14.8)	12.4 (12.4)	19.3 (12.2)	13.0 (13.2)	16.8 (14.9)	15.2 (10.6)	17.4 (14.4)	13.8 (14.1)
Vegetables	13.3 (9.6)	9.9 (6.8)	14.5 (8.2)	14.9 (9.8)	11.2 (10.4)	13.06 (8.6)	15.5 (9.1)	13.2 (7.3)	14.1 (9)	11.2 (7.3)	14.9 (8.2)	13 (10.1)
Fruit	12.3 (12.6)	15 (12)	11.2 (11.6)	11.9 (13.1)	13.5 ^{†§} (11.3)	17.5 (12.6)	8.9 (9)	11.8 (10)	11.2 (9.6)	15.8 (13.5)	11 (11)	10.8 (9.2)
Fat	0.1 (0.3)	0.16 (0.6)	0.2 (0.4)	0.21 (0.6)	0.12 (0.26)	0.12 (0.4)	0.04 (0.1)	0.08 (0.2)	0.2 (0.73)	0.13 (0.25)	0.6 (0.13)	0.09 (0.2)
Cake and desserts	21.2 ^{†§} (16)	13.2 (11.3)	25.6 (20.3)	19.5 (23.1)	19.4 (16.3)	13.7 (13.7)	28.2 ^{†§} (25.9)	20.3 (22)	21 ^{††} (15.5)	15.5 (15.1)	23.2 ^{††} (19)	13.8 (17.3)
High sugar foods	17.1 (20.6)	13.7 (15.9)	23.5 ^{*§} (25.4)	9.1 (8.6)	12.3 (12.7)	11.2 (15)	19.6 ^{*§} (17.6)	10.3 (11.2)	15.2 (14.8)	14 (17.5)	21.6 ^{†§} (25.7)	10.3 (12.4)
Drinks	11.8 (13)	11.6 (12.3)	15.5 (17.3)	16.2 (20.1)	11.7 (12.2)	10.7 (11.8)	18 (20.2)	13.1 (13.6)	12.4 (13.3)	11.4 (10.4)	21.2 (27.6)	18.7 (21.9)
Savoury snacks	1.6 (4.05)	1.4 (2.7)	5.2 (9)	1.7 (2.8)	1.67 (2.4)	1.13 (3.1)	2.3 (4.3)	1.8 (3.2)	2 (3.7)	42 (1.1)	3.6 ^{†§} (5.7)	1.3 (2.3)

¹ Figures in brackets are standard deviations

*p<0.001, † p<0.05 † paired t-test § Wilcoxon sign rank test

Table 35: The mean ($\pm$ SD) simple sugar intake from each food category for menses 1 to 3 in the treatment and placebo groups

	Menses 1 Treatment		Menses 1 Placebo		Menses 2 Treatment		Menses 2 Placebo		Menses 3 Treatment		Menses 3 Placebo	
Simple sugars	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Cereal	5.6 $\dagger^s$ (5.7) ¹	4.6 (6)	4.04 $\dagger^s$ (3.1)	4 (4.8)	4.85 (5.5)	4.2 (4.1)	4.14 (4.9)	4.2 (5)	4.6 (5.5)	5 (5.2)	4.2 (4.5)	4.7 (5.4)
Milk	8.4 $\dagger^s$ (7.6)	7.1 (5.7)	9.3 (7.9)	9 (8.5)	7.7 (6.1)	8 (6.4)	10.7 (8)	9.45 (7.1)	8 (7.6)	8.6 (8.3)	11.8 (9.1)	12 (9.7)
Meat, poultry, fish and eggs	0.27 (1.1)	0.32 (1.0)	0.06 (0.14)	0.06 (0.2)	0.16 (0.36)	0.32 (0.8)	0.1 (0.2)	0.36 (1.0)	0.28 (0.95)	0.04 (0.12)	0.11 (0.2)	0.09 (0.2)
Savoury foods	2.5 (1.7)	3.4 (2.9)	3.4 (3.0)	3.2 (2.9)	3.5 (3)	2.5 (2.2)	3.5 (2.5)	2.6 (2.3)	3 (2.5)	2.9 (2.1)	3 (2.3)	3.0 (2.9)
Vegetables	2.8 (2.6)	2.7 (2.3)	3.4 (2.5)	3.9 (2.7)	3.1 (2.6)	3 (2.3)	4.3 (3.1)	4.2 (3)	3.3 (2.4)	3.4 (2.2)	3.5 (2.5)	3.7 (3)
Fruit	11.2 (11.3)	13.8 (11.1)	9.8 (10.2)	10.7 (11.7)	12.4 $\dagger^s$ (10.1)	15.8 (11.1)	7.9 (7.9)	10.7 (9)	10.1 $\dagger^s$ (8.8)	14.4 (12.1)	9.9 (10)	9.3 (8)
Fat	0.1 (0.3)	0.14 (0.6)	0.16 (0.3)	0.21 (0.6)	0.12 (0.3)	0.12 (0.4)	0.04 (0.1)	0.8 (0.2)	0.2 (0.7)	0.13 (0.25)	0.6 (0.14)	0.09 (0.2)
Cake and desserts	11.7 $\dagger^s$ (9.9)	7.5 (6.3)	15.7 (13.5)	11.7 (13.4)	12.3 (12.4)	8.25 (8.7)	16.4 $\dagger^s$ (14.9)	10.9 (11.2)	12.2 $\dagger^s$ (10.1)	9.4 (9.7)	12.8 $\dagger^s$ (11.3)	7.8 (9.4)
High sugar foods	16.3 (20)	13.6 (15.8)	22* $\dagger^s$ (24.2)	8.8 (8.3)	11.5 (12.3)	10.5 (13.9)	18.6 $\dagger^s$ (17)	10.1 (10.9)	14.4 (13.8)	13.4 (16.5)	20.8 $\dagger^s$ (25)	9.9 (11.5)
Drinks	11.2 (12.7)	11.1 (12.3)	15 (17.3)	15.7 (20.1)	11.1 (12.2)	10.2 (11.6)	17.2 (20.2)	12.4 (13.6)	12 (13.4)	10.8 (10.4)	20.5 (27.7)	18.1 (22)
Savoury snacks	0.3 (0.8)	0.2 (0.5)	0.26 (0.6)	0.22 (0.5)	0.17 (0.3)	0.25 (0.96)	0.31 (0.6)	0.54 (1.5)	0.14 (0.35)	0.13 (0.8)	0.37 (0.8)	0.27 (0.6)

¹ Figures in brackets are standard deviations

* $p < 0.001$, $\dagger p < 0.05$ $\dagger$ paired t-test $\dagger^s$ Wilcoxon sign rank test

Table 36: The mean ($\pm$ SD) complex carbohydrate intake from each food category for menses 1 to 3 in the treatment and placebo groups

	Menses 1 Treatment		Menses 1 Placebo		Menses 2 Treatment		Menses 2 Placebo		Menses 3 Treatment		Menses 3 Placebo	
Complex carbohydrates	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Cereal	51.6 (20) ¹	50.2 (21.4)	61 (22)	56 (21.8)	51.8 (22.4)	48.6 (23.3)	61.8 (24.2)	57.5 (19.9)	50.2 (20.1)	48.3 (24.3)	59.4 (22.9)	62.7 (25)
Milk	0	0	0.24 (1.5)	0.39 (2.5)	0	0	0.56 (3)	0.5 (3.0)	0	0	0.4 (2.3)	0.48 (2.8)
Meat, poultry, fish and eggs	1.6 (2.6)	1.8 (2.5)	1.6 (2.4)	1.6 (2.6)	1.8 (3.0)	2.3 (3.4)	2.4 (4.1)	2.1 (3.5)	2.8 (3.8)	1.6 (2.6)	1.75 (2.6)	1.85 (2.7)
Savoury dishes	11.3 (8.7)	1.8 (3.0)	14.2 (11.6)	11.8 (10.9)	13.1 (12.5)	10.1 (11.1)	15.9 (10.7)	10.5 (11.6)	13.9 (13)	12.5 (9.7)	14.3 (12.9)	10.2 (12)
Vegetables	10.1 [†] (8)	7.2 (5.4)	11 (7.1)	11 (8.5)	8.1 (9.1)	10 (7.4)	11.2 (7.4)	8.8 (5.95)	10.9 (7.7)	7.9 (5.9)	11.5 (7.2)	9.3 (8.2)
Fruit	0.8 (1.3)	0.8 (1.2)	1.03 (1.2)	0.9 (1.4)	0.8 [†] [§] (1.1)	1.2 (1.5)	0.67 (1.1)	0.85 (0.98)	0.6 (0.8)	0.87 (1.2)	0.8 (1.1)	0.96 (1.2)
Fat	0	0	0	0	0	0	0	0	0	0	0	0
Cake and desserts	9.5 [§] (7.8)	5.8 (6.2)	9.5 (9.4)	7.8 (10.6)	7.1 (6.6)	5.5 (5.8)	11.7 (14)	9.25 (12.3)	8.3 (7.3)	6.03 (6.3)	10.2 [†] [§] (10.8)	6 (8.9)
High sugar foods	0.75 (1.2)	0.51 (1.3)	1.05 [†] [§] (1.6)	0.3 (0.5)	0.8 [§] [†] (1.1)	0.51 (1.2)	0.9 (1.5)	0.25 (0.5)	0.74 (1.4)	0.46 (1.3)	0.75 [†] [§] (0.98)	0.4 (1.1)
Drinks	0.5 (0.49)	0.5 (0.5)	0.7 (0.6)	0.6 (0.56)	0.54 (0.6)	0.46 (0.5)	0.76 (0.75)	0.7 (0.6)	0.49 (0.5)	0.51 (0.6)	0.75 (0.7)	0.71 (0.7)
Savoury snacks	1.3 (3.9)	1.2 (2.4)	4.9 (8.6)	1.5 (2.7)	1.5 (2.3)	0.87 (2.3)	2 (3.9)	1.2 (2.7)	1.8 (3.45)	0.27 (0.8)	3.1 [†] [§] (5.4)	1.05 (1.9)

¹ Figures in brackets are standard deviations

*p<0.001, † p<0.05 [‡]paired t-test [§]Wilcoxon sign rank test

Table 37: The mean ($\pm$ SD) kilojoule contribution from each food category for women that complete all 3 cycles

	Menses 1 Treatment		Menses 1 Placebo		Menses 2 Treatment		Menses 2 Placebo		Menses 3 Treatment		Menses 3 Placebo	
Kilojoules	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Cereal	1294 (528) ¹	1283 (517)	1502 (499)	1420 (478)	1254 (557)	1162 (515)	1493 (568)	1364 (494)	1208 (514)	1197 (599)	1403 (550)	1517 (593)
Milk	525 (394)	507 (361)	671 (363)	632 (371)	540 (391)	547 (470)	631 (376)	593 (296)	475 (332)	558 (355)	734 (381)	705 (393)
Meat, poultry, fish and eggs	673 (613)	686 (413)	802 (463)	810 (552)	678 (420)	658 (399)	802 (560)	751 (480)	786 (428)	586 (487)	728 (503)	737 (444)
Savoury foods	663 (432)	620 (487)	793 (595)	696 (580)	728 (536)	600 (587)	896 (592)	637 (573)	800 (597)	741 (547)	823 (671)	619 (654)
Vegetables	437 (304)	353 (252)	449 (258)	423 (297)	365 (316)	408 (309)	464 (271)	376 (226)	451 (334)	328 (275)	440 (241)	379 (270)
Fruit	230 (228)	279 (213)	195 (217)	201 (240)	239 (198)	312 (224)	162 (165)	213 (177)	201 (170)	284 (240)	198 (201)	194 (166)
Fat	175 (173)	176 (157)	362 (299)	359 (404)	245 ^{†§} (234)	160 (172)	273 (229)	257 (234)	202 (164)	221 (234)	285 (293)	226 (207)
Cake and desserts	655 ^{†§} (506)	417 (368)	795 ^{†§} (650)	634 (795)	596 (524)	425 (436)	903 ^{†§} (831)	618 (671)	623 ^{†§} (487)	474 (466)	702 ^{†§} (590)	398 (503)
High sugar foods	417 (555)	309 (371)	561 ^{*§} (607)	220 (212)	305 (354)	254 (362)	473 ^{*§} (412)	243 (274)	398 (427)	322 (447)	568 ^{†§} (745)	252 (389)
Drinks	311 (264)	331 (367)	549 (568)	516 (629)	320 (312)	309 (277)	698 (610)	447 (452)	422 (387)	335 (274)	636 (697)	693 (537)
Savoury snacks	104 (213)	125 (314)	267 (384)	114 (161)	115 (174)	144 (537)	143 (244)	123 (189)	121 (209)	59 (174)	201 ^{†§} (282)	103 (223)

¹ Figures in brackets are standard deviations

*p<0.001, † p<0.05

‡ paired t-test § Wilcoxon sign rank test

Table 38: The mean ($\pm$ SD) protein contribution from each food category for women that have completed all 3 cycles

	Menses 1 Treatment		Menses 1 Placebo		Menses 2 Treatment		Menses 2 Placebo		Menses 3 Treatment		Menses 3 Placebo	
Protein	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Cereal	10.2 (4.3) ¹	10.04 (4.2)	12.2 (4.4)	11.7 (3.6)	9.8 (4.2)	9.1 (4.0)	11.7 (4.1)	11.1 (3.9)	9.8 (4.4)	9.5 (4.6)	11.3 (4.2)	12.4 (4.7)
Milk	8.8 (7.05)	8.05 (5.9)	10.95 (5.9)	10.5 (6.2)	9 (7.2)	8.9 (8.1)	10.2 (6.1)	9.9 (5.2)	8 (6.3)	9.2 (6.8)	12.2 (6.3)	12.04 (6.95)
Meat, poultry, fish and eggs	19.7 (18.6)	19.8 (13.3)	21.6 (13.1)	24.5 (16.9)	17.4 (11.5)	18.3 (10.7)	20.9 (11.3)	20.9 (13.5)	20.4 (10.9)	16.5 (12.9)	21 (14.8)	20.4 (11.4)
Savoury foods	7.6 (4.9)	7.4 (7.7)	8.9 (6.8)	7.8 (7.1)	7.6 (5.5)	6.5 (5.7)	9.3 (6.7)	7.6 (6.4)	9.0 (6.8)	8 (5.7)	8.8 (8)	6.5 (7.3)
Vegetables	3.3 (2.3)	2.9 (1.9)	3.9 (1.97)	3.8 (2.3)	3.2 (2.6)	3.7 (2.5)	4.2 (2.6)	4 (2.3)	3.7 (2.1)	2.99 (2.1)	4.1 (2.1)	3.5 (2.8)
Fruit	0.78 (0.9)	0.88 (0.83)	0.82 (0.97)	0.82 (0.87)	0.75 ^{†§} (0.8)	1.04 (0.95)	0.71 (0.96)	0.72 (0.67)	0.65 ^{†§} (0.6)	1.02 (1.1)	0.8 (1.03)	0.74 (0.7)
Fat	0.03 (0.1)	0.01 (0.08)	0.08 (0.3)	0.11 (0.47)	0.1 ^{†§} (0.4)	0.01 (0.04)	0.01 (0.06)	0.02 (0.09)	0.05 (0.1)	0.07 (0.2)	0.04 ^{†§} (0.1)	0.01 (0.04)
Cake and desserts	3.4 ^{†§} (3.1)	2.2 (1.9)	4.5 ^{†§} (4.3)	2.8 (3.3)	3.6 (3.2)	2.6 (2.8)	4.6 (4.3)	3.0 (3.3)	3.4 ^{†§} (2.8)	2.7 (2.9)	3.7 ^{†§} (3.3)	1.95 (2.4)
High sugar foods	0.95 (1.8)	0.7 (1.1)	1.6 ^{†§} (2.0)	0.5 (0.76)	0.78 ^{†§} (1.3)	0.6 (1.3)	1.2 ^{†§} (1.4)	0.47 (0.75)	1.01 (1.5)	0.8 (1.7)	1.6 ^{†§} (2.4)	0.6 (1.5)
Drinks	2.03 (2)	2.03 (3.3)	2.9 (3)	2.8 (3.2)	2.2 (2.1)	2.5 (3.1)	3.2 (3.8)	3 (2.5)	2.5 (3)	2.4 (3)	3.7 (3.8)	3.5 (3.3)
Savoury snacks	0.48 (0.9)	0.93 (3.0)	1.25 (1.8)	0.66 (1.1)	0.71 (1.6)	1.34 (5.7)	0.82 (1.5)	0.99 (2.1)	0.7 (1.6)	0.55 (1.8)	1.04 (1.6)	0.64 (1.6)

¹ Figures in brackets are standard deviations

*p<0.001, † p<0.05

‡ paired t-test § Wilcoxon sign rank test

Table 39: The mean fat ($\pm$ SD) contribution from each food category for women that have completed all 3 cycles

	Menses 1 Treatment		Menses 1 Placebo		Menses 2 Treatment		Menses 2 Placebo		Menses 3 Treatment		Menses 3 Placebo	
Fat	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Cereal	3.9 (2.7) ¹	3.8 (2.6)	4.6 (2.6)	4 (2.12)	3.4 (3)	3.1 (1.7)	4.5 (2.9)	3.67 (1.9)	2.9 (1.9)	3.3 (3.3)	3.7 (2.3)	4.55 (2.8)
Milk	6.6 (5.2)	6.7 (5.3)	8.2 (5.9)	7.5 (5.2)	7.2 (5.6)	7.2 (7.3)	7.4 (5.6)	7.1 (4.8)	5.7 (3.8)	7.2 (4.9)	8.9 (5.5)	7.98 (5.3)
Meat, poultry, fish and eggs	8.3 (7.6)	8.8 (5.9)	10.8 (6.8)	9.4 (7.1)	9.3 (6.5)	8.1 (5.4)	10.7 (9.2)	9.5 (7.1)	10.4 (6.4)	7.5 (6.8)	10.4 (6.4)	9.7 (6.8)
Savoury foods	8 (5.8)	7.6 (7.0)	9.5 (7.8)	8.5 (7.6)	8.6 (6.6)	7.6 (8.3)	11.0 (8.2)	7.9 (7.6)	9.9 (7.1)	9.5 (8)	10.3 (8.6)	7.4 (8.5)
Vegetables	4.15 (4.6)	3.05 (3.9)	3.4 (3.3)	2.7 (3.2)	3 (4.5)	3.2 (4.5)	3.05 (3.2)	2.16 (2.4)	3.8 (5.4)	2.1 ^{†§} (3.8)	2.9 (2.9)	2.35 (2.7)
Fruit	0	0	0.03 (0.12)	0.03 (0.12)	0	0	0.03 (0.13)	0.02 (0.11)	0.03 (0.2)	0	0	0
Fat	4.7 (4.5)	4.4 (3.9)	9.85 (7.68)	9.3 (10.1)	6.52 ^{†§} (6.3)	4.3 (4.6)	7.6 (6.5)	6.93 (6.3)	5.4 (4.3)	5.9 (6.2)	7.7 ^{†§} (7.9)	5.9 (5.3)
Cake and desserts	6.4 (5.4)	4.4 (4)	7.5 (7.4)	6 (8.9)	6 (6.2)	4.2 (5.2)	9.16 ^{†§} (9.8)	6.3 (7.3)	6.14 (5.8)	4.7 (5.1)	7 ^{†§} (7.03)	3.74 (5.2)
High sugar foods	3.04 (5.3)	2.1 (3.4)	5.74 ^{†§} (8.7)	1.3 (2.1)	2.5 (4.1)	1.7 (3.3)	3.8 ^{†§} (3.9)	1.8 (2.75)	3.7 (5.1)	2.2 (4.5)	5.2 ^{†§} (8.3)	2.04 (4.9)
Drinks	0.4 (0.96)	0.42 (1.3)	0.4 (1.3)	0.56 (1.4)	0.34 (0.77)	0.45 (1.1)	0.72 (1.9)	0.56 (1.1)	0.6 (1.3)	0.49 (1.1)	0.9 (1.8)	0.79 (1.63)
Savoury snacks	1.8 (3.5)	2.5 (6.3)	4.1 ^{†§} (5.9)	1.98 (2.9)	2.04 (3.3)	2.8 (10.7)	3 (5.0)	2.1 (3.28)	2.03 (3.7)	1.17 (3.5)	3.3 ^{†§} (4.6)	1.9 (4.4)

¹ Figures in brackets are standard deviations

*p<0.001, † p<0.05 ‡paired t-test §Wilcoxon sign rank test

Table 40: The mean ($\pm$ SD) carbohydrate contribution from each food category for women that have completed all 3 cycles

	Menses 1 Treatment		Menses 1 Placebo		Menses 2 Treatment		Menses 2 Placebo		Menses 3 Treatment		Menses 3 Placebo	
Carbohydrate	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Cereal	57.9 (24.3) ¹	57.2 (23.4)	66.9 (23)	63.2 (22.8)	56.6 (25.3)	53 (24.8)	66.2 (25.3)	61.4 (22.5)	55.2 (23.5)	53.7 (26.9)	63.3 (25.2)	67.1 (27.1)
Milk	8.4 (7.6)	7.3 (5.8)	10.24 (8)	9.9 (9.2)	7.7 (6.1)	8.0 (6.4)	11.1 (8.6)	10 (7.7)	8 (7.6)	8.6 (8.3)	12.2 (9.1)	12 (9.2)
Meat, poultry, fish and eggs	1.9 (3.2)	2.4 (2.8)	1.8 (2.6)	1.9 (2.8)	2 (3.1)	2.6 (3.8)	2.6 (4.2)	2.6 (4.2)	3.1 (4.0)	1.7 (2.6)	1.9 (2.8)	1.9 (2.7)
Savoury foods	14 (9.7)	15.5 (17.1)	17.3 (13)	15 (13.4)	16.5 (14.8)	12.4 (12.4)	19.4 (12.4)	13.0 (13.1)	16.8 (14.8)	15.2 (10.6)	17.4 (14.4)	13.8 (14.1)
Vegetables	13.1 (9)	10.3 (6.8)	14.67 (8)	14.5 (9.9)	11.2 (10.4)	13.06 (8.6)	15.8 (9.04)	13.2 (7.3)	14.1 (9)	11.2 (7.3)	14.9 (8.2)	13 (10.1)
Fruit	12.9 (12.9)	15.8 (12.2)	10.8 (11.9)	11.1 (13.5)	13.5 ^{†§} (11.3)	17.5 (12.6)	8.9 (9.1)	11.8 (10)	11.2 (9.6)	15.8 (13.5)	11 (11)	10.8 (9.2)
Fat	0.07 (0.2)	0.17 (0.7)	0.16 (0.4)	0.18 (0.6)	0.12 (0.26)	0.12 (0.4)	0.04 (0.1)	0.08 (0.2)	0.2 (0.73)	0.13 (0.25)	0.6 (0.13)	0.09 (0.2)
Cake and desserts	21.8 ^{†§} (16.9)	13.3 (11.8)	26.25 (20.6)	20.9 (24.2)	19.4 (16.3)	13.7 (13.7)	29 (25.9)	20.3 (22)	21 ^{†§} (15.5)	15.5 (15.1)	23.2 ^{†§} (19)	13.8 (17.3)
High sugar foods	17.6 (20.4)	13.7 (15.9)	21.8 ^{*§} (20.5)	9.6 (8.9)	12.3 (12.7)	11.2 (15)	19.6 ^{†§} (17.9)	10.3 (11.3)	15.2 (14.8)	14 (17.5)	21.6 ^{†§} (25.7)	10.3 (12.4)
Drinks	11.3 (12.6)	10.3 (11.3)	16.5 (18.1)	16.7 (20.8)	11.7 (12.2)	10.7 (11.8)	18 (20.4)	13.1 (13.6)	12.4 (13.3)	11.4 (10.4)	21.2 (27.6)	18.7 (21.9)
Savoury snacks	1.7 (4.2)	1.2 (2.6)	5.3 (9.2)	1.9 (2.9)	1.67 (2.4)	1.13 (3.1)	2.2 (4.3)	1.8 (3.2)	2 (3.7)	42 (1.1)	3.6 (5.7)	1.3 (2.3)

¹ Figures in brackets are standard deviations

*p<0.001, † p<0.05 ‡ paired t-test § Wilcoxon sign rank test

Table 41: The mean ($\pm$ SD) simple sugars contribution from each food category over for women that have completed all 3 cycles

	Menses 1 Treatment		Menses 1 Placebo		Menses 2 Treatment		Menses 2 Placebo		Menses 3 Treatment		Menses 3 Placebo	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Simple sugars												
Cereal	5.6 (5.9) ¹	4.9 (6.1)	4.3 (3.2)	4.4 (5.04)	4.85 (5.5)	4.2 (4.1)	4.2 (5.0)	4.2 (5)	4.6 (5.5)	5 (5.2)	4.2 (4.5)	4.7 (5.4)
Milk	8.4 (7.8)	7.3 (5.9)	9.7 (7.8)	9.5 (8.9)	7.7 (6.1)	8 (6.4)	10.5 (8.1)	9.45 (7.1)	8 (7.6)	8.6 (8.3)	11.8 (9.1)	12 (9.7)
Meat, poultry, fish and eggs	0.3 (1.1)	0.3 (1.1)	0.05 (0.1)	0.06 (0.2)	0.2 (0.4)	0.31 (0.8)	0.1 (0.2)	0.4 (1.0)	0.3 (0.9)	0.04 (0.1)	0.11 (0.25)	0.1 (0.2)
Savoury foods	2.5 (1.7)	3.4 (2.9)	3.3 (3.2)	3.2 (2.9)	3.5 (3)	2.5 (2.2)	3.5 (2.5)	2.6 (2.3)	3 (2.5)	2.9 (2.1)	3 (2.3)	3.0 (2.9)
Vegetables	2.6 (2.1)	2.8 (2.3)	3.45 (2.5)	3.9 (2.7)	3.1 (2.6)	3 (2.3)	4.4 (3.1)	4.2 (3)	3.3 (2.4)	3.4 (2.2)	3.5 (2.5)	3.7 (3)
Fruit	11.7 (11.5)	14.6 (11.2)	9.4 (10.4)	10.0 (12.0)	12.4 ^{†§} (10.1)	15.8 (11.1)	7.9 (8.04)	10.7 (9)	10.1 ^{†§} (8.8)	14.4 (12.1)	9.9 (10)	9.3 (8)
Fat	0.1 (0.21)	0.16 (0.6)	0.15 (0.35)	0.19 (0.6)	0.12 (0.3)	0.12 (0.4)	0.04 (0.1)	0.8 (0.2)	0.2 (0.7)	0.13 (0.25)	0.6 (0.14)	0.09 (0.2)
Cake and desserts	12.1 ^{†§} (10.1)	7.5 (6.6)	16.0 (13.8)	12.6 (13.9)	12.3 (12.4)	8.25 (8.7)	16.8 ^{†§} (14.9)	10.9 (11.2)	12.2 ^{†§} (10.1)	9.4 (9.7)	12.8 ^{†§} (11.3)	7.8 (9.4)
High sugar foods	16.7 (20.4)	13.7 (16.7)	20.7 ^{*§} (19.9)	9.3 (8.6)	11.5 (12.3)	10.5 (13.9)	18.7 ^{*§} (17.3)	10.1 (10.9)	14.4 (13.8)	13.4 (16.5)	20.8 ^{†§} (25)	9.9 (11.5)
Drinks	10.7 (12.1)	9.8 (11.3)	16.0 (18.1)	16.1 (20.8)	11.1 (12.2)	10.2 (11.6)	16.8 (20.4)	12.4 (13.6)	12 (13.4)	10.8 (10.4)	20.5 (27.7)	18.1 (22)
Savoury snacks	0.3 (0.8)	0.2 (0.5)	0.28 (0.59)	0.23 (0.54)	0.17 (0.32)	0.25 (0.96)	0.27 (0.6)	0.54 (1.5)	0.14 (0.35)	0.13 (0.8)	0.37 (0.8)	0.27 (0.62)

¹ Figures in brackets are standard deviations

*p<0.001, † p<0.05 ‡ paired t-test § Wilcoxon sign rank test

Table 42: The mean ($\pm$ SD) complex carbohydrate contribution from each food category for women that have completed all 3 cycles

	Menses 1 Treatment		Menses 1 Placebo		Menses 2 Treatment		Menses 2 Placebo		Menses 3 Treatment		Menses 3 Placebo	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Complex carbohydrates												
Cereal	52.1 (20.7) ¹	50.2 (21.4)	62.7 (22.2)	58.9 (21.2)	51.8 (22.4)	48.6 (23.3)	62.3 (24.3)	57.5 (19.9)	50.2 (20.1)	48.3 (24.3)	59.4 (22.9)	62.7 (25)
Milk	0	0	0.28 (1.6)	0.44 (2.6)	0	0	0.58 (3)	0.5 (3.0)	0	0	0.4 (2.3)	0.48 (2.8)
Meat, poultry, fish and eggs	1.5 (2.6)	2 (2.6)	1.7 (2.5)	1.7 (2.7)	1.9 (3)	2.3 (3.4)	2.4 (4.1)	2.1 (3.5)	2.8 (3.7)	1.6 (2.6)	1.75 (2.6)	1.9 (2.7)
Savoury foods	11.6 (8.8)	10 (8.0)	13.8 (10.5)	11.5 (11.0)	13.1 (12.5)	10.1 (11.1)	16 (10.8)	10.5 (11.6)	13.9 (13)	12.5 (9.7)	14.3 (13.9)	10.2 (12)
Vegetables	10.1 (8)	7.5 (5.5)	11.1 (6.8)	10.5 (8.5)	8.1 (9.1)	10 (7.4)	11.4 (7.4)	8.8 (5.95)	10.9 (7.7)	7.9 (5.9)	11.5 (7.2)	9.3 (8.2)
Fruit	0.86 (1.3)	0.8 (1.2)	0.96 (1.2)	0.9 (1.5)	0.8 ^{†§} (1.1)	1.2 (1.5)	0.65 (1.1)	0.85 (0.98)	0.6 (0.8)	0.87 (1.2)	0.8 (1.1)	0.96 (1.2)
Fat	0	0.1 (0.08)	0	0	0	0	0	0	0	0	0	0
Cake and desserts	9.7 ^{†§} (8.1)	5.8 (6.4)	9.79 (9.7)	8.2 (11.1)	7.1 (6.6)	5.5 (5.8)	12.0 (14)	9.25 (12.3)	8.3 (7.3)	6.03 (6.3)	10.2 ^{†§} (10.8)	6 (8.9)
High sugar foods	0.8 (1.2)	0.52 (1.3)	0.91 ^{†§} (1.4)	0.3 (0.5)0	0.75 (1.1)	0.51 (1.2)	0.9 (1.5)	0.25 (0.5)	0.74 (1.4)	0.46 (1.3)	0.75 ^{†§} (0.98)	0.4 (1.1)
Drinks	0.47 (0.48)	0.45 (0.47)	0.7 (0.6)	0.6 (0.58)	0.54 (0.58)	0.46 (0.53)	0.78 (0.75)	0.7 (0.6)	0.49 (0.5)	0.51 (0.58)	0.75 (0.73)	0.71 (0.66)
Savoury snacks	1.4 (4)	1.0 (2.2)	5.0 (8.8)	1.7 (2.8)	1.5 (2.3)	0.87 (2.3)	1.9 (3.9)	1.2 (2.7)	1.83 (3.45)	0.27 (0.78)	3.1 ^{†§} (5.4)	1.05 (1.9)

¹ Figures in brackets are standard deviations

*p<0.001, † p<0.05 ‡ paired t-test § Wilcoxon sign rank test

Table 43: The mean ($\pm$ SD) percent of kilojoules from each food category for women over 3 menstrual cycles

Percent kilojoules	Menses 1 Treatment		Menses 1 Placebo		Menses 2 Treatment		Menses 2 Placebo		Menses 3 Treatment		Menses 3 Placebo	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Cereal	24.1 (9.5) ¹	24.7 (10.2)	22.3 (8.3)	23.5 (9.2)	23.3 (8.7)	23.9 (9.9)	22.6 (8.9)	25.5 (8.7)	21.6 (8.3)	23.5 (9.8)	21.4 ^{†‡} (8.4)	26.5 (9.1)
Milk	10.0 (7.4)	9.8 (6.4)	9.2 (4.8)	9.98 (5.5)	9.7 (6.2)	10.95 (6.7)	9.6 (5.6)	11.2 (5.9)	8.4 ^{†§} (5.4)	11.1 (7.4)	11.2 (6.2)	12.1 (6.4)
Meat, poultry, fish and eggs	11.8 (8)	13.2 (8.6)	11.1 (6.2)	13.2 (6.9)	13.2 (8.9)	14.1 (8.6)	11.6 (6.2)	13.3 (8.9)	13.9 ^{†§} (6.9)	11.2 (8.0)	11.1 (7.7)	13 (7.5)
Savoury foods	12.3 (8.6)	13.5 (10.2)	11.9 (9.7)	12.2 (9.6)	13.8 (9.4)	11.0 (10.3)	12.9 (7.7)	11.1 (9.2)	14.2 (9.8)	15 (10.4)	12.1 (9.2)	10.1 (10.2)
Vegetables	8.2 (5.9)	6.8 (5.4)	6.8 (4.04)	7.3 (4.5)	7.0 (5.9)	8.7 (6.5)	6.8 (4.6)	6.9 (4.2)	8.3 (6.8)	6.7 (6.2)	6.9 (3.7)	6.5 (4.5)
Fruit	4.4 (4.9)	5.4 (4.3)	3.4 (4.2)	4.2 (4.9)	4.8 ^{†§} (5.2)	6.5 (4.6)	2.4 (2.7)	3.8 (3.4)	3.7 ^{†§} (3.4)	5.7 (4.5)	3.04 (3.2)	3.6 (3.3)
Fat	3.0 (2.7)	3.3 (2.8)	5.2 (3.6)	5.5 (4.7)	4.5 (3.4)	3.2 (3.3)	4.4 (3.5)	4.7 (4.6)	3.7 ^{†§} (3.1)	4.2 (4.6)	4.3 (4.2)	4.0 (4.3)
Cake and desserts	11.5 (9.2)	8.1 (6.6)	10.8 ^{†§} (7.8)	8.8 (8.9)	10.5 (8.3)	8.5 (8.9)	11.7 ^{†§} (9.1)	9.2 (8.1)	10.4 (7.9)	8.9 (8.3)	9.9 ^{†§} (7.2)	6.1 (6.8)
High sugar foods	6.8 (7.8)	5.96 (6.6)	8.5 * [§] (9.1)	3.2 (2.8)	5.6 (6.2)	5.1 (7.3)	6.7 ^{†§} (4.8)	4.4 (5.0)	7 (7.8)	6.1 (8.2)	7.7 ^{†§} (9.3)	4.2 (6.1)
Drinks	5.95 (5.1)	6.8 (6.0)	7.1 (6.9)	7.6 (7.3)	5.6 (4.9)	6.1 (4.9)	8.8 (7.7)	7.9 (7.5)	6.8 (5.4)	6.6 (5.3)	9.2 ^{†§} (9.1)	11.8 (8.6)
Savoury snacks	1.7 (3.5)	2.2 (4.7)	3.6 (5.0)	1.9 (2.9)	1.99 (2.7)	1.9 (5.3)	2.5 (4.5)	2.1 (3.2)	2.1 (3.8)	0.99 (2.7)	3.1 ^{†§} (4.3)	1.8 (3.9)

¹ Figures in brackets are standard deviations

*p<0.001, † p<0.05

‡ paired t-test § Wilcoxon sign rank test

Table 44: The mean ($\pm$ SD) percentage of protein contributed by each food category over 3 menstrual cycles

	Menses 1 Treatment		Menses 1 Placebo		Menses 2 Treatment		Menses 2 Placebo		Menses 3 Treatment		Menses 3 Placebo	
Percent Protein	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Cereal	18.7 (8.6) ¹	19.2 (10.1)	18.7 (7.2)	17.6 (6.7)	18.9 (10.2)	17.0 (7.7)	18.1 (7)	19.1 (6.5)	16.7 (6.8)	18.3 (9.5)	17.3 ^{†§} (7.2)	20.6 (8)
Milk	15.8 (11.8)	14.5 (9.5)	15.5 (8.1)	14.5 (7.8)	15.1 (10.3)	15.9 (10.7)	15.5 (8.6)	16.7 (8.3)	12.9 ^{†‡} (8.7)	17.2 (11.8)	18.1 (8.8)	18.7 (9.6)
Meat, poultry, fish and eggs	31.1 (17.8)	32.7 (19.3)	29.4 (13.0)	34.2 (16.5)	30.1 (17.1)	33.2 (16.8)	30.6 (11.2)	31.9 (17.0)	33.4 (13.9)	28.3 (16.9)	29.5 (16.8)	32.3 (16)
Savoury foods	13.5 (9.6)	15.1 (13.4)	13.9 (11.5)	12.2 (9.8)	14.9 (10.5)	12.1 (11.9)	13.6 (9.2)	12.4 (9.9)	16 (11.7)	19.5 (16.9)	12.6 (10.2)	14.0 (11.9)
Vegetables	5.9 (4)	5.2 (3.4)	5.88 (3.2)	6.8 (6.5)	5.7 (4.5)	7.6 (6.4)	5.99 (3.5)	6.5 (3.3)	6.6 (4.1)	6.1 (5.6)	6.2 (3)	5.6 (4.1)
Fruit	1.3 (1.3)	1.6 (1.8)	1.34 (2.4)	1.5 (1.6)	1.7 ^{†§} (2.8)	2.1 (2)	1.0 (1.3)	1.2 (1.3)	1.2 ^{†§} (1.3)	1.95 (2)	1.1 (1.6)	1.3 (1.6)
Fat	0.1 (0.2)	0.03 (0.2)	0.098 (0.3)	0.095 (0.3)	0.3 ^{†§} (1.3)	0.01 (0.07)	0.02 (0.07)	0.04 (0.14)	0.08 (0.2)	0.1 (0.5)	0.07 (0.2)	0.01 (0.06)
Cake and desserts	6.2 ^{†§} (6.3)	4.1 (3.7)	6.5 ^{†§} (6.1)	4.0 (4.3)	6.7 (6.1)	5.1 (6)	6.4 ^{†§} (5.5)	4.5 (4.5)	5.8 (4.7)	4.8 (4.9)	5.5 ^{†§} (5.3)	2.8 (3.3)
High sugar foods	1.6 (3)	1.3 (2.2)	2.9 ^{*§} (4.4)	0.6 (1.04)	1.5 (2.5)	1.3 (3)	1.8 ^{†§} (1.7)	0.9 (1.8)	1.9 (3.4)	1.4 (3.1)	2.4 ^{†§} (4)	0.97 (2.3)
Drinks	3.95 (4)	4.1 (4.8)	3.8 (3.7)	3.8 (4.1)	4.2 (3.9)	4.3 (4.4)	4.7 (5)	4.5 (3.4)	4.1 (4.1)	4.7 (5)	5.3 (4.8)	5.7 (4.9)
Savoury snacks	0.8 (1.6)	1.6 (5.1)	1.8 (2.5)	1.0 (1.8)	1.2 (2.4)	1.4 (4.6)	1.6 (3.3)	1.6 (2.6)	1.03 (2.2)	0.96 (3.2)	1.7 (2.6)	1.1 (2.4)

¹ Figures in brackets are standard deviations

*p<0.001, † p<0.05

‡ paired t-test § Wilcoxon sign rank test

Table 45: The mean ($\pm$ SD) percentage of fat contributed by each food category over 3 menstrual cycles

	Menses 1 Treatment		Menses 1 Placebo		Menses 2 Treatment		Menses 2 Placebo		Menses 3 Treatment		Menses 3 Placebo	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Percent Fat												
Cereal	8.7 (5.4) ¹	9.4 (6.8)	7.9 (4.7)	8.5 (4.8)	6.9 (4.8)	8.7 (6.5)	7.7 (5.4)	8.7 (5.2)	6.2 (4.5)	7.8 (6.2)	6.7 ^{†§} (5.2)	10.2 (5.7)
Milk	14.8 (12.3)	15.6 (11.4)	13.3 (9.4)	15.3 (9.8)	13.8 (9)	17.8 (12.7)	13.4 (10.2)	16.2 ^{†§} (10.0)	11.5 (7.7)	16.3 (9.1)	15.4 (9.5)	18.0 (11.5)
Meat, poultry, fish and eggs	17.2 (12.6)	19.6 (13.6)	16.8 (11.2)	18.2 (10.5)	20.4 (14.7)	21.8 (13.2)	16.9 (10.2)	21.3 (12.9)	20.8 (11.6)	16.7 (12.9)	15.9 (13.2)	16.7 (12.9)
Savoury foods	17.3 (13.1)	19.4 (16.4)	15.4 (13.8)	17.5 (14.6)	18.6 (13.3)	15.5 (14.2)	18.2 (13.7)	16.5 (13.2)	20 (13.6)	22.4 (16.9)	16.9 (12)	15.0 (15.1)
Vegetables	9.0 (11.5)	6.8 (8.7)	5.4 (5.2)	4.7 (4.7)	5.9 (8.5)	7.1 (8.4)	5.2 (5.5)	4.6 (4.9)	7 (9.2)	4.7 ^{†§} (8.8)	5.2 (4.9)	4.8 (5.8)
Fruit	0	0	0.08 (0.4)	0.05 (0.2)	0	0	0.007 (0.04)	0	0.06 (0.4)	0	0	0.02 (0.1)
Fat	9.4 (8.3)	9.9 (8.3)	14.6 (9)	16.1 (13.2)	13.3 (9.3)	10.4 (10.1)	12.8 (9.4)	13.9 (12.9)	10.8 (8.9)	12.7 (13.2)	12.6 (11.8)	12.5 (11.2)
Cake and desserts	13.3 (10.8)	10.2 (9.3)	10.9 (9.2)	9.7 (11.1)	11.3 (9.6)	9.8 (11.9)	13.5 (11.7)	10.8 (9.3)	11.1 (9.8)	10.3 (10.7)	10.9 (9)	7.3 (8.5)
High sugar foods	5.7 (7.9)	4.3 (6.4)	8.3 ^{*§} (11.2)	2.3 (3.5)	4.6 (6.9)	3.7 (6.5)	5.99 (5.6)	3.5 (5)	6.9 (10.4)	4.5 (9.4)	7.6 ^{†§} (10.8)	4.1 (9.9)
Drinks	0.9 (2.0)	0.8 (2.1)	0.6 (1.6)	0.99 (2.4)	0.7 (1.6)	0.99 (2.2)	1.2 (3)	0.9 (1.9)	1.1 (2.4)	1.2 (2.6)	1.4 (2.7)	1.5 (3.0)
Savoury snacks	3.2 (5.9)	4.5 (10.2)	6.1 (8.5)	3.9 (7.0)	3.9 (5.5)	3.6 (8.8)	4.8 (8.6)	4.2 (5.9)	3.9 (6.3)	2.2 (5.8)	6.4 (9.2)	3.7 (7.1)

¹ Figures in brackets are standard deviations

*p<0.001, † p<0.05

‡ paired t-test § Wilcoxon sign rank test

Table 46: The mean ($\pm$ SD) percentage of carbohydrate from each food category over 3 menstrual cycles

	Menses 1 Treatment		Menses 1 Placebo		Menses 2 Treatment		Menses 2 Placebo		Menses 3 Treatment		Menses 3 Placebo	
Percent Carbohydrate	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Cereal	36.8 (14.3) ¹	38 (14.1)	35 (11)	37.5 (14)	36.7 (12.5)	36.6 (13.6)	35.8 ^{††} (13.3)	40.6 (12.3)	35.0 (12.2)	36.1 (14.3)	34.4 ^{††} (13.0)	42.0 (13.8)
Milk	5.3 (4.5)	5.1 (3.8)	5.0 (3.6)	5.5 (4.7)	5.2 ^{†§} (4.1)	5.95 (4.8)	6.0 ^{†§} (4.3)	6.7 (5.3)	5.2 (5.3)	6.3 (7.4)	6.6 (5.2)	7.1 (6.2)
Meat, poultry, fish and eggs	1.2 (1.9)	1.6 (2.1)	0.9 (1.4)	1.05 (1.4)	1.3 (2.2)	2.0 (2.9)	1.3 (2.1)	1.8 (2.9)	2.02 (2.7)	1.1 (1.7)	1 (1.5)	1.3 (1.8)
Savoury foods	8.8 (6.2)	11.9 (12.8)	9.9 (8.5)	9.8 (8.4)	10.8 (8.9)	8.1 (8.0)	10.2 (5.6)	8.4 (8.8)	10.3 (8.1)	10.7 (7.4)	9.6 (8.5)	8.5 (8.7)
Vegetables	8.5 (5.7)	7.3 (5.6)	7.9 (4.4)	9.2 (5.5)	8.1 (8.1)	9.8 (6.7)	8.2 (5.0)	8.8 (5.3)	9.6 (6.9)	7.8 (5.5)	8.4 (4.4)	8.0 (5.5)
Fruit	8.0 (8.6)	10.2 (7.9)	6.3 (7.1)	8.0 (8.7)	9.1 ^{†§} (8.9)	12.7 (9.1)	4.6 ^{†§} (5)	7.2 (6.4)	7.4 ^{†§} (6.8)	10.7 (8.6)	5.7 (5.8)	7.1 (6.2)
Fat	0.07 (0.2)	0.1 (0.5)	0.09 (0.2)	0.1 (0.3)	0.08 (0.2)	0.09 (0.3)	0.02 (0.05)	0.06 (0.1)	0.12 (0.5)	0.1 (0.2)	0.03 (0.06)	0.05 (0.1)
Cake and desserts	12.99 (10.3)	8.9 ^{†§} (7.1)	12.8 (9.1)	10.8 (9.8)	12.1 (9.4)	9.4 (9.7)	13.6 (9.3)	10.7 (9.5)	12.6 (9.3)	10.0 (9.4)	11.3 ^{†§} (7.8)	7.6 (8.6)
High sugar foods	10.0 (10.8)	9.7 (11.1)	11.6 ^{* §} (10.7)	5.4 (4.6)	8.1 (8.0)	7.9 (10.4)	9.6 ^{†§} (7.2)	6.7 (7.6)	9.4 (9.0)	9.1 (10.3)	10.4 ^{†§} (10.6)	6.2 (6.9)
Drinks	7.5 (7.9)	7.7 (7.9)	7.9 (8.5)	9.3 (10.4)	7.1 (7.2)	6.8 (6.3)	9.6 (10.2)	8.3 (8)	7.3 (6.7)	7.9 (7.2)	10.6 (12.7)	10.8 (11.8)
Savoury snacks	1.03 (2.7)	0.9 (1.8)	2.8 (4.8)	1.0 (1.7)	1.1 (1.6)	0.7 (1.8)	1.3 (2.6)	1.2 (2.5)	1.5 (3.4)	0.3 (0.6)	2.1 (3.9)	0.8 (1.5)

¹ Figures in brackets are standard deviations

*p<0.001, † p<0.05 ‡ paired t-test § Wilcoxon sign rank test

Table 47: The mean ($\pm$ SD) percentage of simple sugars from each food category over 3 menstrual cycle

	Menses 1 Treatment		Menses 1 Placebo		Menses 2 Treatment		Menses 2 Placebo		Menses 3 Treatment		Menses 3 Placebo	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Percent simple sugars												
Cereal	8.6 (7.9) ¹	7.5 (7.9)	5.2 (3.7)	6.1 (5.2)	7.3 (7.4)	6.7 (6.1)	4.9 ^{†§} (3.7)	6.4 (5.1)	7.0 (7.7)	7.9 (7.6)	5.4 ^{†§} (4.6)	7.1 (5.3)
Milk	13.1 (10.8)	12.3 (11.2)	11.6 (9.3)	13.8 (12.4)	13.0 (12.4)	13.9 (12.0)	14.7 ^{†§} (12.8)	17.1 (13.7)	13.0 (13.1)	13.5 (13.4)	15.9 (14.7)	18.7 (14.9)
Meat, poultry, fish and eggs	0.37 (1.4)	0.6 (2)	0.08 (0.2)	0.08 (0.23)	0.3 (0.6)	0.8 (3.1)	0.1 (0.3)	0.5 (1.2)	0.6 (2.3)	0.1 (0.3)	0.14 (0.3)	0.3 (1.1)
Savoury foods	3.9 (3.0)	5.8 (5)	5.0 (5.7)	5.9 (6.7)	6.0 (5.7)	4.2 (4.4)	4.9 (5.3)	4.8 (5.1)	5 (4.1)	4.4 (3.1)	4.2 (3.9)	5.2 (5.7)
Vegetables	4.4 (3.7)	5.0 (4.6)	4.4 ^{†§} (3)	6.6 (4.7)	5.6 (5.1)	5.3 (4.1)	5.9 (4.7)	7.4 (6.2)	5.7 (4.8)	5.5 (4.5)	5.4 (4.8)	6.2 (4.9)
Fruit	16.4 (15.8)	21.4 (16.8)	12.96 (15.6)	18.0 (17.8)	18.7 ^{†§} (17.3)	25.4 (17)	9.7 ^{†§} (10.5)	17 (16.1)	15.2 ^{†§} (13.7)	21.0 (16.8)	11.9 (11.5)	15.6 (13.3)
Fat	0.1 (0.4)	0.2 (0.8)	0.2 (0.4)	0.3 (0.7)	0.2 (0.4)	0.2 (0.7)	0.04 (0.1)	0.1 (0.3)	0.3 (1.1)	0.2 (0.5)	0.06 (0.2)	0.1 (0.3)
Cake and desserts	16.7 (13.7)	12.1 (10.4)	18.0 (14.7)	15.3 (14.5)	16.6 (14.3)	12.6 (12)	17.8 ^{†§} (12.1)	13.7 (11.4)	16.95 ^{†§} (13.2)	12.7 (12)	14.9 ^{†§} (11.6)	10.4 (12)
High sugar foods	19.8 (18.4)	20.3 (20.8)	24.6 ^{*§} (17.8)	13.1 (12.8)	16.7 (14.4)	15.5 (17.5)	21.5 ^{†§} (15.9)	15 (14.5)	19.9 (18)	18.5 (18.5)	21.7 ^{†§} (17.1)	13.5 (14.6)
Drinks	16.0 (15.7)	15.6 (14.1)	17.1 (17.4)	18.9 (19.2)	15.1 (14.2)	15 (14.5)	20.0 (20.9)	17.2 (15.5)	16.0 (14.6)	18.5 (18)	20.8 (20.6)	13.5 (14.6)
Savoury snacks	0.4 (0.9)	0.2 (0.6)	0.3 (0.6)	0.3 (0.7)	0.2 (0.4)	0.3 (1.2)	0.4 (0.7)	0.9 (3.3)	0.2 (0.5)	0.2 (0.4)	0.40 (1.0)	0.4 (1.1)

¹ Figures in brackets are standard deviations

*p<0.001, † p<0.05 ‡paired t-test § Wilcoxon sign rank test

Table 48: The mean percentage ($\pm$ SD) of complex carbohydrate from each food category over 3 menstrual cycles

	Menses 1 Treatment		Menses 1 Placebo		Menses 2 Treatment		Menses 2 Placebo		Menses 3 Treatment		Menses 3 Placebo	
Percent complex carbohydrates	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Cereal	58.5 (16.2) ¹	61.3 (15.3)	58 (13.8)	59.8 (18)	59.5 (17.0)	60.7 (20.2)	57.5 ^{†‡} (15.1)	64.1 (15)	56 (17.1)	59.3 (16.2)	57.3 ^{†‡} (13.6)	66.7 (16.1)
Milk	0	0	0.25 (1.5)	0.3 (2.1)	0	0	0.4 (2.2)	0.36 (2.0)	0	0	0.4 (2.3)	0.50 (2.9)
Meat, poultry, fish and eggs	1.7 (2.8)	2.4 (3.4)	1.6 (2.5)	1.7 (2.5)	2.1 (3.6)	3.1 (4.3)	2.1 (3.4)	2.8 (5.1)	3.04 (4.1)	1.8 (2.8)	1.7 (2.5)	2.4 (3.5)
Savoury foods	13.1 (9.5)	14.4 (12.2)	13.2 (10.7)	12.5 (10.4)	14.8 (11.5)	11.4 (12.1)	15.1 (9.5)	11 (11.8)	14.6 (11.7)	17.3 (14)	13.2 (11.5)	10.5 (11.7)
Vegetables	12.0 (9.9)	9.7 (7.4)	10.8 (6.9)	11.9 (8.6)	10.0 (11.1)	13.7 (10.6)	10.6 (7.6)	10.2 (7.7)	12.5 (9.1)	10.5 (9)	11.7 (7.6)	10.1 (8)
Fruit	1.1 (2.1)	0.98 (1.4)	1.1 (1.3)	1.1 (1.7)	1.2 ^{†§} (1.8)	1.75 (2.2)	0.7 (1.1)	0.97 (1.2)	0.7 (1.1)	1.2 (1.7)	0.8 (1.1)	1.2 (1.7)
Fat	0	0.02 (0.13)	0.007 (0.05)	0.01 (0.05)	0	0.01 (0.04)	0	0	0.01 (0.08)	0	0	0
Cake and desserts	10.7 ^{†§} (9.5)	7.5 (8.0)	8.7 (7.8)	7.5 (7.2)	8.7 (9.1)	6.85 (8.3)	9.7 (9.1)	8.5 (9.3)	9.2 (8.1)	7.8 (8.9)	9.4 (9.8)	5.95 (7.6)
High sugar foods	0.8 (1.4)	0.7 (1.7)	1.0 ^{†§} (1.6)	0.3 (0.5)	0.85 ^{†§} (1.3)	0.7 (1.8)	0.86 ^{†§} (1.2)	0.3 (0.66)	0.8 (1.5)	0.8 (2.0)	0.8 (1.1)	0.4 (0.97)
Drinks	0.6 (0.7)	0.6 (0.67)	0.6 (0.6)	0.6 (0.6)	0.7 (0.86)	0.6 (0.68)	0.7 (0.75)	0.8 (0.7)	0.6 (0.6)	0.7 (0.97)	0.8 (0.8)	0.8 (0.7)
Savoury snacks	1.4 (3.9)	1.6 (3.1)	4.8 (8.6)	1.5 (2.6)	1.7 (2.8)	1.06 (2.6)	2.1 (4.5)	1.7 (5.1)	1.95 (4.1)	0.4 (1.14)	3.8 ^{†§} (7.1)	1.2 (2.2)

¹ Figures in brackets are standard deviations

*p<0.001, † p<0.05 ‡ paired t-test § Wilcoxon sign rank test

4.5 Frequency of daily meal intake over three menstrual cycles

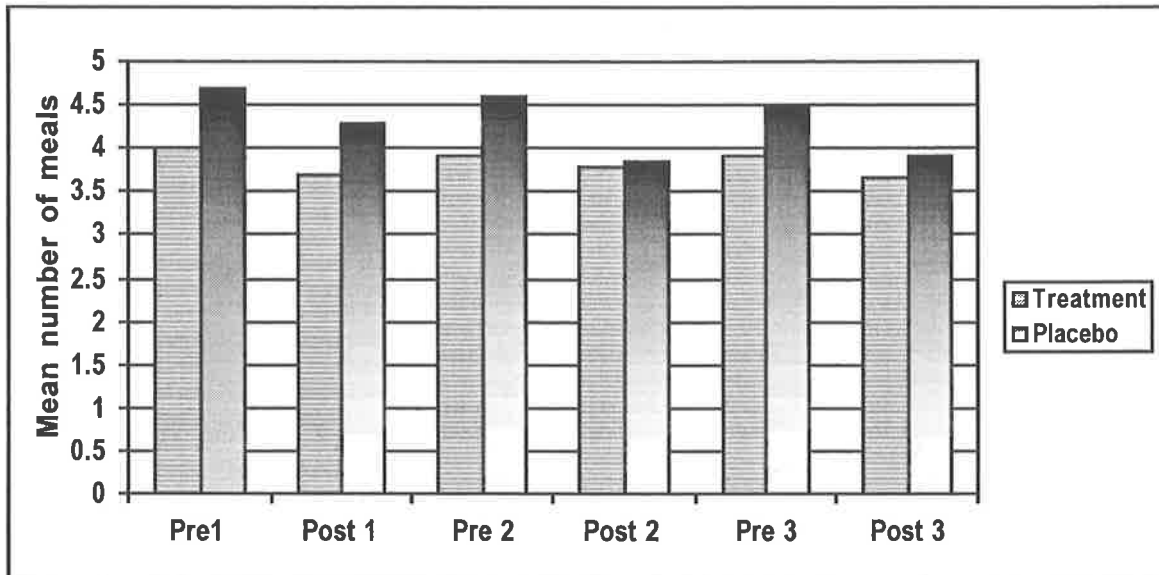
Table 49 shows the mean number of 'episodes of eating' for the treatment and placebo groups for all women participating in the study. Graph 3 presents the data from women who completed all three menstrual cycles. The placebo group for menses 1 to 3 and the treatment group at menses 1 and 3 consumed more meals premenstrually. This was also statistically significant when analysed for women that completed all three cycles. A comparison of the 'number of episodes' of eating between the treatment and placebo groups showed a significantly higher mean number of meals for the placebo group, premenstrually. This was also the case for the postmenstrual number of meals at menses 1 and 3.

Table 49: The mean ($\pm$ SD) number of episodes of eating over 3 menstrual cycles for women in the treatment and placebo groups

	Menses 1			Menses 2			Menses 3		
	Pre 1	Post 1	*P value	Pre2	Post 2	P value	Pre 3	Post 3	P value
Treatment	4.1 (0.94)	3.74 (0.94)	0.04	3.9 (0.92)	3.8 (0.83)	0.35	3.9 (0.9)	3.65 (0.84)	0.035
Placebo	4.7 (1.2)	4.2 (0.97)	0.04	4.6 (0.96)	3.8 (0.90)	0.000	4.5 (0.95)	3.9 (0.9)	0.000 1
¹ P value	0.01	0.03		0.00 4	0.8		0.006	0.3	

* *t*-test p values ¹ *t*-test p values for the comparison of placebo and treatment groups

Graph 3: The mean number of meals consumed by women who completed all three cycles in the placebo and treatment groups



4.6 Relationship between Steiner self-rated PMS questionnaire, Nottingham Health Profile and nutrient intake

4.6.1 Steiner self-rated questionnaire

The Steiner self-rated questionnaire median scores for pre and post menses for the treatment and placebo groups appear in Table 50. There was a significant difference between the pre and postmenstrual PMS scores for both the treatment and placebo groups over the three menstrual cycles ($p < 0.001$).

Table 50: The median score for the Steiner self-rated questionnaire over 3 menstrual cycles for all women

Score (median)	Menses 1		Menses 2		Menses 3	
	Treatment	Placebo	Treatment	Placebo	Treatment	Placebo
Premenstrual score	8 (1-35)	19 (0-32)	7 (0-34)	12 (0-33)	5 (0-35)	14 (0-33)
Postmenstrual score	2 (0-18)	1 (0-20)	0 (0-8)	1 (0-15)	0 (0-16)	0 (0-11)
P score	p=0.000	p=0.000	p=0.000	p=0.000	p=0.000	p=0.000
Pre -post score	6 (-4-34)	15 (-7-32)*	5 (-2-34)	11 (0-32) [†]	10 (0-31)	5 (-12-35)*

#p< 0.001, *p<0.01 † p<0.05

The change in score (Pre-post PMS score) also differed significantly between the treatment and placebo groups, with the treatment groups exhibiting a lower difference in score.

GEE analysis of the premenstrual scores indicated a significant treatment effect for all menstrual cycles (menses 1 p=0.01, menses 2 p=0.005 and menses 3 p=0.002). Adjusting for baseline scores supported this, where the treatment group exhibited a greater reduction in premenstrual score than the placebo group (p=0.002).

GEE analysis of the postmenstrual scores revealed no significant difference between the treatment and placebo groups (menses 1 p=0.6, menses 2 p=0.3 and menses 3 p=0.8). This was also the case after scores were adjusted for the baseline scores. Analysis of the change in scores (pre-post menstrual scores) also revealed a significant treatment effect

(menses 1 $p=0.005$, menses 2 $p=0.004$ and menses 3 $p=0.0007$). When adjusting for the base line score differences the difference in score was greater for the treatment group ($p=0.0008$).

Unlike for the screening data there was no consistent relationship between the initial self-perception of the severity of PMS symptoms and pre or postmenstrual scores for either the placebo or the treatment groups. There was a small significant correlation at menses 2 for the placebo group (Spearman's ρ 0.35, $p=0.033$).

4.6.2 Nottingham Health Profile scores

The Nottingham Health profile was scored according to seven subareas. These were: *physical mobility*, *pain*, *energy*, *sleep*, *social isolation*, *emotional reaction* and *daily life activities*. For the placebo, there was a significant difference between the pre and postmenstrual scores for *energy*, feeling of *social isolation*, *emotional reaction* and *daily life activities* for all 3 cycles (Table 51). For *sleep*, there was a significant difference for menses 1 and 2, but not 3 and for *physical mobility* there was a significant difference for menses 2 and 3.

Subjects receiving dexfenfluramine also exhibited a significant difference between pre and postmenstrual scores (Table 51). These were for *energy*, *emotional reaction* and *daily life activities* for all 3 cycles. There was also a significant difference in menses 3 for *pain* sub score. This suggests that dexfenfluramine did not contribute to an

improvement for *energy*, *emotional reaction* and *daily life activities*, but did for *sleep* and *social isolation* when compared to the placebo group.

There was no significant difference between the scores of the treatment group and placebo for most subsections of the questionnaire (Table 51). The differences that were of significance were for the pre menses score for *emotional reaction* over at all 3 cycles and, the pre menses 1 and 3 scores for *social isolation*. The change in score (Pre-post menses score) was significantly different for *social isolation* and *emotional reaction* for all the cycles. In addition, there was a significant difference for the score change between treatment and placebo groups for *sleep* at menses 1 and *daily life activities* at menses 1.

GEE analysis support these findings. The premenstrual *social isolation* scores showed a significant treatment effect (menses 1 $p=0.008$, menses 2 $p=0.031$, and menses 3 $p=0.01$). Adjusting for baseline also showed that the treatment group had a larger reduction in score compared to the placebo group ($p=0.005$). The postmenstrual *social isolation* did not differ between the two groups, while the change (pre-post menstrual) also exhibited a significant treatment effect (menses 1 $p=0.007$, menses 2 $p=0.03$ and menses 3 $p=0.01$). Adjusting for baseline showed that the treatment group had a greater decrease in score compare to the placebo group.

Table 51: The median pre and postmenstrual Nottingham Health Profile scores for each subsection of the questionnaire for all women

Item scored (median)	Menstrual phase	Menses 1		Menses 2		Menses 3	
		Treatment	Placebo	Treatment	Placebo	Treatment	Placebo
Physical mobility	Pre menses	0 (0-54)	0 (0-33)	0 (0-54)	0 (-24)	0 (0-66)	0 (0-33)
	Post menses	0 (0-54)	0 (0-22)	0 (0-54)	0 (0-11) ^{1†}	0 (0-11)	0 (0-11) ^{1†}
	Pre- post	0 (-11-31)	0 (-22-33)	0 (-11-39)	0 (-11-24)	0 (0-66)	0 (0-33)
Pain	Pre menses	0 (0-100)	0 (0-67)	0 (0-100)	0 (0-87)	0 (0-100)	0 (0-80)
	Post menses	0 (0-100)	0 (0-100)	0 (0-100)	0 (0-0)	0 (0-0) ^{1†}	0 (0-0)
	Pre- post	0 (-84-66)	0 (-100-67)	0 (-9-41)	0 (0-87)	0 (0-49)	0 (0-80)
Energy	Pre menses	24 (0-100)	39 (0-100)	0 (0-100)	0 (0-100)	0 (0-100)	30 (0-100)
	Post menses	0 (0-100) ^{1#}	0 (0-100) ^{1#}	0 (0-63) ^{1*}	0 (0-63) ^{1#}	0 (0-100) ^{1†}	0 (0-100) ^{1#}
	Pre- post	0 (-37-100)	24 (-39-100)	0 (-39-100)	0 (0-100)	0 (-100-100)	37 (0-100)
Sleep	Pre menses	0 (0-100)	13 (0-78)	0 (0-78)	0 (0-78)	0 (0-78)	0 (0-78)
	Post menses	0 (0-100)	0 (0-43) ^{1#}	0 (0-78)	0 (0-29) ^{1†}	0 (0-78)	0 (0-50)
	Pre- post	0 (-78-60)	6 (0-78) ^{2*}	0 (-38-78)	0 (-78)	0 (-22-78)	0 (-50-40)
Social isolation	Pre menses	0 (0-100)	16 (0-100) ^{2*}	0 (0-100)	0 (0-100)	0 (0-100)	0 (0-100) ^{2*}
	Post menses	0 (0-80)	0 (0-22) ^{1#}	0 (0-23)	0 (0-19) ^{1#}	0 (0-42)	0 (0-42) ^{1#}
	Pre- post	0 (-38-100)	16 (0-100) ^{2#}	0 (-23-100)	0 (0-100)	0 (-42-100)	0 (0-100) ^{2*}
Emotional reaction	Pre menses	0 (0-93)	24 (0-100) ^{2*}	0 (0-100)	17 (0-100) ^{2*}	0 (0-100)	24 (0-84) ^{2*}
	Post menses	0 (0-100) ^{1*}	0 (0-77) ^{1#}	0 (0-51) ^{1*}	0 (0-32) ^{1#}	0 (0-33) ^{1*}	0 (0-46) ^{1#}
	Pre- post	0 (-42-93)	18 (-35-100) ^{2*}	0 (-17-100)	17 (-32-100) ^{2†}	0 (-22-100)	24 (-4-76) ^{2*}
Daily life activities	Pre menses	1 (0-7)	1 (0-7)	1 (0-7)	1 (0-7)	1 (0-7)	1 (0-6)
	Post menses	0 (0-7) ^{1*}	0 (0-4) ^{1#}	0 (0-7) ^{1†}	0 (0-3) ^{1*}	0 (0-2) ^{1*}	0 (0-3) ^{1#}
	Pre- post	0 (-3-6)	1 (-4-7) ^{2*}	0 (-2-6)	0 (0-5)	0 (-1-6)	0 (0-6)

¹ Comparison of pre and postmenstrual scores.

² Comparison between treatment and placebo groups for pre menses, post menses and pre-post menses. #p< 0.001, *p<0.01 † p<0.05

For the premenstrual *emotional reaction* score the treatment and placebo groups did not differ. However after adjusting for baseline scores there was a significantly greater decrease in score ($p=0.03$). The treatment effect was significant for menses 2 ($p=0.04$) and 3 ($p=0.04$) and borderline for menses 1 ($p=0.07$). The change in scores (pre-postmenstrual scores) also showed no difference between the two groups. Adjusting for the baseline scores revealed the treatment group to have a greater decrease in score compared to the placebo ($p=0.01$). The effect of treatment over the three menstrual cycles were either of borderline significance or significant (menses 1 $p=0.058$, menses 2 $p=0.055$, and menses 3 $p=0.02$).

4.6.3 Relationship between the Nottingham health profile scores and the Steiner self- rated score

Table 52 displays the Spearman's correlation coefficients between the changes in the Nottingham health profile subarea scores and the Steiner self- rated scores. For the placebo group, as would be expected there was a moderate to high correlation between the change in PMS score and several subsections of the Nottingham Health profile for menses 1 to 3. For example, in menses 1 the correlations were as follows: physical *mobility* (Spearman's ρ 0.45, $p<0.01$), *energy* (Spearman's ρ 0.52, $p<0.001$), *social isolation* (Spearman's ρ 0.58, $p<0.001$) *emotional reaction* (Spearman's ρ 0.83, $p<0.001$) and *daily life* (Spearman's ρ 0.62, $p<0.001$) *activities*.

Table 52: Correlation coefficient scores (Spearman's rho) between the pre and postmenstrual change in each subarea of the Nottingham Health Profile and the Steiner self-rated score for the treatment and placebo groups

Item scored (median)	Menses 1		Menses 2		Menses 3	
	Treatment	Placebo	Treatment	Placebo	Treatment	Placebo
Physical mobility	0.06	0.45*	0.09	0.45 *	0.36 †	0.48 †
Pain	0.27	0.3	0.22	0.1	0.43 *	0.07
Energy	0.48 *	0.52 #	0.5 *	0.55 #	0.63 #	0.53*
Sleep	0.37 †	0.26	0.36 †	0.39 †	0.13	0.32
Social isolation	0.42 *	0.58 #	0.51 *	0.53 *	0.45 *	0.58 *
Emotional reaction	0.62 #	0.83 #	0.54 *	0.7 #	0.76 #	0.73 #
Daily life activities	0.42 *	0.62 #	0.43 †	0.48 *	0.74 #	0.55 *

#p< 0.001, *p<0.01 † p<0.05

For the treatment group there was a significant correlation between Steiner self-rated score and the Nottingham health profile subgroups of *energy*, *social isolation*, *emotional reaction*, and *daily life activities* for menses 1 to 3.

4.6.4 Relationship between Steiner self-rated score and energy and macronutrient intake

There was no consistently significant correlation between the change in macronutrient and energy intake and the Steiner self rated PMS score (Table 53). Significant correlations only occurred in menses 1 for the placebo, with energy (Spearman's rho 0.54, p< 0.001) and fat (Spearman's rho 0.57, p<0.001) being positively correlated and

Table 53: Correlation coefficient (Spearman's rho) score between the change in nutrient intake and PMS score

Pre -post difference in nutrient intake	Menses 1		Menses 2		Menses 3	
	Treatment	Placebo	Treatment	Placebo	Treatment	Placebo
Energy	0.22	0.54#	0.17	0.26	-0.02	0.22
Protein	0.42*	0.28	0.11	0.17	-0.14	0.18
Fat	0.28	0.57 #	0.23	0.28	0.008	0.294
Carbohydrate	-0.003	-0.36 [†]	-0.08	-0.32	0.06	-0.11
Complex carbohydrate	-0.13	0.15	0.18	0.31	-0.03	0.11
Simple sugars	0.18	0.25	-0.09	0.13	0.02	0.05

#p< 0.001, *p,0.01 [†] p<0.05

carbohydrate (Spearman's rho, -0.36, p<0.01) being negatively correlated. In the treatment group there was a moderate correlation for protein (Spearman's rho 0.42, p<0.01) at menses 1. This is indicative of a lack of relationship between the severity of PMS (as measured by the change in score) and total nutrient intake.

Table 54: Correlation coefficient (Spearman's rho) score between the premenstrual energy or macronutrient intake and PMS score for *high sugar foods* category

Nutrient contribution by high sugar food category	Menses 1		Menses 2		Menses 3	
	Treatment	Placebo	Treatment	Placebo	Treatment	Placebo
Energy	0.05	0.6#	0.12	0.39 [†]	0.25	0.41 [†]
Protein	0.25	0.67#	0.18	0.44*	0.32 [†]	0.31
Fat	0.28	0.68#	0.22	0.48*	0.3	0.29
Carbohydrate	0.05	0.52#	0.07	0.34 [†]	0.25	0.4 [†]
Complex carbohydrate	0.13	0.48*	0.2	0.43*	0.42 [†]	0.24
Simple sugars	0.07	0.50*	0.07	0.34 [†]	0.23	0.42 [†]

#p< 0.001, *p,0.01 [†] p<0.05

Analysis using the Steiner self-rated scores and food categories also showed a lack of significant correlation except for the *high sugar food* category (Table 54). For this category, there was a significant relationship between kilojoule, carbohydrate and simple sugar contribution and PMS score for all three menstrual cycles in the placebo group. This correlation was the strongest at menses 1 and of greater significance. Also for menses 1 and 2, there was a significant correlation between PMS score and protein and fat contribution.

There was also a lack of consistent significant correlation between the change in pre and postmenstrual Nottingham Health Profile subareas scores and energy and macronutrient intake. Correlations, if significant, tended to occur in menses 1 for the placebo group. This also applied when the food category data was analysed. As with the analysis using the Steiner self-rated scores (except for the *high sugar*

food category), there does not appear to be a strong link between the subareas, total nutrient intake or the types of foods consumed.

For the *high sugar food* category, there were significant relationships between some nutrients and the Nottingham Health Profile subareas of *energy* and *emotional reaction*. These relationships tended to be significant for the placebo group's premenstrual intake. The treatment group exhibited isolated significant relationships and were not consistent over the three menstrual cycles. The following nutrients from the *high sugar food* category exhibited a premenstrual relationship with the Nottingham Health Profile subarea of energy for the placebo group:

- Menses 1 for kilojoule (Spearman's $\rho=0.43$, $p=0.007$), protein (Spearman's $\rho=0.45$, $p=0.0049$), carbohydrate (Spearman's $\rho=0.39$, $p=0.016$) and simple sugars (Spearman's $\rho=0.38$, $p=0.017$).
- Menses 2 for protein (Spearman's $\rho=0.39$, $p=0.022$), fat (Spearman's $\rho=0.38$, $p=0.024$), and complex carbohydrate (Spearman's $\rho=0.39$, $p=0.02$).

There was no significant relationship between the Nottingham Health Profile *energy* subarea and any macronutrients or kilojoule intake at menses 3.

For the Nottingham Health Profile subarea *emotional reaction*, the significant relationships again occurred premenstrually in menses 1 and 2 but not menses 3. These were at:

- Menses 1 for kilojoules (Spearman's rho, 0.57 $p=0.0002$) protein (Spearman's rho 0.62 $p=0.0001$), fat (Spearman's rho, 0.64 $p=0.0001$) , carbohydrate (Spearman's rho 0.46, $p=0.004$), complex carbohydrate (Spearman's rho 0.46, $p=0.004$) and simple sugars (Spearman's rho 0.46, $p=0.0045$)
- Menses 2 for protein (Spearman's rho 0.37, $p=0.027$), fat (Spearman's rho 0.39, $p=0.02$) and complex carbohydrate (Spearman's rho 0.34, $p=0.04$).

4.6.5 Relationship between PMS score and the number of episodes of eating

Spearman's rank correlation was used to detect whether there was a relationship between the premenstrual, postmenstrual and the change in the Steiner self rated scores, and the number of 'episodes of eating'. Analysis of the data (not shown) found there to be no relationship between the Steiner self-rated score and the number of episodes of eating for either the placebo or the treatment groups.

4.7 Summary of results

4.7.1 Macronutrient and energy intake

The findings of this study have consistently shown an elevated absolute premenstrual energy and macronutrient intake for all subjects compared to postmenstrual intake. For the subjects in the placebo group this increase was significant for energy and fat and carbohydrate but not protein.

Dexfenfluramine suppressed the overall food consumption when compared to the placebo group. However, there still appears to be a reduced intake postmenstrually in the dexfenfluramine group. This may indicate that Dexfenfluramine is not totally suppressing the increased appetite and consumption of food that occurs in relation to PMS in these women. Alternatively as the findings are not consistent through the three menstrual cycles it may reflect normal variations in intake. The kilojoule intake and carbohydrate is significantly greater premenstrually for menses 1 and 3. Also in menses 3 there is a significantly greater premenstrual consumption of all macronutrients as well as energy. What is interesting is that there is no significant difference in the contribution from 'sugar' for the treatment group, but there is for 'complex carbohydrate for menses 1 and 3. This could possibly indicate that dexfenfluramine is suppressing the intake of foods contributing, 'simple sugars' in the diet. However as most foods consist of a combination of nutrients and taking into

consideration the analysis of the food categories this is unlikely to be the case.

The proportion of energy provided by carbohydrate however remains constant for all three menstrual cycles between pre and post menses for both the placebo and treatment groups. This is similar to the findings by Johnson et al (1995) in a study of women without PMS, where the percent of carbohydrate was unchanged over the three phases of the menstrual cycle as was protein. Similarly Barr et al (1995), observed a greater mean luteal intake of 1259kJ/day but no significant change in percent of macronutrients. When divided into the percentage of sugars and complex carbohydrate there continues to be no significant difference between the pre and postmenstrual contribution. This could indicate that the elevated premenstrual energy and macronutrient does not reflect carbohydrate craving but an overall increased premenstrual appetite and supports the findings of the screening data.

4.7.2 Food category consumption over the menstrual cycle

Few studies have investigated food consumption in terms of the groups of foods eaten by women over the menstrual cycle. These studies have tended to be in women without PMS and have primarily looked at consumption of sweet foods and drinks and not all the food consumed (Fong et al, 1993). The majority of those reported have used retrospective methods such as 24 hour food recall and questionnaires.

Other studies have examined the food preferences of women when offered a range of foods in a controlled environment. For example, Bowen et al (1988) offered women sweet, salty or bland foods. They found that there was a preference for sweet foods regardless of phase of menstrual cycle and this preference was the highest during the luteal phase.

In a study reported by Tomelleri et al (1987), college students completed a questionnaire listing 32 foods as well their menstrual symptoms over a 6-week period. The foods were scored according to how much each food was 'craved'. There was no difference in food cravings between the 4 stages of the menstrual cycle used.

4.7.2.1 *Energy contribution by food categories*

In both the placebo and treatment groups kilojoule intake from 'sweet foods' was higher premenstrually (Graph 1). For the placebo group this was significantly higher over the whole study (Table 30). It was also significantly higher in the treatment group in Menses 1 and 3 for the *cake and dessert* category. These foods also contributed a significantly higher percentage of kilojoules in the placebo group.

No other food category consistently contributed either a higher energy or percentage of energy premenstrually. Therefore, these two categories were primarily responsible for the higher energy intake observed in the placebo. Dexfenfluramine appears to have dampened

overall food consumption including these foods. However, it did not completely suppress intake of these foods.

4.7.2.2 *Macronutrients*

The *cake and desserts and high sugar food* categories contributed both a significantly greater number of grams of protein and percentage of protein premenstrually for the placebo group. In the case of the treatment group, the contribution from protein reflected the energy intake.

The contribution of these two food categories in the placebo group in terms of other macronutrients was less consistent over the three menstrual cycles. However, the *high sugar* category but not *cake and dessert* category provided a significantly greater premenstrual contribution of fat, carbohydrate, and simple sugars. Treatment with dexfenfluramine reduced overall food consumption as discussed above. However, it did not totally suppress desire for sweet foods. There was a significantly greater contribution premenstrually from the *cake and dessert* category in menses 1 and 2 towards carbohydrate and simple sugars.

Analysis of the food categories in terms of the percentage of each macronutrient and energy they contribute to the total diet found that the *high sugar foods* consistently provided a greater proportion premenstrually for the placebo group. The treatment group was less consistent. The percentage of nutrient contribution was elevated

premenstrually for 'sweet' foods for all macronutrients as well as energy. However, the pattern of significance was variable.

4.7.3 PMS scores, Nottingham Health Profile Scores and their relationships to food intake

The Steiner self-rated showed a significant change between the premenstrual and postmenstrual scores for both the placebo and treatment groups. There was some suppression of the treatment group scores and analysis showed that there was a significant difference between the treatment and placebo groups' scores. Therefore, dexfenfluramine led to less PMS related symptoms being identified in this group.

For the placebo group there was no consistent relationship between total energy and nutrient intake and the Steiner self-rated score or the Nottingham Health Profile subarea scores. This was also the case for the treatment group.

However, analysis of the premenstrual data according to food categories did reveal a moderate to strong relationship between the *high sugar food* category and the Steiner PMS scores in the placebo group. This relationship was consistent across all three cycles for kilojoules, carbohydrate, and complex carbohydrate. Subjects in the treatment group, did not show a link between their consumption of this food category and their Steiner PMS scores. There was a weaker

relationship and less consistent between the Nottingham Health Profile subareas of *emotional reaction* and *energy* and kilojoule and macronutrient intake.

Dexfenfluramine reduced the strength of the relationship between the Steiner PMS scores and intake from the *high sugar food* category. A possible interpretation of this finding is that improvement in premenstrual symptoms led to a reduced desire to consume foods from this food category, as well as reducing overall food consumption.

CHAPTER 5

Discussion

5. Introduction

The types and quantities of food eaten by humans are complex. Food consumption is influenced by interactions between neurological, hormonal, physiological, psychological, social, economic, and cultural aspects. In some premenopausal women, there is an increase in appetite and food intake during the luteal phase of the menstrual cycle. This increase in appetite is more pronounced in a subgroup of women with PMS. A review of the literature has shown that there have only been a limited number of studies reporting on food and nutrient intake in women with premenstrual syndrome. No studies investigating food intake in overweight women with PMS symptoms have been reported in the literature.

The following discussion will include the findings of this present work within the context of current knowledge in this area, as well as drawing on other work in relation to appetite control. It will also provide some suggestions for future work in this area.

5.1 Premenstrual syndrome and food consumption

5.1.1 Evidence for premenstrual increase in food consumption in overweight women with PMS

One of the selection criteria for entry into this study was an increase in premenstrual carbohydrate intake. This criterion was based on the limited number of human studies (Wurtman et al, 1989, Wurtman, 1990) that reported a premenstrual increase in carbohydrate in women with PMS as well as animal studies (Czaja JA, 1975; Kemnitz et al, 1989).

This current study hypothesised (Hypothesis 1) that there are women with PMS who premenstrually increased their carbohydrate intake and that this reflected an increased preference for carbohydrate containing foods.

The screening data of women meeting the criteria for entering into the study showed not only an elevated premenstrual carbohydrate, but also a premenstrual increase in the other macronutrients (protein and fat) and kilojoule intake. A significant difference between pre and postmenstrual macronutrient and kilojoule intake was also observed during this study for the placebo group. These findings confirm other published work, mainly in women not identified as suffering from PMS, that there is a premenstrual increase in food consumption (Lyons et al, 1989; Tarasuk et al, 1991; Martini et al,

1994; Dye et al, 1997). However, although there is a consistency in the literature about increased premenstrual kilojoule intake, this is not the case when food intake is analysed in terms of macronutrients. For example, Martini et al (1994) found all the premenstrual macronutrients, protein, fat, and carbohydrate, to be significantly higher than the postmenstrual macronutrients. In comparison, Tarasuk et al (1991) only found fat intake to be significantly elevated. Both these studies did not identify whether the women participating had symptoms associated with PMS.

As previously stated, few published studies have reported energy and macronutrient intake in women with PMS. The study that has had a major influence in this area has not been in 'free-living subjects', but rather under controlled conditions (Wurtman et al, 1989). The advantage of this study has been that it has enabled food consumption in women with PMS to be documented more accurately. Moreover, there is a greater control over the types of foods being offered and subsequently consumed. Self-reported food consumption has limitations such as under reporting (Poppitt et al, 1998), the inability to control the foods eaten, and the variability in the accuracy of the recording of quantities consumed. These factors all contribute towards a decreased accuracy of nutrient data analysis. Advantages of self-reporting food consumption include that it is more likely to reflect usual dietary habits and there is a capacity to use a larger number of participants due to reduced cost.

Neither the screening data, nor the placebo data support the hypothesis that in this group of overweight and obese women there is a premenstrual preference for high carbohydrate foods. The findings show that there was an overall premenstrual increase in food consumption, but not a significant change in the proportion of macronutrients being consumed. This is similar to the findings by Johnson et al (1995) in a study of women without PMS, where the percent of carbohydrate was unchanged over the three phases of the menstrual cycle as was protein. This has also been found by Barr et al (1995), who observed a greater mean premenstrual kilojoule intake of 1259kJ/day but no significant change in percent of macronutrients.

Analysis of the screening data according to food categories revealed a significantly elevated premenstrual energy and macronutrient contribution from most categories except for the *milk* and *fruit* categories. When analysed according to the percentage that each food category contributed to the total macronutrient and energy intake, the categories *cakes and desserts* and *high sugar foods* contributed a higher premenstrual percentage for energy as well as all macronutrients. Analysis of the data from the participants in the placebo arm of study confirmed that there was no preference for high carbohydrate foods. The preference was for 'sweet tasting foods' excluding fruit.

5.1.2 The effect of increasing brain serotonin availability using Dexfenfluramine on food consumption

5.1.2.1 *Dexfenfluramine influence on energy and macronutrient intake during the pre and postmenstrual phases*

Dexfenfluramine reduced the absolute premenstrual energy and macronutrient intake when compared to the placebo group. However, this suppression was not total. A comparison between the premenstrual and postmenstrual kilojoule and macronutrient in subjects taking dexfenfluramine revealed the premenstrual intake to be higher. This elevated premenstrual intake was significant for carbohydrate for menses 1 ($p=0.025$) and in menses 3 ($p=0.02$). Also at menses 3, the premenstrual energy and all other macronutrients were significantly greater. This is at variance to the findings of Brzezinski et al (1990) who found that dexfenfluramine premenstrually suppressed energy, carbohydrate and fat intake, but not protein intake when compared to subjects taking a placebo. Their findings were attributed to dexfenfluramine '*selectively reducing excessive intake of carbohydrate rich, protein poor foods*' in these subjects. This group of researchers found similar findings in a study where obese subjects who reported to crave carbohydrates, received dexfenfluramine or a placebo (Wurtman et al, 1985).

Both of these studies were of similar design concerning the types of foods provided. The snacks provided were either high in carbohydrate or high in protein. Three of the five high carbohydrate snacks were sweet tasting while those high in protein were savoury in taste. The preference for foods high in carbohydrate, in particular the snacks could be attributed to a preference for sweet tasting food rather than a desire for carbohydrate per se. A preference for sweet tasting foods has been widely reported in the literature for both men and women (Drewnoski et al, 1992). Bowen et al (1988) compared women's taste preferences over the menstrual cycle. They found a preference for sweet tasting foods throughout the menstrual cycle and this was accentuated during the late luteal or premenstrual phase. In another study Rossignol et al (1991) found a relationship between chocolate intake and the severity of PMS symptoms.

Calculation of the mean percentage of energy, using the data presented in their paper, contributed by each macronutrient in the study by Brzezinski et al (1990) revealed a relatively high fat, lower carbohydrate diet. In the placebo group, the mean premenstrual percentage of energy from protein, fat, and carbohydrate was 15.4%, 48.9%, and 35.7% respectively. When women received dexfenfluramine, the mean percentage of intake from protein, fat, and carbohydrate was 18.9%, 49.4% and 31.7%. The higher proportion of fat may reflect their addition of fat to the meals to ensure they

were isocaloric. The proportion of macronutrients is lower than expected in an average diet. For example, the Australian National Nutrition Survey (1995) data found that, the mean percent contribution towards the total energy of the diets of women aged 25-44 years were as follows: protein 16.8%, fat 33% and carbohydrate 46.7%. This is comparable to the findings reported here. The premenstrual percent contribution in the current study for the placebo group was protein 16.7-17.5%, fat 33-34.1%, and carbohydrate 44.7-44.9%. In the group receiving dexfenfluramine the premenstrual contribution to the total energy intake was protein 17.8-18%, fat 31.9-33%, and carbohydrate 44.8-46.7%. The proportion of carbohydrate in the group receiving dexfenfluramine was slightly higher.

Drawing on the findings of other work contributes towards interpreting the current findings. There have been several studies using dexfenfluramine or other serotonin enhancing drugs such as fluoxetine in other subject groups such as obese subjects that indicate that dexfenfluramine does not selectively reduce carbohydrate consumption (Goodall et al, 1992 Lawton et al, 1995, Breum et al, 1996). Lawton et al. (1995) used fluoxetine in a double blind randomised cross over study in 12 obese women. They found that fluoxetine suppressed energy and macronutrient intake but not the percentage of energy from protein, fat, or carbohydrate. Analysis of food consumption according to the energy contribution by main

meals and snacks found that fluoxetine had its greatest effect on snacks providing 100-199kcal (420- 836kJ).

There are some similarities in the findings presented in this thesis to Lawton et al's (1995). Dexfenfluramine did not significantly alter the proportion of energy contributed by macronutrients. In particular, the percentage of energy provided by carbohydrate remained relatively constant for all three menstrual cycles for both the placebo and treatment groups. When analysed in terms of its two main constituents, the percentage of simple sugars and complex carbohydrate there continues to be no major difference between the pre and postmenstrual contribution. This further supports the evidence that that the elevated premenstrual energy and macronutrient does not reflect carbohydrate craving but rather an overall increased premenstrual appetite.

5.1.3 The influence of dexfenfluramine in the types of foods consumed over the menstrual cycle

Few studies have investigated food consumption in terms of the groups of foods eaten by women over the menstrual cycle. These studies have tended to be in women not identified to have PMS and have primarily looked at consumption of sweet foods and drinks (Fong et al. 1993, Bowen et al, 1988). The majority of those reported have used retrospective methods such as 24-hour food recall and

questionnaires. Other studies have examined the food preferences of women when offered a range of foods in a controlled environment. Bowen et al (1988), offered women sweet, salty or bland foods. They found that there was a preference for sweet foods regardless of phase of menstrual cycle and this preference was the highest during the luteal phase.

In a study reported by Tomelleri et al (1987), college students completed a questionnaire listing 32 foods as well their menstrual symptoms over a 6-week period. The foods were scored according to how much each food was 'craved'. There was no difference in food cravings between the four stages of the menstrual cycle used.

5.1.3.1 *Energy contribution by food categories*

In both the placebo and treatment groups the kilojoule intake from 'sweet foods' was higher premenstrually. For the placebo group this was significantly higher over the whole study. It was also significantly higher in the treatment group in Menses 1 and 3 for the *cake and dessert* category. These foods also contributed a significantly higher percentage of kilojoules in the placebo group. No other food category consistently contributed either a higher energy or percentage of energy premenstrually. Therefore, these two categories were primarily responsible for the higher energy intake observed in the placebo. Dexfenfluramine appears to have

dampened overall food consumption including these foods. However, it did not completely suppress intake of these foods.

The findings within the study are inconsistent to those of the screening data. Analysis of the screening data found a significantly greater energy contribution premenstrually by the *cereal, fat, drinks, savoury foods*, and *savoury snack* categories. The reason or reasons for this difference are unclear. The most likely reason could be that it is a result of the placebo effect, for example arising from the perception that by the placebo group that they were taking medication. Another reason, which may be linked with the placebo effect, is that subjects were underreporting. However, the energy contribution by the food categories was consistent over the study period.

5.1.3.2 *Macronutrient contribution by food categories*

The *cake and dessert* and *high sugar food* categories contributed both a significantly greater number of grams of protein and percentage of protein premenstrually for the placebo group. In the case of the treatment group, the *cake and dessert* category contributed significantly more protein premenstrually but not the *high sugar food* category.

The contribution of these two food categories in the placebo group for the other macronutrients was less consistent over the three

menstrual cycles. The *high sugar foods* category but not *cake and dessert* category provided a significantly greater premenstrual contribution of fat, carbohydrate, and simple sugars. Treatment with dexfenfluramine reduced overall food consumption as discussed above. However, it did not totally suppress the consumption of sweet tasting foods. There was a significantly greater contribution premenstrually from the *cake and dessert* category in menses 1 and 2 to the total carbohydrate and simple sugars.

Analysis of the food categories in terms of the percentage of each macronutrient and energy they contribute to the total diet found that the high sugar foods consistently provided a greater proportion premenstrually for the placebo group. The treatment group was less consistent. The percentage of nutrient contribution was elevated premenstrually for 'sweet' foods for all macronutrients as well as energy. However, the pattern of significance was variable.

These findings, taken together with the total energy and macronutrient intake of subjects, supports other published findings that increasing the availability of serotonin (eg through the use of dexfenfluramine) in the brain reduces appetite in women with PMS. However, the increased preference for 'sweet foods' is still apparent in the treatment group. In addition, the frequency of eating was also not completely suppressed in subjects receiving dexfenfluramine.

This indicates that low brain serotonin levels does not solely explain the desire for sweet foods and that other factors, such as biological, psychological, behavioural, or environmental are involved. The preference in humans for sweet foods is well documented. Young children exhibit a preference for these foods together with high fat foods up to adulthood. Studies on food preferences in adults show that there is a preference for high sugar foods, with about 68% men and most women exhibiting this preference (Weingarten et al, 1991). In addition, the observation that the consumption of other high carbohydrate foods such as cereals and breads were not significantly greater premenstrually in subjects receiving the placebo supports this view.

In terms of the hypothesis being tested here, there does not appear to be an overall preference for foods high in carbohydrates, but rather a preference for sweet tasting foods. This finding differs from Wurtman's et al. (1989) study that showed a preference for both sweet and savoury high carbohydrate foods. In their study, it was suggested that low brain serotonin might explain the observed increase in intake. Subjects showing a preference for these foods were described as 'craving carbohydrate'. Neither does dexfenfluramine specifically reduce carbohydrate take.

The definition of food craving and its identification in individuals has been debated in the literature. In a review of the literature on food craving including the craving reported during the menstrual cycle, Weingarten et al (1990) highlights the lack of a standardized tool to measure and define what is meant by craving. They point out those studies relating food craving and the menstrual cycle are descriptive. Indeed studies reviewed as part of the work presented here varied greatly in their definition of craving.

Work that has investigated food craving has found that the foods most commonly 'craved' were sweet foods, in particular chocolates. Rozin et al (1991) found that both men and women liked chocolate. Women tended to like or crave it most and this tended to peak at the late luteal phase. Gendall et al (1997) investigated food craving in 101 women aged 18-45years. They found that the most commonly 'craved' foods were sweet foods (100%), then cereal and potato based products (26%) and lastly snack type foods (pizza, pies, hamburgers and nuts (5%)). Another earlier study (Drewnowski et al, 1992) that reported their findings on the food preferences of obese patients (93 men and 386 women) attending an outpatient clinic, questions the concept of food cravings. In this study, women tended to list more sweet foods among their favourite food, while men listed high fat high protein foods such as meat based dishes most frequently as their favourite foods. The concept of 'craving' was not investigated.

The authors base their contention because of claims that such craving for carbohydrate is widespread among obese individuals. They propose that if this was the case then it would not differ between men and women, as they had observed and that carbohydrate craving would lead to a preference for these foods regardless of whether they were sweet or not. In relation to the elevation of brain serotonin levels they propose that as carbohydrate foods with a high glycemic index are believed to be the most effective *then such foods as potato starch* should be most commonly craved.

Buffenstein et al. (1995) suggests that as foods that are reported to be 'craved' premenstrually tend to be sweet, women are not craving carbohydrate but are craving '*a combination of pleasant tasting, sweet, high fat foods*'. In a more recent study, Evans et al (1999) using a Food Desirability questionnaire found that women with PMS had a small increase in desire for both sweet and savoury carbohydrate/ fat foods as well as protein/fat foods. However, the desire for carbohydrate containing foods although high did not alter over the menstrual cycle.

Other work highlights the cultural and psychological influences on food craving. Zellner et al (1999) found a cultural as well as gender differences between American and Spaniard in chocolate craving , with 44 % of American women craving chocolate compared with

28.6% of Spanish women. The cravings for sweet foods overall was not culturally different, but did exhibit significant gender differences, with women having a higher preference for sweet foods and men savoury. The role of stress also seems to influence the types of food consumed (Oliver et al , 2000)

Thus, there is substantial support for there being a preference for sweet tasting foods. The current study provides further evidence for an increase in premenstrual preference for these foods.

However, although these studies provide support for the preference of 'sweet tasting 'foods they do not help to explain why there is a premenstrual increase in appetite and a preference for sweet foods. One of the most frequently referred to theories is that women with PMS and other disorders such Seasonal Affective Disorder and in some obese subjects is that the desire for high carbohydrate foods is a response to low brain serotonin levels. This theory proposes that individuals with low brain serotonin levels are attempting to self medicate by consuming high carbohydrate foods. The success of a range of medications that increase the availability of brain serotonin and suppress appetite, in particular for 'high carbohydrate containing foods have been used to support this theory.(Brzezinski et al, 1990; Wurtman et al, 1985). Other support for the role of serotonin in PMS is from studies on blood tryptophan levels and the effect of

high carbohydrate fluids or meals on mood and tryptophan levels (Sayegh et al, 1995). However these findings are not consistent. Rapkin et al (1991) found no difference between women with PMS and controls in the ratio of blood tryptophan: neutral amino acids levels.

Therefore the evidence from this study does not support the first two hypotheses. Based on the current findings both hypotheses have been revised and are presented below.

Revised Hypothesis 1

There are overweight women who as part of their PMS symptoms significantly increase their premenstrual food consumption when compared to their premenstrual intake. A major proportion of this increased intake is accounted for by foods that are sweet tasting.

Revised Hypothesis 2

Increasing the availability of brain serotonin by the use of dexfenfluramine in overweight women with PMS reduces overall energy and macronutrient consumption over the menstrual cycle

5.2 PMS and alleviation of symptoms by dexfenfluramine

PMS symptoms as measured by the Steiner self rated questionnaire, were reduced by dexfenfluramine in the current study. There was also an improvement in some of the subareas (eg emotional reaction, social isolation) of the Nottingham Health Profile. These findings support other work reported in the literature, where dexfenfluramine has been shown to reduce the premenstrual symptoms experienced by women with PMS. The amelioration of these symptoms by dexfenfluramine has been linked with the elevation of brain serotonin levels. The symptoms experienced have been attributed to reduced brain serotonin levels and have been compared to conditions such as depression.

The proposal that reduced brain serotonin levels contribute to PMS symptoms is based on studies where L-Tryptophan, the precursor of serotonin has been administered to women with PMS. In a pilot study, Steinberg et al (1994) and a subsequent clinical trial (Steinberg et al, 1999) observed an improvement in mood, but not physical symptoms after administering tryptophan to women with PMS.

5.3 The relationship between PMS symptoms and food consumption

Although there appeared to be a weak correlation between the changes in the Steiner self-rated PMS score and macronutrient intake

during the screening process, this relationship was not consistently observed in the study. There was a more consistent relationship between the Steiner self-rated PMS score and kilojoule intake. The strength of this relationship lessened when analysed according to whether subjects were taking dexfenfluramine or the placebo. The reduction in detecting a significant relationship may be related to a smaller sample size.

Investigation of a possible relationship between the Steiner PMS scores and intake according to food categories revealed a relationship to the consumption of the *high sugar food* category in the placebo group, but for none of the other food categories. Dexfenfluramine led to the disappearance of this relationship. These findings support previous discussion regarding the findings of this study, that there is a preference for 'sweet tasting' foods. The improvement in PMS symptoms may lead to a reduced desire for these foods, as well as the overall effect of the suppression of food intake by dexfenfluramine. Whether this is the case cannot be directly implicated from this findings of this study. However, the relationship between PMS symptoms and nutrient intake in the placebo group indicates that this is a possibility.

There was also no relationship found between the Steiner self-rated score and the number of episodes of eating.

The inconsistency in the findings therefore cannot lead to support for the third hypothesis - that there is a relationship between the severity of PMS symptoms and carbohydrate and kilojoule intake and that the frequency of food intake is greater in women with more severe symptoms.

Other previously published works either have found a lack of association between mood and food intake or detected a relationship. Bancroft et al (1988) found that 46% of women experienced premenstrual food craving prior to mood changes. Bancroft et al's (1988) findings are supported by a more recent study that investigated food cravings and mood over a five-week period in normal women (Hill et al 1994). They found that there was no relationship between food craving and mood. While MacKay Rossignal et al (1991) who investigated intake of sweet foods in women aged 18-22 found that there was a relationship between reported severity of premenstrual symptoms and the preference for sweet foods and drinks. Dye et al (1995) also detected a relationship between depression and the severity of craving.

A major reason for a lack of detection of a relationship between the subjects PMS scores and nutrient intake relates to the use of the mean nutrient intake over 4 days and the PMS score for one day. If there were little variation in food intake over the four days, then this

would have little effect. A large variation may significantly influence the relationship. In retrospect, the completion of daily PMS scores at the same time as the diet diaries would have improved the study. The findings may also be confounded by a placebo effect, by reducing the difference between premenstrual and postmenstrual intake and thus reducing the ability to detect a relationship. Another possible reason for the lack of a detectable difference could be related to the sample size.

5.4 Future work

The findings of the work reported here support some of the other published work and gives rise to some new questions.

This study could have been improved in several areas and future work should take this into account. Ideally further work in this area should use multiple measures including nutrient intake analyses, psychological aspects, analyses of relevant biochemical indices and hormones and the determination that ovulation has occurred. For example, the delineation of meals and snacks to determine snacking behaviour in women and the measurement of restrained eating among participants would have improved the study. In relation to food consumption and PMS symptoms additional information linking food consumption and why food was eaten could have been more rigorously collected. For example by instructing women to document feelings and reasons for eating when documenting food

intake. Other improvements could have included the confirmation of ovulation in participating women.

The understanding of why some women, both with and without PMS increase the amount of food they consume is an area that requires more investigation. Such understanding will contribute towards providing reliable dietary advice to women where increased food consumption is an issue. Currently in both the published scientific literature and popular media there is a wide range of dietary modifications recommended, but little available evidence published to support them.

The cyclic nature of PMS symptoms including food consumption, have led to the investigation of the possible links between gonadal hormones and PMS symptoms. To date, evidence continues to be conflicting. Low brain serotonin levels have also been postulated to be responsible for the premenstrual increase in appetite as well as contributing to the other PMS related symptoms. The findings of the current study could be interpreted as supporting this theory, as there was a reduction in food consumption and PMS symptoms in women taking dexfenfluramine. However, a direct link between serotonin levels and appetite is unlikely and current work suggests that serotonin may have a modulating effect in relation to PMS symptoms. To progress work in the area of PMS and food consumption, several questions need to be addressed and some of

these are discussed below. These questions assume the current definition of PMS.

Firstly, an important question that needs to be investigated is whether the observed increase in appetite and food consumption should be considered as part of PMS. Measurement of BEE over the menstrual cycle have shown there to be a premenstrual increase in BEE. The scale of this increase varies among ovulating women. It therefore could be argued that an increase in food intake coincides with a normal change in energy requirements and the inclusion of this symptom as part of the diagnosis of PMS requires review.

Secondly, the concept of 'craving' needs to be more clearly defined. The literature often refers to women with PMS craving certain foods, but there is no consistent way currently being used that identifies such subjects. Gendall et al (1997) has already done work in this area and more recently White et al (2002). This would enable the area of 'craving' in PMS to be more fully investigated.

Thirdly, it may be that an increase in food consumption in women with PMS is a result of a combination of influences. In part, the increase may coincide with the increase in premenstrual energy requirements (Solomon et al, 1982; Webb, 1986). Other influences are likely to be based on psychological and physiological changes

occurring premenstrually. This would include the effect of alterations in mood on food intake.

A review of the research findings in this area together with other work on the control of appetite and the psychosocial aspects of eating would also be beneficial. Work in the sociological literature links the types of food consumed with cultural views. Lupton (1996) in her book 'Food, the body and self' discusses and reviews research in the area of gender-based associations of food. In Western society sweet foods are associated with women, while foods such as meat are associated with male preferences. Seiderman et al (1990) found that women undergoing an education program exhibited fewer symptoms as well as less severe symptoms.

The advancement of technology will also contribute to our understanding of the factors involved in modulating food consumption. For example, recently published work by Gautier et al (2001), used positron emission tomography to measure regional cerebral blood flow (a marker of brain neuronal activity) to investigate satiation in lean and obese women. They found a difference in cerebral blood flow in some areas of the brain between lean and obese women after consuming a liquid meal. Their findings included a greater blood flow in the prefrontal cortex and a reduced blood flow in areas such as the frontal cortex in the obese compared to the lean women.

Conclusion

This study brings together two aspects of PMS, a comparison of the nutrient intake and the effect of increasing the availability of serotonin using dexfenfluramine. The findings show that there is a dampening of food consumption by dexfenfluramine. This decrease is particularly noticeable with sweet tasting foods. Within the context and limitations of this study there does not appear to be support for the concept that women with PMS increase their consumption of carbohydrate containing foods nor that there is a link with PMS symptoms as measured by the Steiner self rated questionnaire. However this work does indicate that there is a relationship between sweet tasting foods and PMS scores.

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FOOD DIARY

INITIALS: _____

Patient No: _____

Weight Kgs

Height cm

Date diary commenced:

Is this Premenstrual _ or Postmenstrual _

When recording the foods you eat:

1. Write down **everything** you eat and drink
2. Keep to your **usual** diet
3. Be as **specific** as possible when describing the foods you eat :
 - ω eg 1 thin slice of multi grain bread, grilled rump steak , fat not removed,
 - ω if you are eating out eg take a way, please write down the name of the take a way or restaurant
 - ω if you are using commercial products eg sauces, soups, frozen meals write down the brand used.
4. Be as accurate as you can when writing down the quantities of food you eat.
An example on how to fill out the diary is given in the middle of this booklet.
Please use the measurement cup provided and standard teaspoon and tablespoon measures
5. The usual length of time to keep the diary is 4 days.

Example of a page of the diet diary used in the study

DATE: DAY:

[illegible]

Example of how to fill out this diet diary

DATE: DAY:

TIME	FOOD	AMOUNT	REASON FOR EATING	AMOUNT	CODE
7.15am	Multigrain bread, thinly sliced	2 slices	Hungry		
	Strawberry jam	2 tsp			
	Black coffee	1 cup			
	Sugar	2 tsp			
10.30am	Rockbun (from XX bakery)	1 large	Hungry		
	Coke	1 can			
12.30	Cheese and salad sandwich made with white bread, no margarine (from shop)	1			
	Coffee	1 cup			
	Full cream milk	2 tbsp			
	Sugar	2tsp			
4.00pm	Mars bar	30g	Headache, felt as if		
	Chocolate milk , low fat	300mls	Needed to eat		
6.00pm	Roast chicken, with skin	2 drumsticks	Tea time, not hungry		
	White rice, boiled	1 cup			
	Peas, steamed	1/3 cup			
	Brussel sprouts, steamed	4 small			
	Pumpkin , roasted with chicken	3x4cm piece			
8.30pm	Tim tam	2	Watching TV, felt		

APPENDIX

QUESTIONNAIRE

Nottingham Health Profile

Listed below are some problems that individuals may experience in their daily life. Please tick "yes" for any problem that you have at the moment and tick "no" for any problem you do not have. Please answer every question. If you are not sure whether to say "yes" or "no", tick whichever answer you think is more true at the moment.

	YES	NO		YES	NO
I'm tired all the time	☐	☐	I lose my temper easily these days.	☐	☐
I have pain at night.	☐	☐	I feel there is nobody I am close to.	☐	☐
Things are getting me down	☐	☐	I lie awake for most of the night.	☐	☐
I have unbearable pain.	☐	☐	I feel as if I'm losing control.	☐	☐
I take tablets to help me sleep	☐	☐	I'm in pain when I'm standing.	☐	☐
I've forgotten what its like to enjoy myself.	☐	☐	I find it hard to dress myself	☐	☐
I'm feeling on edge	☐	☐	I soon run out of energy.	☐	☐
I find it painful to change position.	☐	☐	I find it hard to stand for long (for example, at the kitchen sink, waiting for the bus).	☐	☐
I feel lonely	☐	☐	I'm in constant pain.	☐	☐
I can only walk about indoors	☐	☐	It takes me a long time to get to sleep.	☐	☐
I find it had to bend.	☐	☐	I feel I am a burden to people.	☐	☐
Everything is an effort.	☐	☐	Worry is keeping me awake at night.	☐	☐
I'm waking up in the early hours of the morning.	☐	☐	I feel that life is not worth living.	☐	☐
I'm unable to walk at all.	☐	☐	I sleep badly at night.	☐	☐
I'm finding it hard to make contact with people.	☐	☐	I'm finding it hard to get on with people The days seem to drag.	☐	☐
I need help to walk about outside (for example, [] a walking aid or someone to support me).	☐	☐			
I have trouble getting up and down stairs or steps.	☐	☐	I'm in pain when going up and down stairs the steps. []	☐	☐
I find it hard to reach for things.	☐	☐	I wake up feeling depressed	☐	☐
I'm in pain when I walk.	☐	☐	I'm in pain when I'm sitting.	☐	☐

APPENDIX

Listed below are some activities, which may be affected by your state of health. Please tick "yes" for each activity that is being affected by your state of health. Tick "no" for each activity, which is not being affected, or does not apply.

Is your present state of health causing problems in your:

	YES	NO		YES	NO
Paid employment?	☐	☐	Home life (that is, relationships with other people in your home)	☐	☐
Looking after the home (examples, cleaning and cooking, repairs, odd jobs around the home and So on)?	☐	☐	Sexual relationships	☐	☐
Social relationships (examples, going out, seeing Friends, going to the pub and so on)?	☐	☐	Interests and hobbies (examples, sports, arts and crafts, "do it yourself" projects and so on)?	☐	☐
			Holidays?	☐	☐

APPENDIX

SELF RATING SCALE FOR PRE-MENSTURAL TENSION SYNDROME

Name: Date:/...../.....

Identification No:

Instructions

The following questions are concerned with the way you feel or act today (or the way you feel or acted during the week).

Please answer all questions by circling YES or NO as indicated.

- | | | | |
|-----|--|-----|----|
| 1. | Do you find yourself avoiding some of your social commitments? | YES | NO |
| 2. | Have you gained 5 or more pounds during the past week? | YES | NO |
| 3. | Is your coordination so poor that you are unable to use kitchen utensils, garden tools or unable to drive? | YES | NO |
| 4. | Do you feel more angry than usual? | YES | NO |
| 5. | Do you avoid family activities and prefer to be left alone? | YES | NO |
| 6. | Do you doubt your judgement or feel that you are prone to hasty decisions? | YES | NO |
| | NO | | |
| 7. | Do you feel more irritable than usual? | YES | NO |
| 8. | Is your efficiency diminished? | YES | NO |
| 9. | Do you feel tense and restless? | YES | NO |
| 10. | Do you feel a marked change in your sexual drive or desire during the last week? | YES | NO |
| | If YES, is it <i>increased</i> [] or <i>decreased</i> [] | | |
| 11. | Are your present physical symptoms causing so much pain and discomfort that you are unable to function? | YES | NO |
| 12. | Have you recently cancelled previously scheduled social activities? | YES | NO |
| 13. | Do you feel as if you were unable to relax at all? | YES | NO |
| 14. | Do you feel confused? | YES | NO |
| 15. | Do you suffer from painful or tender breasts? | YES | NO |
| 16. | Do you have an increased desire for specific kinds of foods (eg. cravings for candy, chocolate, etc.)? | YES | NO |
| 17. | Do you scream/ yell at family members (friends, colleagues) more than usual? Are you "short fused"? | YES | NO |
| 18. | Do you feel sad, gloomy, and hopeless most of the time? | YES | NO |

APPENDIX

SELF RATING SCALE FOR PRE-MENSTRUAL TENSION SYNDROME (cont'd)

19.	Do you feel like crying?	YES	NO
20.	Do you have difficulty completing your daily household /job routine?	YES	NO
21.	Was there a marked change in your sexual drive with definitive change in your sexual behaviour during the last week?	YES	NO
27.	Do you find yourself being more forgetful than usual or unable to concentrate?	YES	NO
23.	Do you happen to have more "accidents" with your daily housework /job (cut fingers, break dishes, etc)?	YES	NO
24.	Have you noticed significant swelling of your breasts and/or ankles and /or bloating or your abdomen?	YES	NO
25.	Does your mood change suddenly without obvious reason?	YES	NO
26.	Are you easily distracted?	YES	NO
27.	Do you think that your restless behaviour is noticeable by others?	YES	NO
28.	Are you clumsier than usual?	YES	NO
29.	Are you obviously negative and hostile towards other people?	YES	NO
30.	Are you so fatigued that it interferes with your usual level of functioning?	YES	NO
31.	Do you tend to eat more than usual or at odd irregular hours (sweets, snacks, etc)?	YES	NO
32.	Do you become more easily fatigued than usual?	YES	NO
33.	Is your handwriting different (less neat than usual)?	YES	NO
34.	Do you feel jittery or upset?	YES	NO
35.	Do you feel sad or blue?	YES	NO
36.	Have you stopped calling or visiting some of your best friends?	YES	NO

Changes in nutrient intake during the menstrual cycle of overweight women with premenstrual syndrome

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This study presents the nutrient data collected from women who were being screened for premenstrual syndrome (PMS) for entry into an intervention study. Screening was by the Steiner self-rated questionnaire. One hundred and forty-four overweight women completed the screening process and eighty-eight met the criteria for PMS. All women kept 4 d diet diaries pre- and postmenstrually over two menstrual cycles. The mean energy and macronutrient intakes were compared between the pre- and postmenstrual phases. Energy and macronutrient intake was also calculated according to food categories. Goldberg's cut-off limit for the ratio of energy intake to estimated basal metabolic rate was used to exclude data that was incompatible with predicted energy requirements. The diet diaries were also used to determine the mean number of meals or snacks eaten pre- and postmenstrually. Nutrient analysis of the diet diaries of the women with PMS showed a significant increase ($P < 0.001$) in total energy and all macronutrients premenstrually when compared to nutrient intake postmenstrually. Women who did not meet the criteria for PMS showed a significant increase in energy and fat intake ($P < 0.05$) but not in the other macronutrients. When adjusted for energy, data collected from women with PMS showed a premenstrual significant increase in fat, carbohydrate ($P < 0.05$) and simple sugars ($P < 0.001$). There was a significant decrease ($P < 0.001$) in protein premenstrually. Women not meeting the PMS criteria showed no significant difference between pre- and postmenstrual intakes when adjusted for energy. Analysis according to food categories in women with PMS showed a significantly greater intake premenstrually of energy and all macronutrients for cereals, cakes and desserts and high-sugar foods ($P < 0.001$). In women with PMS there was a significantly greater number of 'episodes of eating' premenstrually ($P < 0.001$). This study provides further evidence, to support the very limited number of earlier studies, that there is a group of women with PMS who increase their nutrient intake during the premenstrual phase. This could potentially be a contributing factor for some women experiencing difficulties adhering to suggested dietary modification and should be considered when counselling premenopausal women.

Premenstrual syndrome: Overweight women: Macronutrient and energy intake

Premenstrual syndrome (PMS) is a group of symptoms of varying degrees of severity, which occurs during the late luteal phase of the menstrual cycle. It is characterised by somatic, appetitive and behavioural changes. These symptoms occur in the week prior to menstruation and cease to be present within a few days of the onset of menses (American Psychiatric Association, 1994). Women have also been reported to have more accidents, suicide attempts and psychiatric admissions premenstrually (Dalton, 1960; Reid, 1986).

Energy and macronutrient intake over the menstrual cycle has been investigated in women with and without

premenstrual syndrome. Studies in women without PMS are inconsistent in their findings. They have reported increases of one or more macronutrients as well as total energy intake during the luteal phase of the menstrual cycle (Dalvit-McPhillips, 1983; Manocha *et al.* 1986; Lissner *et al.* 1988; Gong *et al.* 1989; Martini *et al.* 1994; Barr *et al.* 1995). In a recent review by Dye & Blundell (1997) of thirty studies in thirty-seven groups of women, most of these studies (twenty-five) found energy intake to be increased during the premenstrual phase. The remaining studies detected no significant change and two studies reported a greater energy intake during the postmenstrual

Abbreviation: PMS, premenstrual syndrome.

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phase in women without premenstrual symptoms. This variability in findings may be attributed to the differences in methodology used in obtaining food intake data as well as the selection of the study groups.

The findings with regard to specific changes in macronutrient intakes in women without premenstrual symptoms have been less consistent. Premenstrual increases in one or more macronutrients have been reported. For example, increases in carbohydrate (Dalvit-McPhillips 1983; Johnson *et al.* 1995; Martini 1994) and fat (Tarasuk & Beaton, 1991) have been found premenstrually.

Studies investigating appetite and macronutrient and energy intake in women with PMS are few in the reported literature. Both-Orthman *et al.* (1988), using a daily questionnaire to measure appetite and mood over a period of 2 to 9 months, showed a significant increase in appetite in both women with PMS and controls. However, the effect was greater in women with PMS and this correlated with self-rating of mood.

Wurtman *et al.* found a significant increase in carbohydrate intake in women with PMS premenstrually (Wurtman *et al.* 1989). In this study nineteen women with PMS and nine controls were admitted as inpatients, and their food consumption was monitored for 48 h both premenstrually and postmenstrually. Both the meals and snacks available to the subjects had either a high or low carbohydrate content.

This paper reports the baseline energy and macronutrient data obtained during the screening of overweight women for PMS as part of a double-blind placebo-controlled study. The study investigated whether enhancing serotonin neurotransmission with dexfenfluramine alleviated PMS symptoms, including reducing carbohydrate intake premenstrually in overweight women. The study presented the opportunity to collect dietary data in women during the screening process and the study in detail. The data presented here includes macronutrient and total energy intake from all women completing the screening process, including those women who did not meet the criteria for entry into the above-mentioned study. This paper adds to the very limited dietary data available in this group of women. It also presents nutrient analysis in terms of food categories, which has not been previously reported in free-living women with PMS.

Methods

Subject selection and study entry criteria

Women recruited from poster and newspaper advertisements were screened for entry into the dexfenfluramine study. Participation was voluntary and no financial incentive was given. This study was approved by the Committee on the Ethics of Human Experimentation at the University of Adelaide.

Three hundred and thirteen women who met the initial criteria for entry into the screening process were screened over two menstrual cycles. One hundred and forty-four of these women completed the screening process. Eighty-eight women met the criteria for PMS and fifty-six did not.

All volunteers were required to have regular menstrual

cycles, not be taking an oral contraceptive and have a BMI 24–37 kg/m² (to comply with the product licence of dexfenfluramine), be of a stable weight and not be on any type of special diet. They were excluded from entry into the screening process if there was a history of psychiatric problems, a history of eating disorders, suffered from medical conditions, including diabetes, renal or hepatic diseases, or were taking medication that could interact with the drug used in the study.

As part of the screening process all women completed the Steiner self-rated PMS questionnaire (Steiner *et al.* 1980). Women were identified as experiencing PMS when the difference between the pre- and postmenstrual scores for the Steiner self-rated PMS scale was greater than 10. Women also completed the Nottingham Health Profile (Hunt *et al.* 1981) and completed diet diaries for 4 d during both the premenstrual and postmenstrual phases in each cycle.

Nutritional data

All women with and without PMS kept diet diaries across two menstrual cycles. Initial diaries were commenced postmenstrually on day 5 after menstruation began. Some women also completed diaries for an additional cycle. Diet diaries were recommenced 4 d prior to the predicted onset of menses and on day 5 after the onset of menses for 4 d over one menstrual cycle. If menses did not occur on the predicted day, subjects were instructed to continue recording their food intake until it occurred. In these cases, the food intake for 4 d prior to menses was analysed. In cases where menses occurred early, subjects continued with the screening process for another cycle (sixteen women completed a third cycle). The mean energy and macronutrients were calculated for the premenstrual (late luteal) and postmenstrual (follicular) phases. As an indication of the reliability and level of possible under reporting the recorded energy intake-BMR was calculated. Cases were excluded based on Goldberg's *et al.* (1991) cut-off limits for this ratio (1.06 for records of 4 d). This resulted in six women meeting the PMS criteria being excluded and sixteen from the group not meeting the criteria. Consistency over the two cycles was checked using statistical methods (*t* test).

Previous studies showed that keeping dietary records for 4 d (Basiotis, 1987; Potoska *et al.* 1990) was the appropriate time. The timing of when the diet diaries were kept was based on studies from the literature, which showed that premenstrual symptoms worsened several days prior to the onset of menstruation and had ceased by day 5 from the commencement of menstruation. At the first visit prior to the commencement of screening, weight, height and hip-waist ratios were measured in all women.

All subjects were interviewed and instructed on how and when to fill out the diet diaries. They were requested to continue with their usual diet. Detailed instructions on recording the quantities eaten were given including the use of household metric measures. When composite dishes were eaten, participants were requested to record the recipes used. If eating out, subjects were asked to identify the type of place the food was purchased from and

Table 1. Description of food categories used in nutrient analysis

Food category	Foods included
Cereal products	Breakfast cereals, bread, pasta, rice, dry biscuits
Cakes and desserts	Cakes, buns, sweet biscuits, ice cream, Custard, commercial desserts, Sweet yoghurt (sweetened with sugar or artificial sweetener)
Dairy products	Milk, cheese, unsweetened yoghurt
Fats	Oil, margarine, butter, cream
Composite foods	All meats including processed meats, sausages, chicken, turkey, fish and other mixed meat and vegetable dishes, Vegemite and savoury spreads
Vegetables	All vegetables, fresh, dried and frozen
Fruit	All fresh, tinned, frozen and dried fruit
High-sugar foods	Confectionery, jams, honey, sugar added to cereal and drinks, sweet drink additives, non-dairy iceblocks
Snack foods	Potato crisps, corn chips, extruded snacks, nuts
Beverages	Soft drinks, cordials, fruit juices, fruit juice drinks, flavoured milks, hot chocolate and related drinks, alcoholic beverages

instructed on how to describe the foods and quantities eaten. Diaries were requested to be returned as soon as possible after their completion. Upon return of the diaries, they were checked through and clarified over the phone with the individual subject. Nutritional analyses of the diaries were performed using Diet3 version 4.22 (Xyris Software Pty Ltd, Highgate Hill, Queensland, Australia), with additions to the database obtained from food companies where appropriate. Where quantities were not specified standard portion sizes were used. For each subject, the mean energy and macronutrient intake over the 4 d was calculated for the premenstrual and postmenstrual phases.

The diet diaries were also used to record the number of episodes of eating a meal or a snack over each 4 d interval. 'Episodes of eating' was used due to the differences in the dietary habits in the women and the difficulty in separating snacks from main meals for some women. This enabled a comparison to be made between the two periods, of the number of episodes when food was eaten.

For women with PMS, the nutrient data were also analysed according to food categories. The foods were categorised into groups based, with some modification, on the Australian National Nutrition Survey held in 1995 and Magarey & Boulton (1995). Foods were grouped under the food categories shown in Table 1.

The mean kJ and macronutrients were analysed for each group using the original data. The nutrient data for each food category were also calculated in terms of the percent of total kilojoules, protein, fat, carbohydrate, simple sugars and complex carbohydrates.

Statistical analysis

Statistical analyses were performed using Stata 5.0 (Stata Corporation, 702 University Drive East, College Station, TX, 77840 USA). Paired *t* tests (for normally distributed data) and Wilcoxon sign rank test (non-normal data) were used to compare whether there was a significant difference in energy and macronutrient intake between the premenstrual and postmenstrual phases. Macronutrient intake was also calculated as percent of energy. Spearman's correlation coefficient was used to identify whether there was a

relationship between the severity of PMS symptoms as measured by the Steiner self-rated scores (using total scores) and changes in nutrient and total energy intake.

Results

The eighty-two women identified with PMS had a mean age of 37.2 (SD 5.2) years and a mean BMI of 29 (SD 3.6) kg/m². The mean length of the menstrual cycle was 28 d with a range of 23–38 d. The forty women without PMS had a mean age of 37.2 (SD 6.9) years, a mean BMI of 29.2 (SD 3.1) kg/m². The mean length of the menstrual cycle was 27 d with a range of 23–36 d. There were no great differences between women with and without PMS with regard to age, BMI and length of menstrual cycle.

For women with PMS, the premenstrual median score of the Steiner self-rated questionnaire was 25.5 (range 13.7–34) compared to a median postmenstrual score of 2 (range 0–14.6). In the women who did not meet the criteria for entry into the study, the premenstrual median score of the Steiner self-rated questionnaire was 23 (range 8–34) compared to a median postmenstrual score of 4 (range 0–29).

Table 2 presents the baseline nutritional data for the women who completed the screening process. For the group of women who were identified to be suffering from PMS, there was a statistically significant ($P < 0.001$) greater nutrient intake premenstrually compared with the postmenstrual intake for each nutrient, as well as total intake. In comparison, for women without PMS there were no significant differences between the premenstrual and postmenstrual phases for all nutrients except fat and total energy ($P < 0.05$).

In the eighty-two women with PMS, adjustment of macronutrient intake as a percentage of total energy intake showed significant increases in the percentage of carbohydrate fat ($P < 0.05$), and simple sugar ($P < 0.001$). There was a significant decrease in the percent of protein ($P < 0.001$) in the premenstrual phase as compared with this group's postmenstrual data (Table 3). For complex carbohydrate there was also a decrease premenstrually but this was not significant ($P 0.07$). In the forty women

Table 2. The mean (over 4 d) pre- and postmenstrual energy, macronutrient intake and percentage change for each nutrient for women with and without PMS

(Values are means and their standard deviations)

	Carbohydrate (g)	SD	Complex carbohydrate (g)	SD	Simple sugars (g)	SD	Protein (g)	SD	Fat (g)	SD	Energy (g)	SD
Women with PMS (<i>n</i> 82)												
Premenstrual	245	50.1	131	31	113	40.5	78.7	17.6	81.6	23.5	8648	1727
Postmenstrual	167	36.3	95.9	23.5	71	23.5	65.6	16	53.6	15	6048	1268
Percentage change*	32†		26.8†		37.2†		16.6†		34†		30†	
Women without PMS (<i>n</i> 40)												
Premenstrual	220	50	118	29.7	101	35	74.5	15.3	74.2	21	7895	1347
Postmenstrual	211	53	116	32	94.5	32	71.5	17	67	21	7433	1697
Percentage change	4.1		0.9		6.4		4.0		9.7‡		5.8‡	

PMS, premenstrual syndrome.

* Percentage change between premenstrual and postmenstrual nutrient analysis.

† $P < 0.001$ (paired *t* test).‡ $P < 0.05$.

without PMS, adjustment for energy showed no significant difference between premenstrual and postmenstrual macronutrient intakes.

Tables 4–6 display the mean energy and macronutrient intake analysed, according to food categories, for women with PMS. The kilojoules (Table 4) from all food categories except for the fruit, vegetable and milk categories were significantly greater ($P < 0.001$) premenstrually compared to postmenstrually. The absolute protein, fat, carbohydrate and complex carbohydrate was significantly higher premenstrually than postmenstrually for the cereal, cakes and desserts and the high sugar foods categories ($P < 0.001$; Tables 5 and 6). Composite savoury dishes ($P < 0.001$), drinks ($P < 0.001$) and savoury snacks ($P < 0.05$) contributed more carbohydrate premenstrually (Table 6).

Analysis of the data as the percentage of the total energy and macronutrients that each food category provided is also shown in Tables 4–6. The food categories 'cakes and desserts' and 'high-sugar foods' contributed a higher percentage for all macronutrients and energy premenstrually. When grouped together, these two food categories provided 26.38 % of the total kilojoules premenstrually compared with 15.9 % postmenstrually. They also contributed 27.6 % of the total fat premenstrually, 31.6 % of the total carbohydrate, 15.8 % of the total complex

carbohydrate and 49.6 % total simple sugars compared to 15.8 % total fat, 20.8 % total carbohydrate, 10.1 % of the total complex carbohydrate and 35.2 % simple sugars, postmenstrually. The remaining food groups either contributed a greater percentage postmenstrually or showed no great difference between the two phases.

For women with PMS symptoms the mean number of times per day they consumed food was 5.5 (SD 1.2) premenstrually compared to 4.2 (SD 0.98) postmenstrually. Paired *t* test showed a significant difference ($P < 0.001$). There was no difference for women without PMS.

Spearman's correlation coefficient was used to identify whether there was a relationship between the severity of PMS symptoms, as measured by the Steiner self-rated PMS scale and the change observed in the unadjusted nutrient intake. When Spearman's correlation coefficient was calculated for all subjects (those with and without PMS), there was a weak correlation (Spearman's ρ 0.34, $P < 0.001$, 120 degrees of freedom; d.f.) for carbohydrate. For complex carbohydrate Spearman's ρ 0.29, $P < 0.05$ and simple sugars Spearman's ρ 0, $P < 0.05$. There was also a weak correlation between the change in fat intake and total energy intake with regard to change in PMS score. This was 0.27 ($P < 0.05$) and 0.32 ($P < 0.05$) respectively. The correlation for protein was very weak (Spearman's ρ 0.19, $P < 0.05$). For women with PMS, Spearman's correlation

Table 3. Macronutrient intake for eighty-two women with PMS expressed as percent of total energy intake and for forty women without PMS

(Values are means and their standard deviations)

Macronutrient	Premenstrual % of energy	SD	Postmenstrual % of energy	SD	Significance
Women with PMS					
Carbohydrate	45.58	5.0	44.57		$P < 0.05$
Fat	34.6	4.8	32.61	4.6	$P < 0.05$
Protein	15.66	2.9	18.54	3.2	$P < 0.001$
Simple sugars	20.94	5.8	18.94	5.2	$P < 0.001$
Complex carbohydrates	24.64	5.1	25.58	4.7	$P = 0.067$
Women without PMS					
Carbohydrate	44.32	7.1	45.34	6.5	$P = 0.34$
Fat	35.0	6.6	33.24	5.4	$P = 0.13$
Protein	16.09	2.6	16.59	2.8	$P = 0.28$
Simple sugars	20.1	4.8	20.04	6.6	$P = 0.93$
Complex carbohydrates	23.98	6.1	25.23	5.5	$P = 0.08$

PMS, premenstrual syndrome.

Table 4. The mean energy and percentage intake for each food category for premenstrual and postmenstrual phases for eighty-two women with PMS

Food type	Premenstrual (kJ)	Total nutrients (%)	Postmenstrual (kJ)	Total nutrients (%)
Cereal	1745*†	20.62†‡	1393	23.3
Milk	701	8.3*†	656	10.89
Composite savoury dishes	1797*†	20.8†‡	1454	24.1
Vegetables	482	5.62*†	432	7.19
Fruit	213	2.58*§	227	4.02
Fat	376†§	4.27	276	4.5
Cake and desserts	1327*†	15.02*†	648	10.46
High-sugar foods	995*§	11.24*§	332	5.47
Drinks	588*†	6.67	420	6.76
Savoury snacks	316†§	3.6	175	2.71

PMS, premenstrual syndrome.

* $P < 0.001$.† $P < 0.05$.‡ Paired *t* test.

§ Wilcoxon sign rank test.

coefficient was weak (Spearman's ρ 0.26, $P < 0.05$, 80 d.f.) for carbohydrate. There was also a weak correlation between the change in fat intake and total energy intake with regard to change in PMS score. This was 0.27 ($P < 0.05$) and 0.29 ($P < 0.05$) respectively. Spearman's correlation coefficient for protein, simple sugars and complex carbohydrates were not significant. In women without PMS there were no great correlations between the Steiner self-rated PMS scale and energy and macronutrient intake.

Discussion

This study presents the energy and nutrient intake data, which has not been previously reported, of overweight

women with PMS. The data presented here support the very small number of reports found in the literature in women of normal weight with PMS, where there are increases in both energy and carbohydrate intakes during the premenstrual phase (Wurtman *et al.* 1989). This study also showed a significant increase (g) in both protein and fat. Adjustment for energy also showed a significant increase in total carbohydrate, as well as significant premenstrual increase in simple sugars and premenstrual decrease in complex carbohydrate. After adjustment for energy there was also an increase in fat premenstrually and a decrease in protein. Analysis of the data according to food categories helps to clarify these findings. For all the food categories except for 'milk', 'vegetables' and 'fruit', there was a significantly greater kJ intake premenstrually ($P < 0.001$). However

Table 5. The mean protein and fat and the percentage of the total protein and fat intake for each food category for premenstrual and postmenstrual phases of eighty-eight women with PMS

(Values are means and percentage intake)

Food type	Premenstrual (g)	Total nutrients (%)	Postmenstrual (g)	Total nutrients (%)
Protein				
Cereal	14.1*†	18.5	11.52	18.17
Milk	12.02	15.2	10.9	16.49
Composite savoury dishes	32.88†‡	40.84†‡	29.6	44.2
Vegetables	4.35	5.54	4.02	6.2
Fruit	0.79	1.08	0.78	1.32
Fat	0.16	0.2	0.11	0.18
Cake and desserts	6.3*†	8.12*†	3.53	5.41
High-sugar foods	2.99*§	4.03*§	0.88	1.39
Drinks	2.69	3.38†§	2.5	3.9
Savoury snacks	1.83†§	2.3	1.07	1.6
Fat				
Cereal	5.29*†	6.8	3.82	7.3
Milk	9.35	12.37†§	8.5	16.31
Composite savoury dishes	22.3*†	27.6*†	17.9	34.01
Vegetables	3.63	4.28†§	3.39	6.15
Fruit	0	0	0.03	0.1
Fat	10.03†§	12.07	7.25	13.47
Cake and desserts	14.7*†	16.4*†	6.23	11.6
High-sugar foods	9.6*§	11.2*§	2.31	4.2
Drinks	0.58	0.78	0.46	0.85
Savoury snacks	5.23†§	6.26	3.1	5.02

PMS, premenstrual syndrome.

* $P < 0.001$.† $P < 0.05$.‡ Paired *t* test.

§ Wilcoxon sign rank test.

Table 6. The mean carbohydrate, complex carbohydrate and simple sugars and the percentage of the total intake for each food category for premenstrual and postmenstrual phases for eighty-two women with PMS

(Values are means and percentages)

Food type	Premenstrual (g)	Total nutrients (%)	Postmenstrual (g)	Total nutrients (%)
Carbohydrate				
Cereal	78.0*†	32.26*†	62.15	37.2
Milk	9.82	4.04*§	9.81	5.74
Composite savoury dishes	24.14*†	9.99	16.88	10.24
Vegetables	15.54	6.49*§	13.66	8.29
Fruit	11.83	4.9*§	12.7	7.89
Fat	0.23	0.09	0.22	0.12
Cake and desserts	43.19*†	17.24*†	21.61	12.4
High-sugar foods	36.33*§	14.37*§	14.28	8.39
Drinks	18.85*§	7.6	11.88	7.07
Savoury snacks	5.76†§	2.49	2.66	1.64
Simple sugars				
Cereal	6.42†§	5.99†§	4.9	6.9
Milk	9.55	8.9*§	9.61	13.4
Composite savoury dishes	4.55	4.25	3.21	4.92
Vegetables	3.69	3.6*§	3.64	5.46
Fruit	10.69	10.35*†	11.62	17.17
Fat	0.22	0.19	0.15	0.2
Cake and desserts	24.78*§	22.01†	12.52	17.16
High-sugar foods	35.98*§	27.63*§	13.35	18.15
Drinks	18.06*§	15.3	11.36	15.14
Savoury snacks	0.49	0.52	0.37	0.51
Complex carbohydrates				
Cereal	71.86*†	54.13†	57.32	59.42
Milk	0.27	0.2	0.20	0.20
Composite savoury dishes	19.47*†	14.61	14.06	15
Vegetables	11.77†	9.56	9.6	10.5
Fruit	0.99	0.81	0.89	1.06
Fat	0.01	0.01	0.003	0.003
Cake and desserts	18.51*†	13.87*†	9.17	9.3
High-sugar foods	2.25*§	2.0*§	0.81	0.83
Drinks	0.77†§	0.6	0.50	0.54
Savoury snacks	5.31†§	3.99	2.3	2.43

PMS, premenstrual syndrome.

* $P < 0.001$.† $P < 0.05$.‡ Paired *t* test.

§ Wilcoxon sign rank test.

when analysed in terms of the percentage that each group contributed to the total kilojoule intake, the 'cake and dessert' and 'high-sugar foods' contributed a higher percentage premenstrually, while the other groups either contributed more postmenstrually or there was little difference between the two phases. This was reflected in the analysis of the macronutrients, where there was a greater percentage contribution premenstrually from these two groups. These findings show that there is a preference for sweet high-carbohydrate, high-fat foods in this group of women. They support other findings in women with and without PMS.

Previously reported studies in women, both with and without PMS, have shown increases in energy and macronutrient intake during the premenstrual compared to the postmenstrual phase. However, although many studies have shown increased total energy intake, there is a lack of consistency when macronutrients are analysed. Lissner *et al.* (1988) found in a group of normal weight women without PMS that their mean daily energy intake was 364 kJ higher during the 10 d premenstrually compared to 10 d postmenstrually. Tarasuk & Beaton (1991) retrospectively demonstrated an increase in energy, fat and fat/

1000 Kcal premenstrually but no difference in protein or carbohydrate in women without PMS.

In the few studies of women with PMS, increases in appetite and food intake, in particular foods high in carbohydrates, have been reported during the late luteal phase (Both-Orthman *et al.* 1988). Wurtman *et al.* (1989) monitored the food intake of nineteen women with PMS and nine controls for 48 h pre- and postmenstrually in an inpatient setting. In women with PMS during the late luteal phase there was a 24 and 43 % increase in carbohydrate intake at main meals and snacks respectively. There was no change in protein intake and fat intake rose in proportion to total energy intake. No change in food intake was seen in the control group. In contrast, our study in free-living women showed significant increases in energy and all macronutrients, including protein, in women with PMS. This difference may be due to our study design. In Wurtman *et al.*'s (1989) study, main meals and snacks provided were either high in carbohydrate or protein. In this current study subjects were free living with *ad libitum* food choices. As many foods contain a combination of macronutrients, it is difficult to demonstrate a preference for a specific nutrient. Another reason may be that there is

not a specific preference for craving for carbohydrate, but rather a desire for pleasant tasting sweet high-fat foods as suggested by Hill & Heaton-Brown (1994).

One of the main hypotheses for increased food intake in women with PMS is that these women have low brain serotonin levels premenstrually. Carbohydrate consumption can influence brain serotonin levels by increasing the ratio of tryptophan:large amino acids. Tryptophan, the precursor of serotonin, competes with large amino acids for entry into the brain. Both animal and human studies support the hypothesis that low levels of brain serotonin may play a role in PMS, including increasing carbohydrate intake. Measurement of total blood serotonin, which is believed to reflect brain levels, during the last 10 d of the menstrual cycle, was found to be lower in women with PMS compared to controls (Rapkin *et al.* 1987). A high-carbohydrate meal in comparison to a high-protein meal results in elevated blood tryptophan, which is a precursor of serotonin and can cross the blood-brain barrier. It has been proposed that the observed increase in carbohydrate is an attempt to elevate brain serotonin levels in order to improve mood. A pilot study in women with PMS given L-tryptophan (6 g/d) orally showed a reduction in PMS symptoms (Steinberg *et al.* 1994).

Craving of foods also occurs in women without PMS and conditions such as obesity, bulimia nervosa and seasonal affective disorder. 'Carbohydrate craving', a term used to describe a preference for carbohydrate-containing foods has also been reported in some obese individuals (Lieberman *et al.* 1986) and those with seasonal affective disorder (Rosenthal *et al.* 1989). It has been proposed that carbohydrate craving in obese subjects may be related to reduced brain serotonin levels. This has been supported indirectly by the measurement of 5-hydroxytryptamine, a precursor of serotonin, in platelet-poor plasma (Blum *et al.* 1993). Obese individuals of both sexes and lean males who craved carbohydrate-containing foods had lower plasma 5-hydroxytryptamine compared to lean individuals who were not carbohydrate cravers.

Fernstrom (1994) in a review of dietary amino acids and brain function argues that 'carbohydrate cravers' as a subtype of obese individuals are likely not to exist. These individuals tend to have a preference for high-fat and high-carbohydrate snacks such as chocolate bars. These snacks also have sufficient quantities of protein to prevent a rise in brain tryptophan and therefore serotonin. He suggests that if there were a drive to consume carbohydrate then all carbohydrate foods would be equally craved, which is not the case. Fernstrom theorises that it is the natural human preference for sweet high-fat foods that leads to the choice of these foods.

Other work investigating food cravings in women supports the likelihood that the desire for certain foods is not solely biological, but that psychological factors play an important role. Also, food craving seems to be fairly widespread in the general population. Weingarten & Elston (1991) retrospectively found that in 758 female and 380 male Canadian college undergraduate students, 97 % of the female and 68 % of the male students reported experiencing food cravings. Chocolate was the most frequently craved food among women and they craved it more

frequently than men. In women there also appeared to be more specific triggers (e.g. TV commercials, stress or boredom) compared to men, who most often craved foods as a response to hunger. Hill & Heaton-Brown (1994) report similar findings in a group of twenty-five healthy women over a 5-week period. They found that 49 % of the reported cravings were for chocolate or chocolate-containing foods, 16 % for sweet foods and 12 % for savoury foods. Other foods were much less frequently craved. When relating this to the menstrual cycle, they found an increase in the cravings of food premenstrually. However, there was no selective craving of one food over another and it was concluded, given the mixed macronutrient content of these foods, that the subjects were not carbohydrate cravers.

Our data provide evidence that there is a premenstrual increase in energy and nutrient intake in overweight women with PMS symptoms. The preference for 'sweet foods' that are high in carbohydrate, fat and also contain some protein supports the available literature, that this is not specifically 'carbohydrate craving'. It also presents data, not previously documented, on the frequency of food consumption in women with PMS. This premenstrual increase has implications for women who are experiencing PMS symptoms and trying to lose weight. Increased appetite and difficulty in coping with this may decrease successful longer-term changes in dietary behaviour. Recognition that this could be a contributing factor in individual women is an important consideration during dietary counselling.

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