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DEPARTMENT OF PHYSIOLOGY

UNIVERSITY OF THE WITWATERSRAND

JOHANNESBURG, SOUTH AFRICA

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# Very low energy diets: effects on selected physiological, psychological and sleep measures.

**Amanda Karklin**

A dissertation submitted to the Faculty of Science, University of the Witwatersrand, Johannesburg for the degree of Master of Science.

February 1995

## ABSTRACT

In this dissertation I examine the effects of a long term (one month) and a short term (two week) very low energy diet of 3347 kJ/d (800 kcal/d) on body weight, body composition, cardiac function, nutritional and hormonal status, psychological variables and sleep and temperature variables. In both investigations, data were collected 28 days apart to control for menstrual cycle differences.

In the month long study, nine normal to overweight (weight 71.2 ± 8.0 kg; body mass index 26.1 ± 2.8 kg/m$^2$), premenopausal women (aged 20-36 years) were subjected to the diet regime. The women correctly reported their baseline energy intake and were likely to have correctly reported dietary intake. The women reduced their energy intake by 6130 ± 1650 kJ/d and after a month had lost 8 ± 4% of their initial body mass (1.45 kg/w). Percentage fat and body mass index measurements were reduced by between 6 and 15% depending on the measurement technique used. The women were not malnourished, despite the severity of the diet, as serum glucose, albumin and triglyceride concentrations were unaltered. In the final two weeks of dieting total cholesterol concentration was reduced (from 5.25 ± 0.41 to 4.28 ± 0.59 mmol/L), LDL concentration declined (from 3.34 ± 0.52 to 2.59 ± 0.47 mmol/L) and HDL concentration fell significantly (from 1.39 ± 0.26 to 1.16 ± 0.25 mmol/L). Additional reductions in systolic blood pressure (from 111 ± 4 to 105 ± 6 mmHg) and heart rate (from 66 ± 6 to 61 ± 4 beats/minute) were noted with energy restriction. Although the women reported a lack of vigour and heightened fatigue with dieting, no other psychological changes were noted after four weeks of energy restriction.

Serum $T_3$ was significantly reduced from 5.9 ± 0.7 to 5.1 ± 0.6 pmol/L after four

weeks of dieting, implying a concomitant suppression of metabolic rate. A decline in heat production, due to a reduction in metabolic rate, may be responsible for the slight but significant decrease in minimum nocturnal rectal temperature (from 36.5 ± 0.3 °C to 36.3 ± 0.3 °C) with dieting. Hormonal alterations and/or a hypometabolic state may be responsible for altered sleep variables such as the reduction in slow wave sleep and the prolonged time to fall asleep (due to decreased restorative requirements).

In the two week diet study, six normal to overweight (weight 72.27 ± 10.38 kg; BMI 26.8 ± 4.0 kg/m$^2$), premenopausal women (aged 21-25 years) were investigated. These women were shown to under-report dietary intake. Nevertheless, they showed a significant weight loss of 2.82 ± 0.72 kg, a significant increase in albumin concentration after a week of dieting (from 43.6 ± 2.4 to 46.1 ± 2.2 g/L), and significant reductions in HDL (from 1.40 ± 0.20 to 1.02 ± 0.13 mmol/L) and total cholesterol (from 5.60 ± 1.00 to 4.70 ± 0.73 mmol/L) after two weeks of energy restriction. Unlike the results achieved in the month long study, cardiac function, hormone concentrations, mood, performance, temperature and sleep variables were unaltered.

Irrespective of the degree of energy restriction achieved, there are a number of physiological changes (short term changes) that occur within the first two weeks of dieting. Alterations in cardiac function, hormone concentrations, performance, sleep and temperature measures may be associated with long term (more than two weeks) energy restriction. Previously unreported changes in sleep patterns, minimum nocturnal rectal temperature and performance are important findings in light of the popularity of energy restriction diets among non-obese individuals.

## DECLARATION

I declare that this dissertation is my own work. All assistance has been acknowledged. This dissertation is being submitted for the degree of Master of Science in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination in any other University, nor has it been prepared with the assistance of any other body, organisation or person outside the University of the Witwatersrand.



31 day of December, 1994.

**"... that which we are, we are,**

**one equal temper of heroic hearts**

**made weak by time and fate,**

**but strong in will**

**to strive, to seek, to find...**

**and not to yield."**

Alfred Lord Tennyson (1809-1892), *Ulysses*.

## ACKNOWLEDGMENTS

Firstly, I would like to thank my supervisors Drs Rochelle Buffenstein and Helen Driver for their patience and support. They were both intimately involved in this research and when hundreds of miles away, both continued to offer advise and invaluable knowledge.

I cannot adequately express my appreciation for my family's unwavering tolerance, understanding and encouragement- Thank you all.

To Dr David Fine " Thou wert my guide, philosopher, and friend ".

*Alexander Pope*

Not to mention formatter and proof reader.

Many thanks go to Professor Duncan Mitchell for always making time to share his wisdom and to offer statistical advise.

Thanks to Sheila Taylor and all those who spent many sleepless nights in the laboratory, to all the subjects who participated in this study, to Dr Barry Jacobson and Fiki Makhaye for taking bloods so early in the morning and to all the staff and students of the Department of Physiology, University of the Witwatersrand for their support.

Financial support from Edblo (Pty) Ltd. and the Foundation for Research and Development and the University of the Witwatersrand is greatly appreciated.

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# LIST OF ABBREVIATIONS

| | |
|---|---|
| A + M | Awake and movement time |
| B | Baseline |
| BIA | Bioelectrical impedance analysis |
| BMI | Body mass index |
| BMR | Basal metabolic rate |
| D | Diet |
| E | Energy expenditue |
| EEG | Electroencephalograph |
| EI | Energy intake |
| EMG | Electromyograph |
| EOG | Electro-oculograph |
| HDL | High density lipoprotein |
| LDL | Low density lipoprotein |
| LBM | Lean body mass |
| non-REM | non-rapid eye movement sleep |
| PAL | Physical activity level |
| POMS | Profile of mood states |
| REM | Rapid eye movement |
| ROL | Rem onset latency |
| SM | Skinfold measurements |
| SOL | Sleep onset latency |
| SWS | Slow wave sleep |
| SWS ratio | (Slow wave sleep time in the first sleep cycle)/(slow wave sleep |

| | |
|---|---|
| | time in the second sleep cycle) |
| TEE | Total energy expenditure |
| $T_3$ | Triiodothyronine |
| $T_{re}$ | Nocturnal rectal temperature (°C) |
| ΔLBM:ΔBM | Change in lean body mass:change in body mass |

## PUBLISHED DISSERTATION MATERIAL

**Paper**

Karklin A., Driver H.S. and Buffenstein R. (1994) Restricted energy intake affects nocturnal body temperature and sleep patterns. American Journal of Clinical Nutrition 59: 346-349.

**Abstracts**

Karklin A, Driver H.S. and Buffenstein R. (1993). A very low energy diet affects body temperature and sleep. Proceedings of the XXIII International Congress of Physiological Sciences.

Karklin A., Buffenstein R. and Driver H.S. (1994) Diet induced hormonal changes: effects on mood, performance and sleep. Proceedings of the 22nd Annual Congress. Physiology Society of South Africa.

Driver H.S., Karklin A. and Buffenstein R. (1994) A month long restricted energy intake results in altered sleep patterns and nocturnal body temperature in women. First Swiss Poster Meeting on Basic and Clinical Neuroscience.

# CHAPTER 1

## 1 A review of the effects of energy restriction (specifically very low energy diets) on physiological, psychological and sleep variables.

### 1.1) Obesity

Weight balance is constrained by the laws of thermodynamics within which all exchanges of energy in living matter operate. The chief factor determining body weight is the size of the energy store in the form of fat, mainly in adipose tissue. This energy store is determined by the relationship between energy input and output. Obesity, which is the most prevalent nutritional disorder in prosperous communities, is a state in which an excess of fat has accumulated due to a positive energy balance (Passmore and Eastwood, 1986). The degree of overweight or obesity is generally classified using body mass index (BMI) and a BMI of over 30 $kg/m^2$ is almost always synonymous with obesity (Bray, 1992).

Obesity is a complex, multifactorial disease associated with an increased mortality and with many medical complications (Atkinson, 1993; Bray, 1992). Obesity is an important risk factor for hypertension, hyperlipidaemia, coronary heart disease, gallbladder disease and sleep apnoea (the cessation of breathing during sleep) (Atkinson, 1993; Bray, 1992). Furthermore, weight gain enhances insulin resistance and obesity is thus an important risk factor for non-insulin dependant diabetes mellitus (Bray, 1992). There is strong evidence that individuals with a BMI of $>$ 29 are at a higher risk of disability and mortality (Kopelman *et al*, 1994). The morbidity and mortality related to moderate degrees of obesity (BMI 25 to 29) is less certain (Kopelman *et al*, 1994). There is however convincing data to suggest that individuals with moderate, upper body obesity are at risk

form coronary artery and cerebrovascular disease (Kopelman *et al*, 1994).

Since obesity is a risk factor for so many diseases the need to identify the predictors of obesity and the causes of the disorder is obvious and numerous investigators have examined these issues. It is generally accepted that obesity has a strong genetic component (Ferrell, 1993) which means that individuals with a genetically-determined predisposition become obese when exposed to a particular set of environmental conditions (Astrup, 1994). Astrup (1994) identified dietary fat as an important environmental factor and proposed that obese subjects consume a diet with a higher fat energy percentage than non-obese individuals. It is suggested that the selection of a fat-rich diet is caused by a sensory-specific preference for high fat foods (Astrup, 1994). Likewise, Prentice *et al* (1989) speculate that the etiology of obesity lies in the control of food intake or fat balance as opposed to the theory of a metabolic or behavioural defect in energy expenditure, which has dominated obesity research for many years. Contrary to previous findings Prentice *et al* (1989) noted that when body weight is corrected for, basal metabolic rate and energy expenditure (measured using whole body calorimetry and doubly-labelled water) are very similar in obese and lean subjects. Furthermore, these authors showed that obese subjects are not slothful and inactive as previously thought, but they are shown to under-report food intake and are likely to be hyperphagic in comparison to lean controls (Prentice *et al*, 1989). The importance of appetite defects as opposed to metabolic or behavioural defects in the development of some forms of obesity is therefore emphasised (Prentice *et al*, 1989).

Due to the risks associated with obesity, investigations in to the treatment modalities for obesity are numerous. The principal approaches to obesity treatment include the use of

pharmacological agents that act primarily by modifying hunger and food intake, surgical procedures such as gastroplasty, behaviour modification used to alleviate associated problems of obesity such as poor self-esteem, exercise and diet (Kopelman, 1994). It has been shown that in order to produce long term weight losses a combination of treatments should be used (Kopelman, 1994; Wadden 1993), however the creation of a negative energy balance is essential for weight loss and consequently diet therapy has become the most important treatment used in combating obesity.

## 1.2 Energy restriction

Since the restriction of energy input may be accomplished in numerous ways, a wide variety of diets have become available to the weight conscious individual. Over the past six decades numerous diet philosophies have materialised. In 1953 Dr Alfred Pennington advocated that if a person eliminated carbohydrates from the diet, they could eat as much fat and protein as they liked and they would still lose weight (Llewellyn-Jones, 1993). This theory resulted in the emergence of a number of low carbohydrate diets such as the Scarsdale Diet and the Dr Atkins's diet (Llewellyn-Jones, 1993). In the late 1970's Dr Pritkin revolutionized diet theory by eliminating fats from the diet and by emphasising the importance of complex carbohydrates. Since then numerous diet therapies have captured public attention including very low energy liquid diets (such as the Cambridge Diet), single food diets (such as the Spaghetti diet) and fruit diets (such as the Grape Cure and the Beverley Hills Diet), (Llewellyn-Jones, 1993). It is over 60 years since the first scientific paper on the subject of very low energy diets was published (Evans and Strang, 1929). Very low energy diets produce rapid weight losses and have therefore remained, to this day, an extremely popular sliming tool.

There has been a plethora of scientific literature examining the mechanisms and efficacy of very low energy diets (Foster *et al*, 1992; Garrow and Webster 1989; Pi-Sunyer, 1992; Wadden, 1993). Very low energy diets have been classified as those providing 3349 kJ/d (800 kcal/d) or fewer (Wadden, 1993). Most very low energy diets however provide between 1674 kJ/day (400 kcal/day) and 3349 kJ/day (800 kcal/day) with 45 - 100 g of protein (Foster *et al*, 1992). There are weight loss programmes that employ ultra-low intakes of 334 kJ/day (80 kcal/day), (Foster *et al*, 1992). Despite this wide range of low energy diets Foster *et al* (1992) showed that there is no advantage to using very low energy diets providing less than 3349 kJ/day in terms of weight loss, body composition, acceptability of the diet, mood and a variety of symptoms such as fatigue, tension and concentration.

Very low energy diets also vary considerably with respect to carbohydrate, protein and fat composition. Some researchers believe that if enough protein is given in the diet, weight loss is not accompanied by significant breakdown of body protein and muscle (Apfelbaum *et al*, 1987). Others advocate that the inclusion of carbohydrates in the diet reduces the natriuresis and diuresis associated with protein diets and reduces protein breakdown due to the "protein-sparing" effect of carbohydrate (O'Kane and Wales, 1994). Hill *et al* (1993) suggested that the effects of diet composition are greatest after (rather than during) weight loss. These researchers proposed that a reduction in fat intake and an increased level of physical activity after weight loss, will maximise the chance of weight maintenance (Hill, *et al* 1993).

The success of a very low energy diet depends on the physiological and psychological outcomes associated with the diet. The majority of literature assessing these outcomes has

examine obese subjects. Obese subjects using very low energy diets have reported adverse effects such as gallstone formation, excessive loss of lean body mass, water and electrolyte problems and mild liver dysfunction (Pi-Sunyer, 1993). Very low energy diets should therefore not be used indiscriminately and for extended periods (Pi-Sunyer, 1992; Pi-Sunyer 1993). Despite these adverse effects, very low energy diets have been shown to be successful in terms of weight loss and to reduce many of the health hazards associated with obesity including insulin resistance, hypertension, hyperlipidaemia and sleep apnoea (Atkinson, 1993).

Many normal to slightly overweight individuals select very low energy diets, which may carry some health risk or may lead to physiological and psychological changes in these individuals. In this dissertation the impact of very low energy diets on body composition and weight change, cardiac function, physiological nutritional status (blood glucose, albumin and lipid concentrations), selected hormone concentrations, performance, mood, body temperature, and sleep was assessed in non-obese women.

## 1.3) Effects of energy restriction on weight loss, metabolic rate and body composition

Since the majority of very low energy diets are used for slimming purposes, weight loss and alterations in body composition are the primary indicators used in determining the success of a diet.

### 1.3.1) Weight loss and metabolic rate

Reductions in weight and resting metabolic rate that accompany very low energy diets are more rapid in the first week of energy restriction (Garrow and Webster, 1989). The rapid weight loss phase has been attributed to the loss of glycogen stores and the water

associated with this glycogen (Webster and Garrow, 1989). The introduction of carbohydrates into the very low energy diet regime may reduce this initial diuresis (O'Kane and Wales, 1994). The success of the very low energy diet may be attributed to the weight losses achieved with these energy restriction regimes. Total weight losses for very low energy diets average approximately 20 kg over a duration of about 12 weeks and approximately 35 kg over 6 months or more (Wadden *et al*, 1983). Two-thirds or more of this lost weight may be regained within the first year after weight loss (Wadden and Stunkard, 1986), but behaviour modification programmes (Wadden and Stunkard, 1986) and the inclusion of exercise (Phinney, 1992) can contribute to sustained weight maintenance.

In general, the rate of weight loss is proportional to the severity of the diet. However, there is an apparent threshold at about 5 MJ/d below which, the perceived advantages of rapid weight loss are, in the long term, offset by the suppression of resting metabolic rate that accompanies energy restriction (Prentice *et al*, 1991). This was demonstrated by Foster *et al*, (1992) who showed that weight loss after 24 weeks does not differ significantly between 1758, 2763 and 3349 kJ/day diets and that there is no clinical advantage in using very low energy diets that provide less than 3349 kJ/d.

A reduction in metabolic rate is consistently shown to accompany very low energy diets (Davies *et al*, 1989; de Boer *et al*, 1986; Fransilla-Kallunki *et al*, 1992). The labile nature of energy expenditure was demonstrated by de Boer *et al* (1986) who noted an almost immediate 5 % drop in 24 hour energy expenditure on the first day of a 4.2 MJ/d diet and a 6 % increase in 24 hour energy expenditure on the first day of refeeding. Prentice *et al* (1991) noted that in most studies, resting metabolic rate is suppressed by

between 5 and 25 %. This suppression of resting metabolic rate is dependant on the severity of the diet, with 3 MJ/d diets causing a 15 % suppression and 5 MJ/d diets resulting in a 5 % suppression.

### 1.3.2) Body composition

The quantification of body composition is a fundamental component in determining how effective energy restriction is. Weight loss in humans is almost always accompanied by a loss of lean body mass, as well as fat mass. A curvilinear relationship between these two body compartments has been described by Forbes (1987). The relationship tells us that the relative contribution of lean body mass to the total weight change is inversely related to body fat content (Forbes, 1987). An extremely fat person should therefore have a Δlean body mass:Δbody mass ratio of 0.2, meaning that lean body mass would constitute 20 % of the weight lost, while a thinner person would have a much higher ratio (Prentice *et al*, 1991). Prentice *et al* (1991) advocate that for the fat masses common in dieting women, fat free mass should constitute 25 % of the weight lost and fat mass 75 %. The composition of weight loss is not only determined by the initial fatness of the subject, but is also influenced by the severity of the restriction regime. The greater the energy deficit, the greater the loss of nitrogen and hence lean tissue (Forbes, 1987). So, thinner people and people on more extreme diets lose a greater proportion of lean body mass than fatter people and those on less extreme diets (Prentice *et al*, 1991). Despite this observation, Foster *et al* (1990) noted that no significant changes in body composition occur among subjects who consume 1758, 2763 and 3349 kJ/day diets and they concluded that if very low energy diets provide protein of high biological quality, fat free mass is not unduly compromised. Furthermore, a combination of aerobic and anaerobic exercises added to an energy restrictive diet promotes fat loss and preserves lean tissue mass

(Svendsen *et al*, 1993). So, very low energy diets may be successful, despite concerns of unacceptable reductions in lean body mass.

1.4) **Effects of energy restriction on cardiac function**

Very low energy diets are not only beneficial in terms of weight loss and altered body composition; they have been shown to reduce many of the risk factors associated with cardiovascular disease, such as lipoprotein concentrations and blood pressure (Svendson *et al*, 1993).

Body weight is one of the most important determinants of blood pressure regulation (Tuck, 1985) and hypertension is more frequent in obese people than those of normal weight (Dustan, 1985). Many clinical trials on both normotensive and hypertensive individuals have confirmed that weight reduction is accompanied by significant falls in blood pressure (Cutler 1991; Svendson *et al*, 1993; Tuck, 1985) and, as such, weight loss has become an important antihypertensive therapy. Suppression of the sympathetic nervous system during fasting and semi-starvation has been conclusively demonstrated in obese and normal weight subjects (Landsberg and Young, 1985). A suppression of sympathetic nervous system activity may be responsible for the reductions in blood pressure associated with weight loss, since changes in plasma norepinephrine with weight loss correlate with changes in blood pressure (Tuck, 1985). Furthermore, obese normotensive and hypertensive patients have significant reductions in the levels of renin and aldosterone during weight reduction by very low energy diets (Tuck *et al*, 1981). The mechanisms causing reductions in blood pressure during weight loss are probably complex, since catecholamines are also important in the release of renin and may produce changes in other hormones (Tuck, 1985).

Diminished sympathetic activity may also be responsible for the decrease in heart rate that accompanies energy restriction (Dustan, 1985). Mean heart rate has been shown to fall by 10.9% in obese patients consuming very low energy diets [1757 kJ/day, (420 kcal/day)] and by 9.7% in those consuming balanced-deficit diets [5021 kJ/day, (1200 kcal/day)], (Doherty *et al*, 1991).

Irrespective of the mechanisms involved in blood pressure and heart rate reduction with weight loss, very low energy diets are advantageous because a) when administered as a controlled liquid formula, they may be used to control the intake of various nutrients such as sodium, potassium, calcium and magnesium, all of which have been implicated in the pathogenesis of hypertension (Tuck, 1985), b) they produce normotension in two to four weeks (Tuck *et al*, 1981), c) normal blood pressures can be achieved long before ideal body weight is reached (Eliahou *et al*, 1992; Tuck, 1985) and d) the quantity of antihypertensive drugs needed to reduce blood pressure in overweight hypertensive may be reduced by 50 % when used in conjunction with an efficient hypocaloric diet (Darne *et al*, 1993). Furthermore, weight loss reduces the increased cardiac output and compensatory left ventricular hypertrophy associated with severe obesity, improves ventilation perfusion disturbances and carbohydrate tolerance and decreases serum lipid concentrations (see section 1.4.1) thereby diminishing other risk factors for coronary heart disease and heart failure (Dustan, 1985; Pi-Sunyer 1993). Consequently, the beneficial effects of energy restriction on obese, hypertensive patients are well documented.

Diet composition also alters cardiac functioning: Straznicky *et al* (1993) showed that short term consumption of a low fat diet is associated with reduced 24 hour ambulatory blood pressure and heat rate, a selective decrease in noradrenaline cardiovascular reactivity (without apparent changes in noradrenaline release rate or clearance from plasma), and a reduced systolic blood pressure response to a cold pressor test, when compared to an isocaloric high fat diet. Thus, both reductions in energy intake and alterations in diet composition are shown to improve cardiac functioning.

### 1.5) Effects of very low energy diets on physiological nutritional status

The metabolic status of the body may be assessed by monitoring certain blood variables, namely, lipoprotein, glucose (Fransilla Kallunki *et al*, 1992) and albumin (Scafi *et al*, 1990) concentrations.

#### 1.5.1) Lipoprotein concentrations

The relative proportions of lipoproteins occurring in the blood act as indicators of obesity and are used to identify the risks of coronary heart disease. Increased concentrations of total cholesterol, low density lipoprotein (LDL) cholesterol and plasma triglycerides, and decreased concentrations of high density lipoprotein (HDL) cholesterol accompany obesity (Bray, 1992; Kannel *et al*, 1979). These altered lipoprotein concentrations may be responsible for the increased risk of cardiovascular disease and heart attack associated with obesity. Many studies have therefore attempted to assess whether weight loss is advantageous in normalising altered blood lipids and lipoproteir in the hope of reducing the risk of coronary heart disease (Dattilo and Kris-Etherton, 1992; Svendson *et al*, 1993; Weinsier *et al*, 1992).

There is conclusive evidence that weight reduction is associated with a decrease in total cholesterol, LDL cholesterol, very low density lipoprotein (VLDL) cholesterol and triglyceride concentrations (Dattilo and Kris-Etherton, 1992). Furthermore, a reduction in HDL cholesterol during active weight loss and an increase in HDL at follow up (i.e. at a reduced stabilised weight) is a common finding in weight reduction studies (Dattilo and Kris-Etherton, 1992; Follick *et al*, 1984; Zimmerman *et al*, 1984). Short term changes in lipoprotein concentrations with weight loss have been observed after ten days of energy restriction (Weinsier *et al*, 1992) and long term changes have been observed after a year of energy restriction (Kasim *et al*, 1993). Dietary changes that occur with energy restriction, such as reductions in total dietary fat, saturated fatty acid and cholesterol intakes, may partially explain the changes in lipids and lipoproteins noted with weight loss (Dattilo and Kris-Etherton, 1992). There are however, a number of other mechanisms which may be responsible for alterations in lipoprotein profiles, such as decreased $\beta$-hydroxy-$\beta$-methylglutaryl coenzyme A reductase activity, inhibited hepatic cholesterol synthesis, enhanced cholesterol excretion in the bile and a decreased lipoprotein lipase activity (Dattilo and Kris-Etherton, 1992).

Weight reduction is therefore beneficial in normalizing the plasma lipid concentrations of obese individuals and thereby reduces the risk of coronary heart disease in these individuals.

### 1.5.2) Glucose

The concentration of blood glucose fluctuates little and is tightly controlled by a number of feedback mechanisms namely insulin, glucagon, the sympathetic nervous system, cortisol, growth hormone and the liver. During periods of energy restriction the

gluconeogenesis function of the liver maintains the relatively high blood glucose level necessary for brain function. In addition, the nervous system and brain continue to utilize glucose, but virtually all other organs and tissues reduce their utilization of glucose and increase their utilization of fats during the fasting state. The combined effects of gluconeogenesis and the switch over to fat utilization are the basis of an efficient control system that regulates glucose concentrations with energy restriction. Consequently, plasma glucose concentration is generally unaltered during energy restriction. Krotkiewski *et al* (1990) found no change in blood glucose in obese subjects placed on a 544 kcal/d diet after two and four weeks of dieting. Furthermore, blood glucose was shown to be unaltered by a six week 1680 kJ/d very low energy diet formula (Fransilla-Kallunki, *et al* 1992) and by an 18 day 589 kcal/d diet (Katzeff *et al*, 1986).

Nevertheless, blood glucose may vary in situations of malnourishment and starvation: Webber and MacDonald (1994) noted that acute starvation results in a reduction in plasma glucose in both men and women after 36 and 72 hours. Furthermore, glucose metabolism is altered in the obese: weight gain is associated with an enhanced insulin resistance, characterised by elevations in circulating insulin and a diminished ability to oxidise and store glucose, making obesity a risk factor for non-insulin-dependant diabetes (Bray, 1992; Pi-Sunyer, 1993). Weight reduction, using very low energy diets, in obese and non-insulin-dependant diabetic subjects is beneficial in that it increases insulin sensitivity (Fransilla-Kallunki *et al*, 1992). The reduction in fat mass accompanying very low energy diets results in a reduced supply of lipids for oxidation and because of reduced substrate competition this leads to enhanced glucose oxidation (Fransilla-Kallunki *et al*, 1992).

### 1.5.3) Albumin

The blood protein, albumin, does not vary significantly during the restriction of both energy and protein intakes (Scafi *et al*, 1990). Even anorexic patients do not exhibit hypoalbuminaemia (Passmore and Eastwood, 1986). During protein restriction albumin decreases slowly (even in the presence of a dramatic decrease in its synthesis) because of its relatively long half life of 18 days, the reduction in breakdown rate and the redistribution of extravascular albumin (Scafi *et al*, 1990). It is for these reasons that albumin is not a sensitive index of protein metabolism. Other plasma proteins such as retinol-binding protein, complement component C3 and firbronectin, which have relatively short half-lives, are more sensitive measures used to assess changes in protein metabolism (Passmore and Eastwood, 1986). Moderate reductions in labile proteins prealbumin and retinol-binding protein occur within the first five days of energy restriction (< 2100 KJ/d). However, these labile proteins are not sensitive to changes in dietary composition (provided that > 40 g of high-biological-protein is given) making them unreliable clear cut indices for assessing overall protein status (Scafi *et al*, 1990). Since insulin regulates both sex hormone binding globulin and insulin-like growth factor binding protein 1, both of these proteins are altered by dietary manipulation (Hamilton-Fairley *et al*, 1993). The sensitivity of insulin like growth factor-I to both energy restriction and protein restriction, and it's relatively short half life make it a more sensitive and more specific marker of nutritional status than albumin, prealbumin, transferrin and retinol binding protein (Thissen *et al*, 1994).

## 1.6) Effects of energy restriction on selected hormone concentrations

### 1.6.1) Cortisol

Stress leads to marked increases in cortisol which stimulates protein metabolism and gluconeogenesis and inhibits glucose uptake and oxidation by many body cells. These metabolic changes initiated by cortisol are essential for survival during stressful conditions such as fasting. Cortisol is therefore usually increased during starvation (Passmore and Eastwood, 1986) and in patients with anorexia nervosa and bulimia (Crisp, 1980). An increase in cortisol concentration has been demonstrated in male subjects after 10 days of starvation (Palmblad *et al*, 1977) and in elite male athletes placed on a low fat/high carbohydrate diet (Tegelman *et al*, 1992). In contrast obese female subjects on a weight loss and exercise programme showed reductions in cortisol concentrations (Scavo *et al*, 1988). Since cortisol is found to decrease in obese subjects treated with a month long very low energy diet, it has also been implicated in the control of android fat distribution (Hainer *et al*, 1992).

The hypercortisolism often displayed during natural and experimental starvation is often reflected as incomplete cortisol suppression after dexamethasone (Yanovsky *et al*, 1993). Yanovsky *et al* (1993) demonstrated that obese subjects placed on a 3.4 MJ/d diet do not display disruptions of the hypothalamic-pituitary-adrenal axis before or after weight loss. They postulated that one of the concomitants of energy restriction, perhaps in combination with a threshold body weight, may be of greater importance in causing abnormalities in dexamethasone suppression testing rather than rapid weight loss *per se* (Zelich *et al*, 1993).

1.6.2) **Triiodothyronine ($T_3$)**

Numerous investigators have noticed a clear decrease in circulating $T_3$ levels with energy restriction (Barrows and Snook, 1987; Davies *et al*, 1989; Katzeff *et al*, 1990), to about 70% of the pre-diet level and sometimes down as low as 50% (Prentice *et al*, 1991). In many studies examining changes in $T_3$ with dieting, $T_4$ remains unchanged (Katzeff *et al*, 1990; Prentice *et al*, 1991) and the decrease in $T_3$ is attributed to significantly raised reverse $T_3$. It is therefore the conversion of $T_4$ to $T_3$ that is sensitive to dietary intake (Sherwin, 1985). Short term changes in $T_3$ with energy restriction and starvation have been well documented (Davies *et al*, 1989; Katzeff *et al*, 1990; Palmblad *et al*, 1977). Palmblad *et al* (1977) noted a significant reduction in $T_3$ within three days of fasting. Long term reductions in $T_3$ have also been documented: Barrows and Snook (1987) showed that after a four to six month period $T_3$ is reduced and after 5 weeks of refeeding $T_3$ concentrations and resting metabolic rate still remain below pre-study concentrations.

The change in thyroid hormone status plays a key role in the suppression of metabolic rate (Prentice *et al*, 1991). It is proposed that the reductions in $T_3$ and metabolism associated with energy restriction are an adaptive mechanism employed to conserve energy and to preserve lean body mass (Osbourne *et al*, 1983). Exercise may reduce the diet induced suppression of resting metabolic rate, however, clear scientific evidence for this is unavailable (Prentice *et al*, 1991). Although changes in $T_3$ are significantly correlated with changes in oxygen consumption, additional factors such as the sympathetic nervous system may also be responsible for the reductions in metabolic rate noted with hypocaloric feeding (Sherwin, 1985). As previously noted (see section 1.4) alterations in the sympathetic nervous system may be responsible for the reductions in blood pressure and heart rate observed in conjunction with reductions in energy restriction and metabolic

rate.

## 1.7) Effects of energy restriction on psychological variables

The psychological consequences of energy restriction are as important as the physiological consequences. Psychological outcomes may be measured by examining an individual's performance and mood state.

### 1.7.1) Performance

In general it has been shown that: performance appears to follow a circadian rhythm (Tilley, 1984), motivation may affect performance and complex tasks may be more sensitive to changes in performance than simple tasks (Daftuar, 1972; Norton, 1970).

Despite the fact that millions of people are preoccupied with weight loss in Western society, there is little that is known about weight loss and performance. There are studies that have examined the potential effects of sub-optimal intakes of minerals and vitamins on psychological performance in children (Benton and Butts, 1990; Southon *et al*, 1994). However, many of these studies have not addressed problems such as the reliability of micronutrient intake recordings and the lack of adequate reference limits and cut off points for biochemical indices of mineral and vitamin status in children. Hence a lack of consensus about whether dietary deficiencies hamper neural function in children exists (Southon *et al*, 1994).

There are studies that have examined the effects of a dietary composition on performance and mood (Deijen *et al*, 1989; Spring *et al*, 1983). The authors hypothesized that diet composition may affect behaviour via the influence of precursors (such as tryptophan,

tryosine and choline) on the synthesis and release of brain neurotransmitters (such as serotonin, catecholamines and acetylcholine). Leathwood *et al* (1994) demonstrated that the addition of 500 mg of tryptophan to a meal has a sedative effect, while Deijen *et al* (1989) noted few differences in performance on a variety of tests completed after long term protein and carbohydrate feeding. Significant differences in performance dietary manipulation are conflicting (Deijen *et al*, 1989).

Studies examining relationships between cognitive performance and food intake, have focused mainly on anorexic and bulimic subjects. Performance in these subjects is generally impaired on a number of tasks when compared to controls (Fox, 1981; Laessle *et al*, 1990). Since cognitive deficits in patients with eating disorders may be related to nutritional variables or to the presence of a primary psychopathology, the effects of dietary restraint have been examined in non-psychiatric patients: Rogers *et al* (1993) and Green *et al* (1994) compared performance in low, medium and high restraint eaters and current dieters and both authors demonstrated impaired cognitive performance with dieting. Direct metabolic and physiological consequences of energy restriction may affect performance, however other factors such as stress and anxiety may affect demanding tasks (Green *et al*, 1994).

### 1.7.2) Mood

Studies examining alterations in mood with low energy intake have concentrated primarily on obese patients losing weight. The obese population as a whole does not show an elevated incidence of psychopathology, however, they differ from non-obese groups in psychological and behavioral variables related to weight and eating and more frequently display perceptual and emotional body image anomalies (O'Neil and Jarrell, 1992).

There have been numerous reports of unfavourable emotional responses such as depression, nervousness and irritability during weight reduction (Wadden and Stunkard, 1985). However, Crisp *et al* (1973) showed that the psychoneurotic status of obese patients fluctuates very little during a four month 500 kcal/day diet. Furthermore, a recent review demonstrated that the majority of very low energy diet studies report neutral or positive effects on hunger, depression and anxiety (O'Neil and Jarrell, 1992). Burley *et al* (1992) reported that, in the second week of a two week very low energy diet (1697 kJ/day), subjects were less irritable, less hungry, and had less urge to eat than in the pre-diet week and the first week of the diet therapy. Using three different very low energy diets, Foster *et al* (1992) demonstrated that obese women losing weight all show significant improvements in mood as assessed by the Beck Depression Inventory. The positive effects of very low energy diets on depression are augmented by the use of behaviour modification techniques (O'Neil and Jarrell, 1992).

1.8) <u>Effects of energy restriction on body temperature</u>

Energy provided by substrate oxidation forms part of a homeostatic mechanism required to maintain constant body temperature and the relationship between energy intake and thermoregulation is thus apparent.

Glickmann-Weiss *et al* (1993) examined the relationship between feeding regime (carbohydrate feeding or a 14 hour fast) and thermal responses during 120 minutes of exposure to 8, 20 or 27°C in well nourished men. They found that neither tissue insulation, rectal temperature nor oxygen consumption differed between fed or fasted states at any temperature. Despite this, previous research has shown that low body weight or

undernutrition impairs thermoregulation: Bastow *et al* (1983) found that elderly, thinner patients exhibit impaired metabolic and behavioral responses to a cold environment and Bennet (1981) noted that a 48 hour fast, in young healthy adults impairs peripheral vasoconstriction and exacerbates heat loss. Mansell *et al* (1990) demonstrated an impaired thermoregulatory ability in patients who lose weight due to illness. These investigators propose that impaired thermoregulation with weight loss may be due to a change in central control mechanisms, since the thermogenic response to an infusion of adrenalin is not abolished with weight loss. Abnormal thermoregulation following weight loss, may be a mechanism for energy conservation (Mansell *et al*, 1990), since the thermogenic cost of warming, when energy is restricted, may exceed the energy saved by reducing body temperature.

The phenomenon of reducing body temperature to save energy is displayed by many small mammals and birds who demonstrate daily entrances into shallow torpor during which increasingly lower body temperature and metabolic rate accompany progressive weight loss (Berger and Phillips, 1988). Moreover, certain human populations become torpid at night. The Australian aborigine, Kalahari bushman and the Alacaluf indians of the Tierra de Fuego all exhibit the ability to conserve energy by entering into shallow torpor. Their torpid state may well contribute to their successful survival, when under harsh environmental conditions, they are faced with a relatively meagre diet (Mount, 1979). While a reduction in thermoregulatory ability and/or body temperature in human subjects has been demonstrated in situations of energy restriction, the effects of a very low energy diet on body temperature have not been examined.

## 1.9) Effects of energy restriction on sleep

The relationship between food intake and sleep was described by Charles Dickens who, in his novel **The Pickwick Papers**, described a markedly obese young man who spent most of the time asleep. The term Pickwickian syndrome was thus coined to describe a condition in which somnolence and obesity are combined with respiratory insufficiency, now referred to as obstructive sleep apnoea syndrome.

### 1.9.1) Effects of psychiatric eating disorders on sleep patterns

The evidence for a relationship between food intake and sleep patterns comes mainly from obese patients (similar to the character from Charles Dickens's novel) and anorexic patients. Disturbances in sleep patterns of patients with psychiatric disorders of weight such as anorexia nervosa and obesity have been related to nutritional factors that transcend specific diagnostic and mood states (Crisp and Stonehill, 1973). When obese patients, without obstructive sleep apnoea syndrome, are placed on weight reduction programmes they show reductions in slow wave sleep (SWS) (Crisp *et al*, 1973; Ogilvie and Broughton, 1977) and rapid eye movement (REM) sleep (Ogilvie and Broughton, 1977). Similarly before refeeding, anorexic patients show gross reductions in SWS and REM sleep in association with reduced total sleeping time, and, as weight is gained, SWS and REM sleep increase (Lacey *et al*, 1975).

Alterations in sleep patterns noted in anorexics and obese patients may be linked to alterations in metabolism. The "restorative theory" of sleep advocates that sleep is a time for growth and repair of the body and the brain (Oswald, 1970). Activities of wakefulness are believed to enhance catabolism, while sleep favours anabolism (Adam and Oswald, 1983). Studies have demonstrated that in the majority of tissues, peak rates of protein

synthesis and peak rates of cell division coincide with the time of sleep (Adam and Oswald, 1983; Adam, 1980). Although there is a circadian component, REM sleep has been associated with peaks in brain protein synthesis (Adam, 1980) and evidence for this is provided by Gillin *et al* (1972) who noted a dose related reduction in REM sleep on administration of corticosteroids (which promote protein catabolism). It is however SWS that is thought to be "worth more" for restoration (Adam, 1980). It follows that alterations in metabolism result in alterations in sleep (especially SWS). Consequently studies in which metabolism is altered, by exercise (Shapiro *et al*, 1990), heat load (Shapiro *et al*, 1989), hypo or hyperthyroidism (Carpenter and Timiras, 1982) and weight change in anorexia nervosa patients (Lacey *et al*, 1975) have been used to lend support to the restorative theory.

### 1.9.2) Effects of body composition on sleep patterns

Since there is an association between metabolic rate and lean body mass, Shapiro *et al* (1990) examined whether sleep variables were correlated with alterations in body composition or weight, as opposed to metabolism *per se*. They found that SWS and lean body mass were correlated, in a group of anorexics gaining weight and in a group of women on a physical training programme. No correlation between SWS and lean body mass exists for women losing weight (Shapiro *et al*, 1990). Similarly Nakazawa *et al* (1978) demonstrated no correlation between SWS and weight and Speigel (1981) found no correlation between REM sleep and body weight. Adam (1987) on the other hand showed a positive correlation between REM sleep and body weight.

### 1.9.3) Effects of short term alterations in energy intake on sleep patterns

The relationship between energy intake and sleep variables has been further demonstrated

by studies that have used normal healthy subjects to assess the short term relationships between energy intake during the day and EEG sleep on the following night. High carbohydrate/low fat intake has been associated with decreased SWS and increased REM sleep the following night, when compared with a balanced diet and a low carbohydrate/high fat diet (Phillips *et al*, 1975). Daytime carbohydrate and calorie intakes correlate positively with nighttime REM sleep and negatively with sleep onset latency. Proportions of tryptophan (serotonin precursor) in the diet and alcohol consumption correlate negatively with sleep onset latency (Crisp *et al*, 1986). In contrast, Hartmann *et al* (1979) showed that the short term impact of fat, carbohydrate and protein loads does not influence the percentage of REM sleep.

### 1.9.4) Effects of energy restriction on sleep patterns in animal studies

Alterations in sleep architecture with changes in food intake have also been examined in animal models. Kukorelli and Juhasz (1977) showed that electrical stimulation of the intestine leads to longer sleep episodes in starved animals. In hungry cats, an EEG arousal pattern is replaced by a record of pronounced synchrony similar to that of SWS, when the stomach of the animals are filled with milk and glucose is administered intravenously (Anokhin, 1961). In the early phases of fasting, geese and emperor penguins increase their proportions of SWS and sleep for longer periods (Dewasmes *et al*, 1989). The increase in SWS is thought to be an energy saving mechanism, in support of the "energy conservation" theory of sleep (Dewasmes *et al*, 1989). According to this hypothesis, sleep serves to reduce metabolic rate and body temperature in mammals and birds during periods of declining energy reserves and ambient temperatures, and thereby offset the high energetic costs of endothermy (Berger and Phillips, 1990). The strongest evidence in favour of the theory is the thermoregulatory and electrophysiological

continuities between hibernation, and sleep (Berger and Phillips, 1990). According to the theory, a decline in energy reserves increases SWS. Further evidence for the energy conservation theory is the finding that along with reduced metabolic rate (Ravussin *et al*, 1986) and cardiac output (Miller and Horvath, 1976), systemic glucose utilization also declines (Boyle *et al*, 1994) during sleep. SWS increases in the early phases of fasting in geese and decreases in the later phases of fasting (Dewasmes *et al*, 1984). The reduction in SWS after long term fasting in geese, could mark the end of an energy conservation strategy and the beginning of a new strategy based on survival and the search for food (Dewasmes *et al*, 1984).

1.10) **Effects of energy restriction on sleep and temperature**

In the previous sections (section 1.8 and 1.9) I have discussed some of the effects of energy restriction on temperature regulation and sleep patterns respectively. There is also a link between sleep patterns and temperature regulation. Dijk *et al* (1991), using prolonged sleep duration and circadian studies, suggested that the sleep-temperature link is minor and that the sleep associated drop in temperature is primarily due to the circadian temperature rhythm. However, Barrett *et al* (1993) noted that in conditions where other exogenous influences are controlled, sleep itself has a clear and unambiguous effect in lowering nocturnal body temperature. This fall in body temperature during sleep has been cited as evidence for energy conservation during sleep (Berger and Phillips, 1990). In addition, SWS is associated with specific thermoregulatory effector processors such as vasodilation, sweating and panting (McGinty and Szymusiak, 1990). Consequently, it has been hypothesised that SWS in mammals and birds provides "homeostatic brain and body cooling which would provide several adaptations including lower energy utilisation..." (McGinty and Szymusiak, 1990). Conversely, sleep has also

been thought of as essential for heat production rather than heat loss (Glotzbach and Heller, 1994). It has been proposed that a drop in hypothalamic temperature set points for thermoregulatory responses, at the onset of sleep, can create a thermoregulatory error signal for heat loss (Wehr, 1991). So, in addition to a restorative and energy conservation function, sleep has been afforded a thermoregulatory function.

There are clearly interactions between energy restriction, sleep and body temperature. Despite the common ground between these variables there are no human studies that have investigated the relationships between them, but a number of animal studies attempted to do so.

In concurrence with the energy conservation theory of sleep it is estimated that a 100 g mammal exposed to freezing temperatures and without food can survive one day longer by dropping its temperature by 2°C through sleeping than if it remains resting quietly awake (Heller, 1978). Accordingly Berger and Phillips (1988), demonstrated that when faced with declining diurnal energy reserves, pigeons increase nocturnal resting energy conservation by dropping body temperature by ~ 2°C and by decreasing metabolic rate while displaying predominantly SWS. This phenomenon of a decreasing stepwise pattern of lowering nocturnal body temperature and metabolic rate, alternating with diurnal restoration of euthermia, accompanies progressive weight loss in many relatively small birds (Berger and Phillips, 1988). Larger birds, however, have been shown to employ a different survival strategy: they display increases in SWS (thought to have an energy conserving function), without changes in nocturnal body temperature (Dewasmes *et al*, 1989). Bears on the other hand, only allow their body temperature to drop by 4-6°C during hibernation, since the thermogenic cost of rewarming a large mass may exceed the

energy saved by reducing body temperature and metabolic rate (Berger and Phillips, 1988).

1.11) **Conclusion and motivation for the following dissertation**

Very low energy diets produce rapid weight losses (especially in the first week of energy restriction) and are successful in altering body composition (Foster *et al*, 1992; Webster and Garrow, 1989). Consequently, very low energy diets are popular slimming tools. Very low energy diets also produce other physiological changes which may be beneficial to health, in that they reduce many of the risk factors associated with obesity, such as hypertension, dyslipidemia, hyperinsulinemia and gallbladder disease (Pi-Sunyer, 1993). However, very low energy diets may indeed hamper the slimming programme by reducing resting metabolic rate via reductions in $T_3$ (Prentice *et al*, 1991).

Studies examining the effects of energy restriction on performance have examined short term changes in performance and studies examining changes in mood with energy restriction have yielded conflicting results.

Temperature regulation is affected by changes in metabolism and sleep has been afforded a restorative function, an energy conservation function and a thermoregulatory function. Studies examining the effects of energy restriction on sleep, have examined psychiatric patients, have used animal models and have been short term studies. To date, there are no human studies exploring the relationships between energy restriction, temperature regulation and sleep.

In this dissertation, I have examined the effects of very low energy diets on weight change, body composition, cardiac function, physiological nutritional status, hormone concentrations, mood and performance measures as well as sleep and nocturnal temperature, in normotensive, non-obese, healthy women.

# CHAPTER 2

## 2 Methodology

### 2.1) Protocol

Nine healthy premenopausal women aged 20-36 years, with a mean weight of 71.21 ± 8.06 kg and a mean body mass index of 26.1 ± 2.8 kg/m$^2$, participated in this study. The women were mainly University of the Witwatersrand students and staff members who responded to an advertisement which was placed in the university newsletter.

Before commencing the study, the women were given a physical examination, which included measurements of weight and height, examination of the cardiovascular respiratory system, abdomen and head and neck regions, and urinalysis using reagent strips (Labstix, Miles Inc, Diagnostics Division, Elkhart, IN 46515, USA). Normotensive, healthy women with a body mass index of > 25 or those having > 7 kg of weight to lose were included in the study. A medical history was taken to ensure that all the women were in good health (i.e. they were free from diabetes, cardiovascular, respiratory, hepatic and renal disease, had normal thyroid function, a regular menstrual cycle and were not taking any medications that could interfere with normal sleep patterns and/or weight loss). In addition the women completed a general health questionnaire, (General Practice Research Unit, 1972), (appendix 1) which screened for depression. Only women scoring less than 12 on the general health questionnaire were included in the study. After being shown the research environment, the women gave written, informed consent (appendix 2) to participate in the study. This protocol was approved by the Committee for Research in Human Subjects of the University of the Witwatersrand (26/2/92)

The study was conducted during autumn (maximum temperature 18.7 °C, minimum temperature 7.1 °C). The study design is shown in Table 2.1. Five nonconsecutive baseline nights were spent in the sleep laboratory in the two weeks before commencement of the diet (baseline nights 1, 3, 7, 11 and 15) and five nonconsecutive diet nights were spent in the laboratory 14, 16, 20, 24, and 28 days after commencing the diet (Table 2.1). The first baseline night (baseline 1) and the first diet night (diet 14) spent in the laboratory acted as adaptation nights allowing the women to acclimatize to the laboratory surroundings and procedures. Menstrual cycle differences were attenuated by scheduling measurements made during the diet, 28 days after the corresponding baseline measurements (7 out of 9 subjects were taking oral contraceptives). No attempt was made to avoid taking measurements during ovulation or menstruation.

During the diet phase of the study the women were placed on a four week very low energy diet consisting of 3347 KJ/day (800 Kcal/day). This energy restriction regime was chosen because both Foster *et al* (1992) and Prentice *et al* (1991) showed that there is no advantage for weight loss compared to using a lower energy diet. Diet composition was not specified but the subjects were encouraged to eat a high carbohydrate diet in order to maintain a larger food volume and accordingly they were discouraged from eating fats because of their high caloric density. The diet plan can be found in appendix 3.

The women kept a daily food diary throughout the six week study period (Table 2.1). Measurements recorded on each visit to the laboratory, during baseline and diet phases of the experiment included: nocturnal sleep recordings and rectal body temperature measurements, supine heart rate and blood pressures recorded upon waking, body weight, reaction tests and visual analogue scales determined in the mornings after micturition

(Table 2.1).

In addition mood was assessed before and after two weeks of dieting, using the Profile of Mood States Questionnaire (POMS, McNair *et al*, 1971, appendix 4) . Skinfold measurements and bioelectrical impedance analysis measurements were made and fasting bloods samples were drawn before, after two weeks and after four weeks of dieting (Table 2.1). All measuring techniques are discussed in detail in the following sections.

**Table 2.1** Study design of a four week very low energy diet. Nine healthy women visited the sleep laboratory on baseline (B) nights 1, 3, 7, 11 and 15, and on diet (D) nights 14, 16, 20, 24 and 28.

| | Adaptation | | | | |
|---|---|---|---|---|---|
| Baseline (B) | B1 | B3 | B7 | B11 | B15 |
| Diet (D) | First two weeks of dieting | | | | |
| | D14 | D16 | D20 | D24 | D28 |
| | - Reaction test practices | **Daily Measurements:**<br>- Food diary<br>**Laboratory Measurements:**<br>- Nocturnal sleep & temperature<br>- Heart rate and blood pressure (on waking)<br>- Weights<br>- Reaction tests<br>- Visual analogue scales } (mornings)<br>**Intermitant Laboratory Measurements:**<br>- Blood samples (B1, D14, D28)<br>- Skinfold/Bioelectrical impedance analysis (B15, D14, D28)<br>- Profile of mood states (B1, D14) | | | |

## 2.2) Compliance and energy intake assessment

### 2.2.1) A review of available techniques

The assessment of energy intake has not kept pace with advances in related disciplines because of the general lack of validation studies (Kohlmeier, 1994). Validation studies are difficult because the doubly labelled water method for measuring total daily energy expenditure, which acts as a gold standard, is costly and requires highly specialised equipment (Johnson *et al*, 1994).

Indirect dietary assessment methods may be divided into list based methods and meal based methods (Kohlmeier, 1994). List based methods, such as the food frequency questionnaire, are used to measure the most common foods and "usual" dietary practices of a population, (Kristal *et al*, 1994). The food frequency questionnaire method of dietary assessment is successful in epidemiological studies, however, it is not sensitive to changes in dietary intake. Meal based methods (such as daily food records) are thus preferred for intervention studies (Kristal *et al*, 1994). There are however problems associated with daily food records which include errors in estimations of portion size and the under-reporting of food intake. Prentice *et al* (1986), using the doubly labelled water measure of energy expenditure, demonstrated serious under-reporting by obese adults. The finding that obese individuals under-report food intake significantly more than non-obese individuals has been replicated by numerous investigators (Bandini *et al*, 1990; Black, 1991; Livingston *et al*, 1990), however it has also been established that the use of dietary records results in under-reporting by non-obese, normal adults (Livingston *et al*, 1990). In view of the fact that the doubly labelled water method is too expensive and too technically demanding to use as a regular validator of reported food intake measurements,

Goldberg *et al*, (1991) have defined cut off limits to identify obviously implausible intake values. Black *et al* (1991) used these cut off limits to evaluate the validity of reported energy intake in 37 published dietary studies and showed that dietary assessment methods have a strong bias towards underestimation of habitual energy intake. Nevertheless, since dietary records are easily executed and are commonly used to assess dietary intake, the recording of a food diary was used in this study and the cut off limits of Goldberg *et al* (1991) were used to identify under-reporting.

### 2.2.2) Methods used to assess energy intake

For the duration of the study, the women were asked to weigh and record the quantities of everything they ate and drank in a daily food diary. The food diary included written instructions for recording food intake. Each woman was provided with a kitchen measuring scale and was asked to record food intake in terms of millilitres or grams when possible. They were instructed on estimating food portions when measurements could not be made. The women were also supplied with "The Complete South African Kilojoule Calorie and Carbohydrate Counter" (Barton, 1990) so that they could determine the caloric value of any food eaten.

Changes in energy intake and diet composition were assessed using the *Foodfinder* computer package. (Medical Technologies Tygerburg, South Africa). Energy intake and diet composition were evaluated on five chosen days during both the baseline and diet phases respectively. The five chosen days included a Sunday, since it is well established that women consume more food on a Sunday than on weekdays, (Basiotis *et al*, 1989). The baseline and diet days chosen for dietary evaluation were not matched for menstrual cycle since the five diet days were selected from a month long diet period, while the five

baseline days were from a two week baseline period. The data from these selected days were assumed to be representative of the average dietary intake over the two experimental phases and were meaned to give an average energy intake for the baseline and diet phases respectively.

Goldberg *et al* (1991), using the fundamental principles of energy physiology, developed a cut-off limit (cut-off limit 2) to determine whether reported energy intakes are a plausible measure of food consumption in weight-stable adults. In order to determine whether the baseline energy intakes reported by the women in this study compared with expected levels of energy intake in a sedentary population, the cut-off limits derived by Goldberg *et al* (1991) were applied.

Physical Activity Level (PAL) is defined as the total energy expenditure (TEE) divided by the basal metabolic rate (BMR) (Goldberg *et al*, 1991)

PAL = EE/BMR

In weight stable adults, energy intake (EI) is equal to energy expenditure (EE) and the equation can be rewritten as:

PAL = EE/BMR · EI/BMR

Since most of the inter individual variance arising from differences in weight, height, age and sex are automatically removed by the use of BMR in the denominator, PAL provides a useful index by which activity levels of all individuals can be compared. It can be

shown that it is virtually inconceivable for people to live at PAL values of less than 1.2 (Goldberg *et al*, 1991). When BMR is not measured directly, it can be determined using the equations defined by Schofield *et al* (1985). Goldberg *et al* (1991) present 95% confidence intervals for PAL values calculated using the Schofield equations (Schofield *et al*, 1985) to estimate BMR. A mean PAL value is calculated for a group of subjects and the duration of the study and number of subjects is used to determine a 95% critical PAL value (cut-off limit). If the observed value is less than the critical value then there is a 95% probability that the reported energy intake is insufficient to support weight balance. In this dissertation these calculations have been used to evaluate the validity of dietary reporting during the baseline phase of the study. The assumption was made that subjects who under-report during the baseline phase (weight stable phase) are likely to under-report during the diet phase of the study.

### 2.2.3) Methods used to assess compliance

In addition to determining whether the reported energy intake was a plausible measure of the food consumed (section 2.2.2), compliance was assessed by weighing the women on each visit to the laboratory. Furthermore, reagent strips for urinalysis (Labsix, Miles Inc, Diagnostics Division, Elkhart, IN 46515, USA) were used to determine urine ketone concentrations on a specimen of first-shed, morning urine collected after diet nights spent in the laboratory. Ketones indicate fat utilization (glucose sparing) and may appear in the urine before serum ketone is elevated.

## 2.3) Body composition assessment

### 2.3.1) A review of available techniques

Methods considered "gold standards" for predicting body composition, which are used

as reference methods for comparison with other methods, include measurements of total body water using isotopes of hydrogen, deuterium and tritium, screened scintillation measurements of total body potassium by determining naturally occurring $^{40}K$, and densitometry (underwater weighing) measurements (Kushner *et al*, 1990; Teran *et al*, 1991). Although these reference methods are relatively safe and non-invasive they require sophisticated equipment, a high degree of operator training, and may be time consuming. Similar problems arise with ultrasound, computed tomography, nuclear magnetic resonance imaging, infrared interactance and total body electrical conductivity, (Marshall *et al*, 1990). In this study, body mass index, skinfold measurements and bioelectrical impedance analysis were used to measure changes in body composition. These methods, although less reliable, are portable, simpler, more convenient and do not require expensive equipment.

### 2.3.2) Body mass index (BMI)

The simplest method for assessing body composition is the body mass index (BMI). BMI is calculated by dividing weight by height$^2$ (Quetelet's index, Quetelet, 1869). Garrow (1981) developed this index into an obesity index and classified obesity as either grade I (BMI 25 to 29.9), grade II (BMI 30 to 40) or grade III (BMI > 40) obesity. He described a BMI of over 30 for females and 25 for males as the threshold for adiposity. Three limitations of BMI have been recognised by Garn *et al* (1986): BMI is 1) dependent on stature, ie. standing height; 2) influenced by body proportions ie. relative length or sitting height and; 3) influenced equally by both lean and fat compartments of the body. Despite these limitations, BMI appears to be an adequate index of adiposity (Brodie, 1988) which is more precise than estimates based on resistance or impedance (Jebb *et al*, 1993), and is exceptionally easy to use and requires the most basic of

equipment.

In the mornings the women, barefoot and dressed in light night clothes, were weighed on an electric balance accurate to 0.01 kg (Mettler Instruments, Zurich, Switzerland) and heights (accurate to 0.01 m) were measured. Thereafter BMI was calculated.

### 2.3.3) Skinfold measurements (SM)

Skinfold measurement for assessing body fat is based on the assumption that the thickness of the subcutaneous adipose tissue reflects a constant proportion of the total body fat (Lukaski, 1987). This assumption is not necessarily true since there may be a greater increase in intra-abdominal fat than in subcutaneous fat with increasing body fatness (Gray *et al*, 1990). Skinfold measurements also assume that the selected sites of measurement represent the average thickness of the subcutaneous adipose tissue (Lukaski, 1987). The validity of this measure depends on whether the regression equation used applies to the population tested and the precision of the skinfold measurement is dependant on the skill of the anthropometrist. The inaccuracy in the method lies in the difficulty of raising skinfolds in certain patients (eg. morbidly obese and very thin subjects), (Gray *et al*, 1990; Lukaski, 1987) and the incorrect choice of region of measurement (Lukaski, 1987).

The usefulness of anthropometric equations in assessing changes in percentage body fat during weight loss has been examined by Sherf *et al* (1986), who proposed that they overestimate changes in percentage body fat with weight loss. Conversely, Jebb *et al* (1993) and Teran *et al* (1991) advocated that SM underestimate changes in percentage body fat with weight loss. Despite these differences, Jebb *et al* (1993) highlighted that

when choosing a simple method that can be used in the field or at a bedside, skinfold thickness appears to be the method of choice.

In this study, skinfolds were measured on the right side of the body at the following four selected sites: the triceps, the biceps (measured halfway between the tip of the shoulder and the tip of the elbow), subscapular (measured below the bottom tip of the scapular) and suprailiac (measured just above the hip bone). These measurements were made using Holtain Skinfold Calipers (Holtain Ltd, Wales). To improve the accuracy, the measurements were triplicated at each site and a mean of the three values was used (Lukaski, 1987). The four skinfold values were then added to obtain a total skinfold measurement. The sex and age specific regression equation devised by Durnin and Wormersley (1974) was applied to predict body density.

$$\text{Body Density} = C - [M \times \log(\text{sum of four skinfolds})]$$

where: $C = 1.1599$ and $M = 0.0717$ for women aged 20 to 29 years

$C = 1.1423$ and $M = 0.0623$ for women aged 30 to 39 years.

This prediction equation was chosen as it was derived from a spectrum of lean to moderately obese subjects and is therefore applicable to the women in this study. Furthermore, this equation has been shown to correlate well with densitometry measurements [$r = 0.88$ (Gray *et al*, 1990) and $r = 0.71$ (Teran *et al*, 1991)]. Using body density, percentage body fat could then be calculated using the Siri (1961) equation:

$$\%\ \text{FAT} = (4.95 / \text{body density}) - 4.5 \times 100$$

**2.3.4) Bioelectrical impedance analysis (BIA)**

Bioelectrical impedance analysis measures body composition by estimating total body water. Fat free mass is determined from total body water, and fat mass is then calculated using total mass. The BIA method is based on the assumption that fat free tissues contain all the water and conducting electrolytes in the body and therefore conducts an alternating low frequency current better than adipose tissues (Baumgartner *et al*, 1987). In order to measure the impedance to the flow of current, electrodes are placed on the hands and feet and a constant alternating current is applied between these electrodes. The voltage between these electrodes is measured and Ohm's law is used to calculate the impedance between the electrodes. If one assumes an electrical resistivity of nonfat tissue to be a constant value then the volume of the conducting system can be calculated by using the formula:

$$V = \rho \times L^2 / Z$$

where V is the conducting volume of the body ($m^3$), $\rho$ is the resistivity (in ohms/m) of the conducting system, L is the height in meters and Z is the impedance measured using Ohm's law (ohms).

The method makes certain assumptions. The assumption that the conducting component of the human body is uniform, is untrue (Baumgartner *et al*, 1987) since certain conductive tissues have a smaller impedance than others. Furthermore, the method assumes that there is a constant resistivity, which can be applied to all people. Resistivity is a function of frequency and is likely to be a function of hydration state, age and gender. In the human body impedance can be considered as the sum of the electrical

resistance and reactance of tissue. As the frequency of an alternating current increases so resistance increases and reactance decreases. It follows that the measurement of impedance from a fixed current value and measured voltage is a strong function of alternating frequency.

Few researchers have investigated the use of the BIA technique in measuring changes in body composition. Kushner *et al* (1990) found that BIA could be used as an indicator of change in body composition when compared with deuterium oxide dilution ($D_2O$), and demonstrated that BIA change is more accurate and precise than that of skinfold measurements. In contrast, Jebb *et al* (1993) demonstrated that BIA overestimates changes in fat mass. When compared with densitometry, Deurenberg *et al* (1989) and Jebb *et al* (1993) noted that BIA underestimates loss of fat mass during dieting. Despite the lack of information on the use of BIA in populations with changing body composition the method is used extensively as it does not require examiner skill, is portable, rapid and inexpensive in comparison to other methods.

In this study, BIA measurements were performed with the women in a supine position, with limbs slightly apart, using a portable four terminal impedance analyzer (BIA 101, RJL System, Detroit, USA.), which supplied a current of 800 $\mu$A at a frequency of 50 kHz. Four self adhesive electrodes were positioned on the right side of the body. Two electrodes were positioned on the wrist (one in line with the ulnar tubercle and the second positioned distally, with 2 cm between electrodes) and two electrodes were positioned on the ankle (one directly over the ankle joint in line with the medial malleolus and the second 2 cm distally). The impedance reading, together with weight, height, sex and age, were then used in the Van Loan and Mayclin (1987) regression equation to predict lean

body mass:

$$\text{Lean Mass} = 17.7868 + (0.000985 \times \text{Height}^2 \text{ in cm}) + (0.03736 \times \text{Mass in kg}) - (0.0238 \times \text{Resistance}) - (4.2921 \times \text{Gender}) - (0.1531 \times \text{age in years})$$

Where for Gender: Females = 1 and Males = 0.

Fat mass was extrapolated by subtracting BIA lean body mass from measured mass and a percentage fat mass was calculated.

2.4) **Blood pressure and heart rate monitoring**

Each morning upon waking (while the women were still in the supine position) systolic and diastolic blood pressures were measured with a Littman Classic stethoscope and a mercury manometer (Baumanometer, W.A Baum Co, Inc. Copiague, N.Y., U.S.A.) to the nearest mmHg. Heart rate was also determined from a wrist pulse.

2.5) **Blood Analysis**

Overnight, fasting blood samples were collected by a medical doctor before beginning the diet, after two weeks and again after four weeks of dieting. Samples were collected in the mornings between 07h00 and 09h30. Blood was collected in sterile evacuated blood collection tubes (Vac-U-Test®). For glucose analysis, 3 ml of blood was collected in a tube containing potassium oxalate/sodium fluoride. Blood collected for all other analyses was collected in four, 5 ml silicone coated tubes that contained no additive. The serum was separated from the cells by centrifugation at 3000 g for 5 minutes. The serum was then stored at -70 °C until analyses were performed. All the blood samples collected

from a subject were stored and were measured in one assay. All blood analyses were conducted with commercially available kits in a professional clinical laboratory.

### 2.5.1) Albumin

Serum albumin was determined using the bromcresol-green dye-binding technique originally described by Doumas *et al* (1941) and modified by Technicon® for use by Technicon RA100 commercial kit system (Technicon method Id-2G14-J88). The serum sample was added to the bromcresol green reagent to form the albumin-bromcresol green complex. The analytical solution was mixed for approximately 35 seconds and the absorbance was measured at 610 nm. Absorbance data were then converted to concentration units using the formula:

Albumin concentration = Sample absorbance/Calibrator absorbance x Calibrator concentration

### 2.5.2) Glucose

Serum glucose was determined using an enzymatic colorimetric test described by Trinder (1969) and modified by Technicon® for use by the RA100 commercial kit system (catalogue number: GL-369). Serum glucose was determined by enzymatic oxidation in the presence of glucose oxidase. The formed hydrogen peroxide reacted under catalysis of peroxidase with phenol and 4-aminophenazone to form a red-violet quinoneimine dye that acted as the indicator. Absorbance was measured at 500 nm and glucose concentration was determined from the absorbance using the formula:

Glucose concentration (mmol/L) = Absorbance sample/Absorbance standard x Concentration of standard

The standard glucose concentration was 5.55 mmol/L.

### 2.5.3) Cortisol

Serum cortisol concentration was determined by the radioimmunoassay method described by Foster and Dunn (1974) and the Amerlex Cortisol radioimmunoassay kit (Code IM. 2021, Amersham, Aylesbury, UK) was used. The assay method releases cortisol from transcortin by a chemical blocking agent, contained in an $^{125}$I-labelled cortisol derivative solution. Total cortisol in the sample was then free to compete with the $^{125}$I-labelled cortisol derivative for binding sites on the antibody-coated particles. The amount of $^{125}$I-labelled cortisol derivative bound to antibody was inversely proportional to the concentration of unlabelled cortisol in the serum. The antibody bound $^{125}$I-labelled cortisol derivative was separated by centrifugation and the polymer particles to which it was attached formed a readily observed precipitate in the assay tubes. After removal of the supernatant liquid, the precipitated radioactivity was measured in a gamma counter. The concentration of cortisol was then interpolated from dose response curves prepared using standards.

### 2.5.4) Triiodothyronine ($T_3$)

Serum triiodothyronine ($T_3$) concentration was determined by radioimmunoassay as described by Ekins (1978). The Amerlex-M-Free $T_3$ RIA kit (Code IM.3101, Amersham, Ayelsbury, UK) was used. A high specific activity [$^{125}$I]-triiodothyronine derivative, was used as the radioactive tracer. This tracer was mixed with a serum sample and a specific high affinity $T_3$ antibody and an equilibrium was established in which the free $T_3$ and the [$^{125}$I]-triiodothyronine derivative competed for a limited number of binding sites on the antibody. In common with conventional radioimmunoassay techniques the proportion of

[$^{125}$I]-triiodothyronine derivative bound to the $T_3$ antibody was inversely related to the concentration of free $T_3$ present in the serum. The Amerlex-M antibody suspension contains antibodies that are bound to magnetisable polymer particles. Separation of the antibody-bound fraction was effected by magnetic separation of the Amerlex-M suspension and decantation of the supernatant. By measuring the proportion of known [$^{125}$I]-triiodothyronine derivative bound in the presence of reference standard sera containing known concentrations of free $T_3$, the concentration of free $T_3$ in unknown samples was interpolated.

### 2.5.5) Total Cholesterol

Total cholesterol was determined after enzymatic hydrolysis and oxidation (Randox Laboratories, LTD, Antrim, Northern Ireland, catalogue number: CH 200), using the method originally described by Richmond (1973). The indicator quinoneimine was formed from hydrogen peroxide and 4 aminoantipyrine in the presence of phenol and peroxidase. Absorbance was measured at 500 nm and total cholesterol concentration was calculated from the formula:

> Concentration of cholesterol in sample = Δ Absorbance of sample/Δ Absorbance of standard x concentration of standard
>
> The concentration of the standard was 5.17 mmol/L.

### 2.5.6) Triglycerides

Triglycerides were determined by enzymatic hydrolysis with lipases (Randox Laboratories, LTD, Antrim, Northern Ireland, catalogue number: TR 213). The indicator

quinoneimine was formed from hydrogen peroxide, 4-aminophenazone and 4-chlorophenol under the catalytic influence of peroxidase (Trinder, 1969). Absorbance was measured at 500 nm and triglyceride concentration was determined from the formula:

Triglyceride concentration = absorbance of sample/absorbance of standard x concentration of standard

The concentration of the standard was 2.29 mmol/L.

**2.5.7) High density lipoprotein (HDL)**

High density lipoprotein was determined enzymatically (Randox Laboratories, LTD, Antrim, Northern Ireland.) Low density lipoproteins (LDL and VLDL) and chylomicron fractions were precipitated quantitatively by the addition of phosphotungstic acid in the presence of magnesium ions. After centrifugation, the cholesterol concentration in the HDL fraction, which remained in the supernatant was determined using the same method as that used for cholesterol. This method was originally described by Lopes-Virella *et al* (1977).

**2.5.8) Low density lipoprotein (LDL)**

Low density lipoprotein was determined using the Friedewald formula:

LDL cholesterol concentration (mmol/L) = Total cholesterol - Triglycerides/2.2 - HDL cholesterol, (Friedewald *et al*, 1972).

The values obtained from the formula were considered reliable provided that the

triglyceride concentration did not exceed 4.5 mmol/l.

## 2.6) Psychological variables

### 2.6.1) Performance testing

Visual, auditory vigilance, word memory and addition tasks are some of the numerous ways in which performance can successfully be assessed. In this study visual reaction tests were employed to assess hand-eye coordination performance. Both simple and complex visual reaction tests were used as it has been shown that simple and complex tasks may yield different results in deprivation studies (Hockey, 1970). These tests were performed in the morning following the nights spent in the sleep laboratory. The tests were performed at approximately the same time each morning, since there is evidence of a marked rhythmicity in human performance (Mikulincer *et al*, 1989). On the adaptation nights (baseline 1 and diet 14) the women were required to perform at least six, five minute practises on the complex reaction test. Reaction tests performed on baseline mornings 3, 7, 11 and 15 and those performed on diet mornings 16, 20, 24 and 28 were used for analysis.

The simple reaction test was performed using an IBM compatible PC, a computer keyboard and a monochrome monitor. The test consisted of randomly introduced and positioned single crosses on the monitor screen. On seeing a cross the women depressed a given key, and the reaction time was recorded. The next cross appeared randomly within seconds after a key was depressed. The duration of the test was approximately two minutes. Each test consisted of 50 cross presentations and an average reaction time for the 50 crosses was used for analysis.

Complex reaction tests were performed using a modified version (Wyon *et al*, 1980) of the apparatus originally used by Leonard (1959). The test assessed speed of response and accuracy of response to a variable stimulus. The apparatus was comprised of two panels, an upper panel inclined at 60 ° and a lower panel inclined at 25 °, linked to a microcomputer. On the upper panel 5 small red lights, 45 mm apart, were arranged in a pentagon and on the lower panel 5 brass discs, 90 mm apart, were arranged in a corresponding pentagon. When a light was illuminated, the women reacted by tapping the corresponding brass disc with a stylus. Tapping a disc immediately extinguished the light and another was illuminated at random. The information acquired during each test was recorded on an IBM compatible microcomputer. The women were required to perform two consecutive tests each lasting five minutes, the second of which was used for analysis. The following variables were determined by the computer and were used for analysis:

- Mean Reaction Time: the mean time in milliseconds from the light being lit to the subject hitting the correct disk.
- Correct Hits: the number of times a correct choice of disk was made.

**2.6.2) Mood and psychological profile assessment**

Mood was assessed using the Profile of Mood States (POMS) questionnaire (McNair *et al*, 1971; appendix 4). The POMS was designed as a rapid, economical method of identifying and assessing transient, fluctuating affective states (McNair *et al*, 1992). It is diversely used in studies ranging from psychiatric intervention studies to numerous experimental manipulation studies on normal subjects, and it's use is prevalent in sport and exercise research (McNair *et al*, 1992). The POMS factors correlate significantly well with factors from other popular mood questionnaires such as the Beck Depression

Inventory and the Manifest Anxiety Scale (McNair *et al*, 1992). The test is recommended for research purposes for normal subjects age 18 and older who have at least some high school education.

In this study the POMS was completed before and after two weeks of dieting, in the evenings before retiring to bed. The POMS is a self-administered test and is completed in about three to five minutes. The questionnaire contains 65 items and the women had to respond to each item (eg. angry, worn out, lively) in terms of "how have you been feeling during the past week including today?". The women were required to circle one of five descriptive phrases 0 = Not at all, 1 = A little, 2 = Moderately, 3 = Quite a bit, 4 = extremely. The questionnaire yields a score for six different mood factors: 1) Factor T, is defined by adjectives descriptive of heightened musculoskeletal tension and anxiety; 2) Factor D represents a mood of depression accompanied by a sense of personal inadequacy and dejection, 3) Factor A is characterised by a mood of anger and hostility towards others, 4) Factor V defines a mood of vigour, ebullience and high energy, 5) Factor F represents a mood of fatigue, inertia and low energy levels and, 6) Factor C is characterised by confusion and bewilderment. The scores for each factor were obtained using overlay stencils. These scores were then plotted on a college norm POMS profile sheet (appendix 4). The college norm profile sheet is based on norms collected for 350 men and 516 women. The profile sheet converts raw scores to *T* scores, which were then used for statistical analysis. A measure of global mood was also obtained. The global mood score was computed by adding the scores for the five negative mood states (tension, depression, anger, fatigue and confusion) and subtracting the score for the one positive mood state (vigour). Since this computational procedure sometimes yields negative values, a constant of 100 was added in accordance with the calculations made

by Morgan *et al*, (1987).

Visual analogue scales were used to assess changes in psychological profiles. They were completed in the mornings following each visit to the laboratory (appendix 5). The women were required to make a cross on a series of 10 cm lines. A cross at 5 cm indicated no change from "normal" with respect to the specific question. Variables tested were concentration, mood, vitality, irritability, temperature sensitivity, subjective need for sleep and subjective sleep quality (appendix 5).

2.7) **Sleep Recordings**

Electrophysiological sleep recordings were carried out in the Edblo Sleep Laboratory in accordance with the methods described by Oswald (1987). The women were studied in groups of three, but were allocated to their own bedrooms. Data from the first night of each experimental phase (baseline, night 1 and diet night 14) were excluded from the respective data sets and were considered to be adaptations to the new environment and the electrodes. Sleep recordings from baseline nights 3, 7, 11 and 15 and diet nights 16, 20, 24 and 28 were used for sleep data analysis.

Electrophysiological recordings were made using silver electrodes. The length of the electrode wires (1.5 m) was long enough so that the women could move freely. The electrode wires were plugged into a headbox situated above the bed. From the headbox the wires led to a 16 channel electroencephalograph (Montage 20, Beckman instruments Inc., IL60/70, USA) which was situated in an adjacent room. For sleep recordings or a polysomnograph, measures of electrical potentials from 1) the brain, [the electroencephalograph (EEG)], 2) eye movements, [the electro-oculograph (EOG)] and

3) movement from muscle areas on the chin, [the electromyograph (EMG)] were obtained. Recordings were made at a paper speed of 15 mm/s. The EEG paper used was 30 cm wide and one page was therefore recorded in 20 seconds. This 20 second per 1 page interval is referred to as a "epoch". A calibration voltage of 50 $\mu$V was used with a high frequency filter of 15 Hz to dampen unwanted signals eg. high frequency muscle activity. A time constant (or low frequency filter) of 0.3 seconds was used to detect slow eye movements.

2.7.1) **Electrode Placement**

Prior to placing the electrodes, the skin and scalp were cleaned with alcohol and were then scratched lightly to ensure a low electrode resistance. Electrodes were filled with a jelly containing saline (Electro-Gel, Electro-Cap International Inc, Dallas, Texas, USA) to aid electrical conductance. The facial electrodes were attached to the skin using hypoallergenic dressing tape, and scalp electrodes were attached using collodion 4 % nitrocellulose solution (Merck, Darmstadt, Germany).

Electrode placement followed the method described by Oswald (1987). Eight electrodes and an earth were placed at various positions along the scalp and face. The electromyogram recording was obtained by placing two electrodes approximately 8 cm apart under the point of the jaw, on or beneath the chin [labelled electrodes 1 (right electrode) and 2 (left electrode)], (Table 2.2).

The eye movements were recorded by placing an electrode to the side of the canthus of each eye, [labelled electrodes 3 (right) and 4 (left)]. A further two electrodes were positioned on the forehead above the eyebrow, in line with the middle of each eye, [with

number 5 being on the right and number 6 on the left side of the face], (Table 2.2).

The EEG was measured from two electrodes placed on the middle of the head, electrode 7 on the vertex central ($C_z$) and electrode 8 on the parietal area ($P_z$), (Table 2.2) and the earth electrode was positioned in the centre of the forehead.

The electroencephalograph was recorded by monitoring electrical potentials between two given electrodes on set channels (Table 2.2).

**Table 2.2** Electroencephalograph settings.

| Record | Channel | Electrodes | Time constant (sec) |
|---|---|---|---|
| EOG/Right eye | 1 | 6 + 3 | 0.3 |
| EOG/Left eye | 2 | 5 + 4 | 0.3 |
| EOG/EEG | 3 | 8 + 5 | 0.3 |
| EEG | 4 | 7 + 8 | 0.3 |
| EMG | 5 | 1 + 2 | 0.03 |

### 2.7.2) Sleep Scoring

The criteria used for the visual scoring of sleep records in this study are based on the internationally recognised system of Rechtschaffen and Kales (1968). Scoring a sleep record involves recognition of the different sleep stages and is done by noting a change in sleep stage and the page number when a transition from one stage to another occurs.

The electroencephalogram can broadly be divided into three different states: the waking state, non-rapid eye movement (non-REM) sleep and rapid eye movement (REM) sleep.

The waking state (also referred to as **Stage 0**) is represented in Figure 2.1 (Driver, 1992), and is characterised by alpha activity and/or a low voltage mixed frequency EEG. The amount of alpha varies considerably from subject to subject. Eye blinks are often present in the EOG trace and a relatively high tonic EMG is characteristic of wakefulness.

Non-REM sleep is comprised of stages 1, 2, 3 and 4. **Stage 1** is a transition phase between wakefulness and sleep (Figure 2.2; Driver, 1992). It is identified by low voltage 2-7 $H_z$, mixed frequency EEG activity which comprises more than 50 % of an epoch. Vertex sharp waves may occur during stage 1, however sleep spindles* and K complexes** are absent. This stage is also characterised by slow eye movements of several seconds duration. Rapid eye movements are absent and tonic EMG levels are usually below those of relaxed wakefulness. **Stage 2** is the first bona fida sleep stage (Figure 2.3; Driver, 1992). It is characterised by the presence of sleep spindles* (EEG activity of 12-14 $H_z$ - one should be able to count 6 to 7 distinct waves within a half-second period) and K complexes** (EEG wave forms that have a well delineated negative sharp wave followed immediately by a positive component). The duration of both sleep spindles and K complexes should exceed 0.5 seconds. **Stages 3** and **4** together comprise slow wave sleep. **Stage 3** (Figure 2.4; Driver, 1992) is distinguished by an EEG record in which between 20 % and 50 % of the epoch consists of slow frequency (1-4 $H_z$), high amplitude (greater than 75 $\mu$V) waves. It is important to note that the amplitude of these slow waves

decreases across a night's recording. The amplitude is also influenced by inter-electrode distance, electrode placement and time constants. **Stage 4**, (Figure 2.5; Driver, 1992) is defined by an EEG record in which more than 50 % of an epoch consists of slow frequency, high amplitude waves. Sleep spindles may or may not occur during stages 3 and 4.

Non-REM sleep alternates with REM sleep at about ninety minute intervals. Non-REM and REM continue to alternate throughout the night in a cyclic fashion, with REM sleep episodes becoming longer and non-REM episodes becoming shorter across the night. **REM** (Figure 2.6; Driver, 1992) sleep is characterised by relatively low voltage, mixed frequency EEG activity and episodic rapid eye movements. It differs from stage 1 in that vertex sharp waves are not prominent, instead distinctive 2-3 $H_z$ "saw-tooth" waves frequently occur. Tonic EMG is almost always at it lowest, however, bursts of phasic muscle activity occur during REM. Towards the beginning and end of REM episodes sleep spindles may occur and the scorer should then distinguish between REM and stage 2 sleep by determining which distinguishing features are predominant.

Both non-REM and REM sleep are frequently interrupted by body movements. **Movement** time is scored when, in more than half an epoch, the EEG and EOG tracings are obscured by muscle tension and/or amplifier blocking artifacts associated with movement of the subject. The movement may be followed immediately by an awakening, in which case it is scored as stage 0, or it may lead to a slight arousal, indicated by a brief period of stage 1.

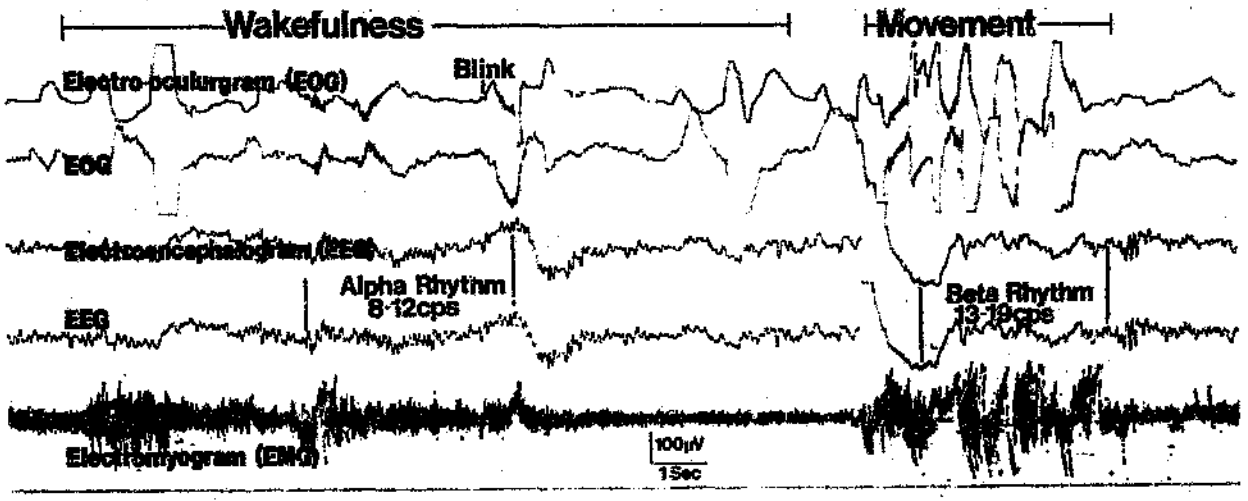



**Figure 2.1** An epoch from a polysomnograph of wakefulness (Driver, 1992)

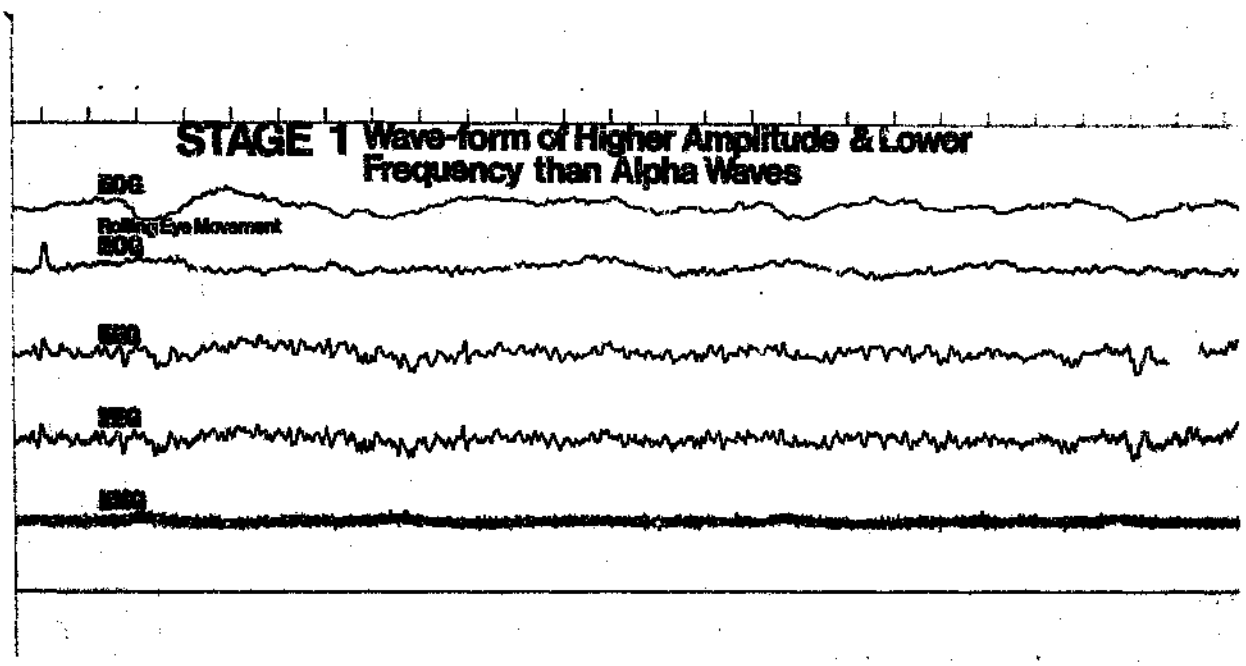



**Figure 2.2** An epoch from a polysomnograph of stage 1 sleep (Driver, 1992)

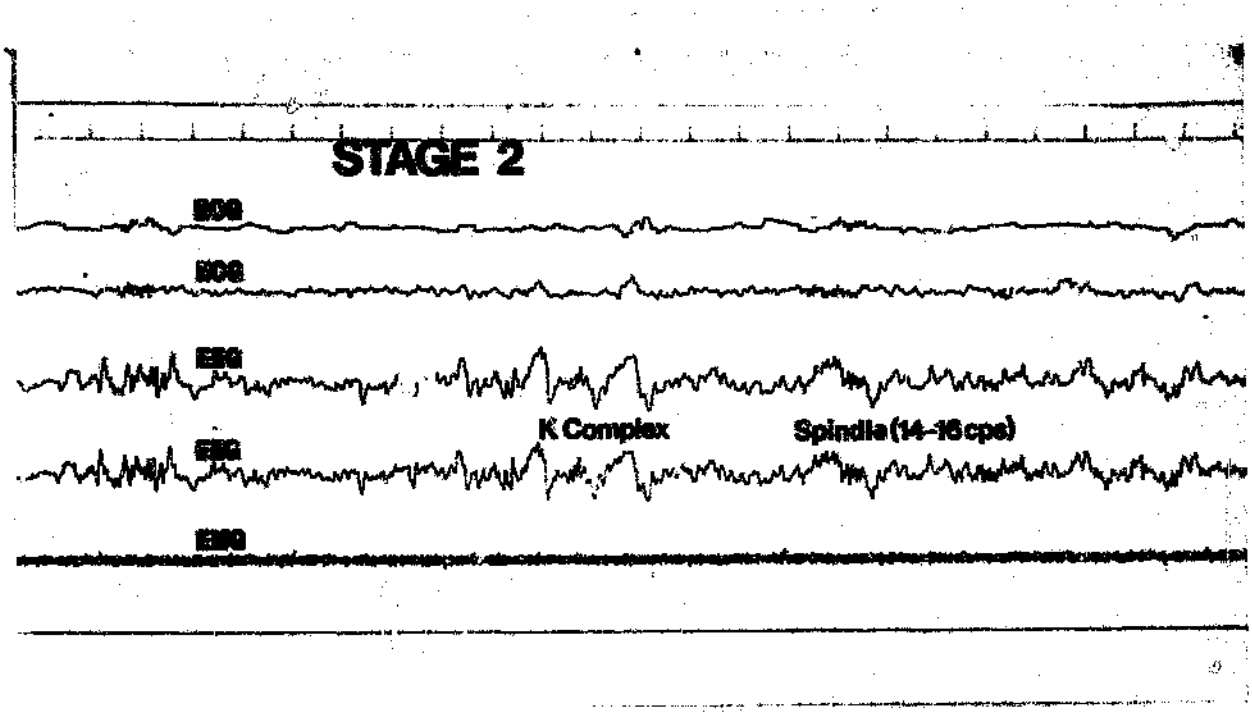



Figure 2.3 An epoch from a polysomnograph of stage 2 sleep (Driver, 1992)

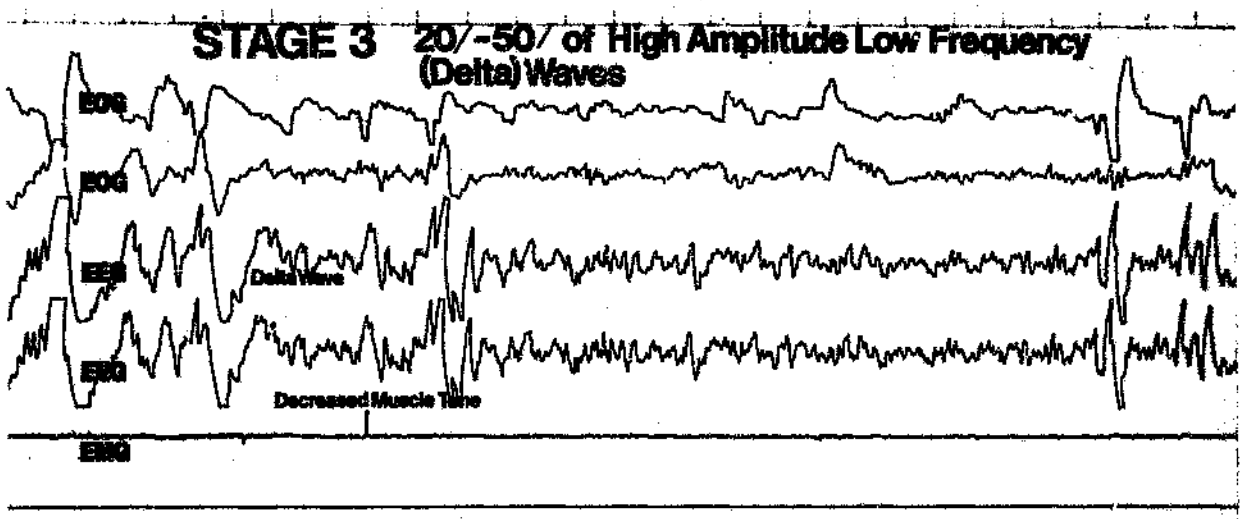



Figure 2.4 An epoch from a polysomnograph of stage 3 sleep (Driver, 1992)

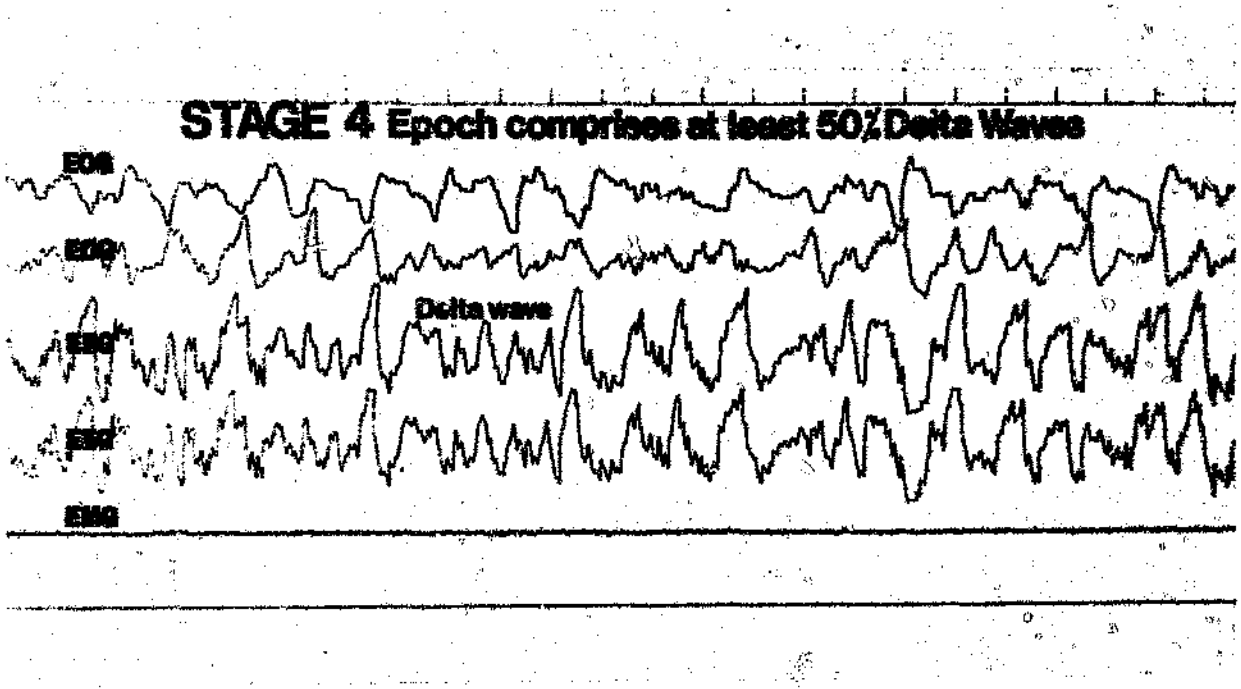



Figure 2.5 An epoch from a polysomnograph of stage 4 sleep (Driver, 1992)

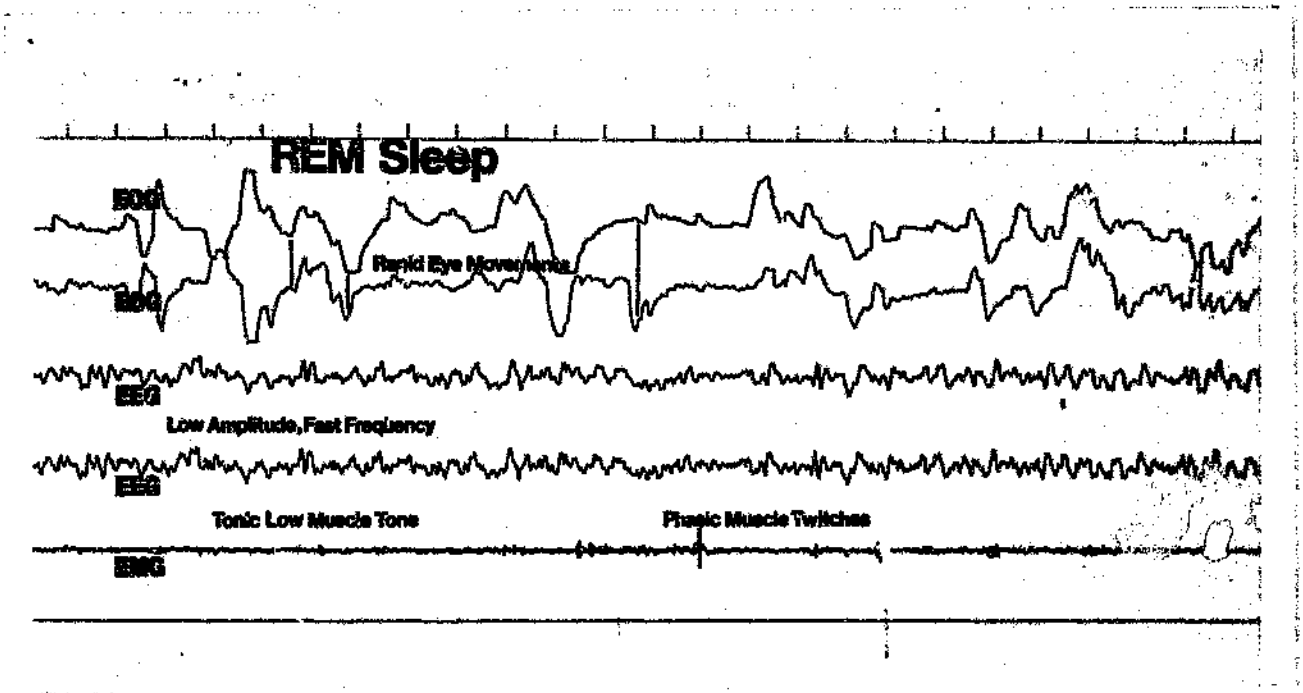



Figure 2.6 An epoch from a polysomnograph of REM sleep (Driver, 19.?)

2.7.3) **Sleep variables**

In this study the following sleep parameters were examined:

- Sleep Onset Latency (SOL): the time taken to the first appearance of three consecutive epochs of stage 2 sleep after lights out.
- REM sleep onset latency (ROL): the time taken to the first REM sleep episode after SOL.
- Slow wave sleep (SWS): the absolute time spent in stages 3 and 4 of non-REM sleep.
- REM : the absolute time spent in rapid eye movement sleep.
- Awake and Movement time (A + M): the time spent in stage 0 and movement time added together.
- The ratio of SWS in the first and second sleep cycles:

Sleep cycles were defined as the time from the beginning of stage 2 sleep in each cycle to the end of the following REM period. (Trinder *et al*, 1982). The first REM period of the night was identified at the first indication of REM sleep characteristics. Subsequent REM periods required 5 minutes of REM within a 7 minute interval. The REM period was considered to have ended when no REM characteristics were detected for 15 minutes.

Lights out time and waking time were not specified in order to allow the women to maintain their normal working routines. Because the women had to be woken up for work it was not possible to measure uninterrupted total sleep duration. Since the mean total recording time was not constant, the time in REM, time in SWS and A + M time were calculated over the first six hours after lights out.

## 2.8) Temperature Recordings

Instantaneous rectal temperatures were measured throughout the night, using plastic covered copper-constantan thermocouples. Approximately fifteen minutes before lights out the thermocouples were inserted approximately 10 cm into the rectum and were connected to an MC-Systems 120-02 data logger (Cape Town, South Africa), this allowed for stabilisation of temperature readings. The thermocouples were calibrated against a standard mercury thermometer to an accuracy of 0.1 °C. Ambient temperatures were maintained at 21 °C ± 3.0 °C. Although ambient room temperatures may seem low the women slept with down duvets and the microclimate to which they were exposed was not considered to be a cold stress.

The following variables were examined:

- Minimum nocturnal temperature
- The time at which the minimum temperature occurred
- The amount of time from lights out until the occurrence of the minimum temperature
- The temperature and time on awakening
- A six hour thermal response index calculated from the area under the curve. This gave an indication of the mean change in nocturnal temperature over the recording time.

## 2.9) Statistical Analyses

For each subject, energy intake and diet composition data from the five selected baseline and five diet days were meaned. These days were assumed to represent the average

energy intake and diet composition for the baseline and diet phases respectively. Baseline and diet values were compared using the paired Student's *t* test. Similarly changes in weight and body composition, calculated after two and four weeks of dieting were evaluated with paired Student's *t* tests and Bonferroni corrections.

The appropriate statistical analysis when comparing indirect body composition techniques is that described by Bland and Altman, (1986). This method is used when the measuring units of each method are the same. Since BMI ($kg/m^2$) yielded a different unit of measurement to SM and BIA (% fat), the three methods were compared using percentage changes. Percentage changes after two and four weeks of dieting were calculated. The differences in the percentages changes between the methods were then calculated. Since the differences are likely to follow a normal distribution (Bland and Altman, 1986) paired Student's *t* tests with Bonferroni corrections were used to determine if the techniques differed.

Bland and Altman (1986) discourage against the use of correlation coefficients when comparing different techniques that measure the same thing, since correlation coefficients measure the strength of a relationship between two variables and not the agreement between them. Furthermore, these authors emphasise that the strength of a correlation can be improved by studying a broad range of subjects. In this study subjects with a narrow range of body fatness were used (n = 9). The failings of correlation coefficients have been recognised but they have been calculated in order to assess linearity between the body composition measurements. Pearson's product-moment correlation coefficients were used to perform linear regression analysis.

For each subject, blood pressure and heart rate data collected on the five baseline and diet days respectively, were meaned to give an average value for the baseline and diet phases. Mean heart rate and blood pressure, and all blood variables and hormone concentrations (which were assessed after two and four weeks of dieting) were analyzed using paired Student's *t* tests and Bonferroni corrections where appropriate.

Differences in the simple and complex reaction test variables and visual analogue scales were determined between corresponding baseline and diet nights B3/D16, B7/D20, B11/D24, and B15/D25 (see Table 2.1). Baseline and diet reaction test variables were compared using paired Student's *t* tests and visual analogue scale variables were compared using the Wilcoxon signed rank test. POMS questionnaire factors (measured before and after two weeks of dieting) were related using paired Student's *t* tests.

All ten recording nights spent in the sleep laboratory were used for temperature data analysis. For each subject the temperature variables from the five baseline nights were averaged as were those from the five diet nights. The mean values were compared using paired Student's *t* tests. Changes in sleep data from corresponding baseline and diet nights B3/D16, B7/D20, B11/D24 and B15/D28 were assessed using the Wilcoxon signed rank test.

When multiple comparisons were made in this study, the Bonferroni *t* test statistic was used. All data were expressed as means $\pm$ standard deviations (SD) and were considered significantly different at $P < 0.05$ for two tailed tests. Calculations were performed in accordance with methods described by Glantz (1992).

# CHAPTER 3

## 3 Alterations in weight, energy intake, and body composition with month long energy restriction.

### 3.1) Introduction

The use and efficacy of very low energy diets in the treatment of obesity, has gained much attention in recent years, (Foster *et al*, 1990; Foster *et al* 1992; Pi-Sunyer, 1992). Most scientific/clinical studies have examined obese subjects with body mass indices greater than 30 kg/m$^2$. Since a great deal of emphasis is placed on body image in modern society, many normal to slightly overweight individuals use very low energy diet as a means of rapid weight loss. In this study, a group of these individuals, women with class 1 obesity (BMI between 25 and 30 kg/m$^2$), were placed on a 3347 KJ/d (800 Kcal/d) diet (Appendix 3). This diet was chosen as there is no advantage to using a lower energy diet (Foster *et al*, 1992), since the perceived advantages of rapid weight loss via extremely low energy diets are in the long term offset by energy sparing mechanisms (Prentice *et al*, 1991). The efficacy of the diet was assessed in terms of both weight loss and changes in body composition.

### 3.2) Methods

The effects of energy restriction and compliance were assessed by monitoring food intake before and during the diet (section 2.2), by comparing calculated PAL values with predefined cut-off limits (section 2.2) and by measuring weight and body composition on a regular basis (as described in sections 2.2 and 2.3). Changes in these variables were assessed using paired Student's *t* tests with Bonferroni corrections (see section 2.9). Pearson product-moment correlation coefficients were used to evaluate the linear

relationships between body composition measurements BMI, SM and BIA as described in section 2.9.

## 3.3) Results

### 3.3.1) Energy intake

During the very low energy diet the women reduced their daily mean energy intake from 9240 ± 1670 KJ/d to 3110 ± 400 KJ/d, a reduction of 6130 ± 1650 KJ/d (1465 ± 394 kcal/d), (Table 3.1). Before dieting, 14 % of daily energy intake was derived from protein, 48 % from carbohydrates and 38 % from fats. The diet composition was altered such that during the energy restriction regime protein contributed 24 %, carbohydrates 59 % and fats 17 % towards energy intake. Absolute protein, carbohydrate and fat intakes declined significantly ($P < 0.05$) with dieting as did cholesterol intake ($P < 0.001$), (Table 3.1). The mean calculated PAL value of 1.49 did not fall below the cut-off limit of 1.4 derived by Goldberg *et al* (1991).

### 3.3.2) Weight

During the two week baseline phase the women significantly gained 0.62 ± 0.47 kg ($P < 0.05$). The women significantly reduced their weight from 71.21 ± 8.06 kg at baseline, to 67.49 ± 7.96 ($P < 0.001$) after two weeks of dieting and to 65.41 ± 7.72 kg ($P < 0.001$) after four weeks of dieting. The women lost a significant amount of weight in the final two weeks of the energy restriction regime ($P < 0.05$). They lost on average 1.45 kg/week (5.80 ± 1.65 kg in total) over the four week diet period, accounting for 8.1 ± 4.2 % of their initial body mass (Table 3.2). Weight loss was significantly more rapid in the first two weeks 3.72 kg (1.86 kg/wk) than in the final two weeks of dieting 2.08 kg (1.04 kg/wk), ($P < 0.05$).

### 3.3.3) Body composition

BMI declined significantly from 26.1 ± 2.9 kg/m$^2$ at baseline, to 24.7 ± 3.0 kg/m$^2$ after two weeks of dieting, and 23.9 ± 2.9 kg/m$^2$ measured after four weeks of dieting. After four weeks of dieting the women displayed a change in lean body mass:change in body mass (ΔLBM:ΔBM) ratio of 0.23 when calculated using BIA, and that of 0.42 when calculated using SM. Percentage changes in BMI, SM and BIA did not differ significantly after two weeks of dieting (Table 3.2). After four weeks of dieting however, the percentage change measured by BIA was significantly larger than that determined by BMI and SM (Table 3.2). Linear regression analyses illustrate that, at baseline, all three methods used to determine body composition correlated significantly with one another. BIA and BMI showing the strongest significant correlation ($r = 0.96$, Table 3.3). As the energy restriction regime progressed, the correlation coefficients between all the techniques decreased (Table 3.3).

**Table 3.1** Energy intake, macronutrient intake and dietary cholesterol intake (mean ± standard deviation) for nine women before (Baseline) and during four weeks of energy restriction (Diet). Mean ± Standard Deviation.

| | Baseline | Diet | Change |
|---|---|---|---|
| Energy (KJ/d) | 9240 ± 1670 | 3110 ± 400 | 6130 ± 1650* |
| Protein (g/d) | 73 ± 17 | 41 ± 15 | 32 ± 23** |
| Carbohydrate (g/d) | 245 ± 50 | 102 ± 15 | 143 ± 46* |
| Fat (g/d) | 96 ± 23 | 15 ± 5 | 81 ± 22* |
| Cholesterol (mg/d) | 261 ± 103 | 86 ± 47 | 175 ± 83** |

* = significantly different from baseline, $P < 0.05$.

** = significantly different from baseline, $P < 0.001$.

**Table 3.2** Percentage changes in weight and body composition as measured by body mass index (BMI), skinfold measurements (SM) and bioelectrical impedance analysis (BIA) after two weeks (2 wk) and four weeks (4 wk) of dieting in nine women. Mean ± Standard Deviation.

| | Weight | BMI | SM | BIA |
|---|---|---|---|---|
| % Δ 2 wks | 5.2 ± 1.2 | 5.6 ± 2.3 | 7.5 ± 3.5 | 9.5 ± 8.3 |
| % Δ 4 wks | 8.1 ± 4.2 | 8.4 ± 2.8* | 6.0 ± 4.0* | 14.6 ± 6.3 |

* = significantly different from BIA, $P < 0.01$.

**Table 3.3** Comparison of body composition techniques, skinfold measurements (SM), body mass index (BMI) and bioelectrical impedance analysis (BIA) using correlation coefficients. Data was obtained using nine premenopausal women before (baseline), after two weeks (2 wk) and after four weeks (4 wk) on an energy restriction diet.

| | SM/BMI | BIA/BMI | BIA/SM |
|---|---|---|---|
| Baseline | 0.71* | 0.96* | 0.71* |
| B - 2 wk | 0.65* | 0.77* | 0.22 |
| B - 4 wk | 0.26 | 0.17 | 0.22 |

* = significant linear correlation, $P < 0.05$.

Baseline regression lines were calculated using absolute values. B - 2 wk (baseline - two weeks) and B - 4 wk (baseline - four weeks) regression lines were calculated using absolute changes.

## 3.4) Discussion

### 3.4.1) Weight and energy intake

The women gained weight during the baseline phase of the experiment. It likely that the women increased their energy intake and/or their intake of high fat foods, in anticipation of the month long energy restriction regime. The weight loss achieved in this study compares favourably with other studies using approximately the same degree of energy restriction (Davies *et al*, 1989; Foster *et al*, 1992; Garrow and Webster, 1989). In an earlier study, eight obese women with a mean weight of 100 ± 14 kg (BMI = 39.3 ± 4.2 kg/m$^2$) on a 780 kcal/d diet, lost an average of 1.45 kg/week (Davies *et al*, 1989),

which is identical to the weight loss achieved in this study using much thinner women (71.21 ± 8.06 kg, BMI 26.1 ± 2.9 kg/m$^2$). A similar weight loss to that reported in other studies might indicate that the women complied with the diet. This is supported by the fact that the mean energy intake reported by the women (Table 3.1) is likely to represent the actual food consumed during the study, since the calculated PAL value falls above the cut-off limit derived to determine implausible reported energy intakes (Goldberg *et al*, 1991). A reduction in the energy contribution of fats towards the total energy intake (from 38 % to 14 %) is likely to have facilitated the weight loss. The phase of rapid weight loss which occurred in the first two weeks of dieting is most probably due to the loss of glycogen stores and associated water pools (Webster and Garrow, 1989).

### 3.4.2) Body composition measurements

Despite the fact that protein contributed 10 % more towards total energy intake during the diet than during baseline (Table 3.1), a loss of lean body mass accompanied the loss of fat mass. Forbes (1987) emphasised that the composition of weight loss is primarily determined by the initial fatness of the subject, with fatter subjects displaying lower ratios of ΔLBM:ΔBM, than slimmer subjects. Prentice *et al* (1991) advocates that, at fat masses common in dieting, a ratio of 0.25 is appropriate. Since the women in this study were slimmer than those usually examined on very low calorie diets, a larger ΔLBM:ΔBM ratio was expected. When body composition was assessed using skinfold measurements a ratio of 0.42 was calculated, implying that the subjects lost 42 % lean mass and 58 % fat mass. However, when BIA was used to assess body composition a ratio of 0.23 was calculated. Since none of the body composition methods used in this study are considered gold standard techniques, it is not possible to determine which method is more precise and so conclusions about the ratios cannot be drawn. The discrepancy between the two

ratios implies an inconsistency between the BIA and SM measurements of body composition.

Body mass index, SM and BIA are all used as indices of obesity and should show broadly similar changes in body composition with time. The different ΔLBM:ΔBM ratios and the dissimilar percentage changes in Table 3.4 reflect that the methods do not measure similar changes in body composition. In a study by Jebb *et al* (1993), various body composition techniques were compared to a gold standard. It was reported that in a comparative underfeeding trial BIA overestimates the change in percentage body fat. The significant increase in percentage change in body composition after four weeks of dieting (Table 3.2), may also imply an overestimation by BIA. Segal *et al* (1988) emphasised that BIA measures hydrated lean tissue and does not measure body fat, either quantitatively (kg of fat) or qualitatively (fat as a percentage of total body weight) and therefore discourages against the use of BIA in this way. Thus, the overestimation by BIA may simply be due to an incorrect assumption that the lean body mass measurement obtained by the BIA method may be converted to percentage body fat units. Alternatively, the discrepancy noted with BIA may be linked to the use of an age and gender specific regression equations compiled from normal subjects, with normal glycogen and water pools (Van Loan and Mayclin, 1987). Deurenberg *et al* (1989) noted that BIA underestimates the mean weight loss of fat free mass when compared to densitometry. Since the current used in the impedance method (800 uA, 50 KHz) does not totally penetrate cell membranes, intracellular water is not fully measured by this method and the decrease in glycogen stores and the corresponding water loss that occurs during weight loss, may not be detected by BIA (Deurenberg *et al*, 1989). Fat free mass in a slimming population may therefore be underestimated (Deurenberg *et al*, 1989).

An underestimation of fat free mass would result in a concomitant overestimation of percentage body fat, as was noted in this study, and furthermore may explain the smaller ΔLBM:ΔBM ratio calculated by BIA when compared to SM. The inaccurate measurement of glycogen and water pool changes may be responsible for the observation that the BIA measurement only deviated from other methods after two weeks of dieting. Deurenberg *et al* (1989) suggest that a correction factor be introduced when impedance is used to follow people during slimming and exercise. To date there are no prediction equations using BIA as a measure of fat change during slimming. Use of prediction equations not designed for this purpose merely give a rough indication of fat changes. Additionally, the assumptions inherent in the BIA method, may not necessarily hold true during weight loss, for example resistivity may not be constant during weight loss.

The discrepancies noted between BIA and SM methods in this study may partly be due to SM underestimating changes in body composition (Jebb *et al*, 1993). SM showed the smallest percentage change in body composition after four weeks of dieting (Table 3.2). Jebb *et al* (1993) noted that skinfold measurements underestimate changes in body composition when compared to a gold standard and Teran *et al* (1991) verified that the use of the Durnin and Wormersly (1974) equation significantly underestimates changes in percentage body fat. SM fat assessment is based on the assumption that the thickness of subcutaneous fat reflects a constant proportion of total body fat. It is therefore assumed that in weight loss studies, the amount of subcutaneous fat lost is proportional to internal fat loss. It is possible that, as a diet progresses, internal fat loss increases in proportion to subcutaneous fat loss, especially in subjects with class 1 obesity. SM may not detect changes in internal fat loss and may therefore underestimate changes in percentage body

fat.

The regression analyses (Table 3.3) show that during a steady state (baseline) the three methods are linear since they are significantly correlated. During energy restriction however, linearity decreases (Table 3.3). Considering the significant differences between the percentage changes in body composition and the differences in the ΔLBM:ΔBM ratios it is possible that the changes in linearity also imply that the three methods differ in their measurement of changing body composition. The results from this study emphasise that the techniques and their associated prediction equations should not be used interchangeably in populations where body composition is changing.

## 3.5) Conclusion

In this study, energy intake and the contribution of fats towards daily energy intake declined significantly and weight loss was comparable to that achieved in studies using similar energy restriction diets. Body composition methods differed significantly in their measurement of changing body composition. However, all the methods showed a significant alteration in body composition with energy restriction. From the reported changes in energy intake, and the reductions in weight and body composition it seems reasonable to assume that a) the women complied with the 3347 KJ/d (800 kcal/d) diet and b) an 800 kcal/d energy restriction regime induces rapid weight loss.

# CHAPTER 4

## 4 Alterations in cardiac function, physiological nutritional status and hormone concentrations with month long energy restriction.

### 4.1) Introduction

Physiological changes other than desired alterations in body composition and weight, commonly occur with energy restriction (Pi-Sunyer, 1993). Plasma concentrations of glucose, albumin, triglycerides and cortisol may be altered by a negative energy balance (Dattilo and Kris-Etherton 1992; Hainer *et al*, 1992; Scafi *et al*, 1990; Webber and MacDonald, 1994) and may thus act as indicators of metabolic state. Indeed plasma lipid profiles change substantially and cardiac risk factors are reduced with weight loss (Dattillo and Kris-Etherton, 1992; Dustan 1985). Furthermore, a reduction in $T_3$ commonly occurs with energy restriction and leads to a corresponding suppression of metabolism (Prentice *et al*, 1991). In this chapter, changes in physiological nutritional status (assessed by measuring changes in glucose, albumin and lipoprotein concentrations), changes in hormone concentrations (serum $T_3$ and cortisol) and changes in blood pressure and heart rate, were assessed in non-obese women.

### 4.2) Methods

Morning, fasting blood samples were taken before commencing the diet, after two and after four weeks of dieting (see section 2.5 and 2.9). Supine blood pressures and heart rates (determined on waking) from the five baseline mornings were meaned, as were those from the five diet mornings (see sections 2.4 and 2.9). Changes in all variables were assessed using paired Student's *t* tests (see section 2.9)

4.3) **Results**

Throughout the duration of this study glucose, albumin, triglycerides, LDL, HDL and $T_3$ serum concentrations were within normal ranges for young healthy women (Smith and Miles, 1991).

Serum cortisol and $T_3$ concentrations were significantly decreased, after two weeks of dieting (by 15.3 % and 22 %, respectively) and after four weeks of dieting by (13.6 % and 18.9 %) when compared to baseline (Figure 4.1). Cortisol concentration was significantly reduced from 1162 ± 415 nmol/L before dieting, to 906 ± 308 nmol/L, after two weeks, and to 942 ± 413 nmol/L, after four weeks of dieting (Figure 4.1 iii). Throughout the study, cortisol concentrations were higher than normal values given for samples taken at 8h00. $T_3$ fell significantly from 5.9 ± 0.7 pmol/L at baseline to 5.0 ± 0.7 pmol/L after two weeks, and to 5.1 ± 0.6 after four weeks on an energy restriction regime (Figure 4.1-iv). The restricted energy intake did not alter serum glucose (Figure 4.1 i), albumin (Figure 4.1 ii) or triglyceride (Figure 4.2 i) concentrations.

Serum total cholesterol, LDL and HDL concentrations were all significantly reduced compared to baseline values (Figure 4.2). The mean baseline total cholesterol concentration (5.25 ± 0.6 mmol/L) was above the normal range for South African women with a mean age of 26 ± 6 years, and fell within the moderate risk factor range for coronary heart disease (Rossouw *et al*, 1988). However, total cholesterol fell significantly after two weeks of dieting (4.27 ± 0.55 mmol/L,) and after four weeks of dieting (4.28 ± 0.59 mmol/L; Figure 4.2 ii), to concentrations considered desirable (Rossouw *et al*, 1988). LDL concentration decreased by 0.62 ± 0.29 mmol/L after two weeks of dieting (Figure 4.2 iii). Neither total cholesterol nor LDL concentrations

decreased further in the third and fourth weeks of energy restriction. Although, HDL concentration was significantly decreased from baseline (1.39 ± 0.26 mmol/L) after four weeks of energy restriction (1.16 ± 0.25), it increased significantly by 0.11 ± 0.13 mmol/L from week two to week four of the diet (Figure 4.2 iv). HDL/LDL ratios were not significantly different from baseline (0.45 ± 0.15), after two (0.41 ± 0.12) or four weeks (0.48 ± 0.13) of dieting. Furthermore, there were no significantly differences between two and four week ratios of HDL/LDL.

Systolic blood pressure was significantly reduced by 5.4 % (from 111 ± 4 to 105 ± 6 mmHg, $P < 0.05$) and heart rate was significantly reduced by 7.6 % (from 66 ± 6 to 61 ± 4 beats/minute, $P < 0.05$), with energy restriction. Dieting did not alter diastolic blood pressure [(baseline) 75 ± 6 mmHg; (diet) 70 ± 6 mmHg]. Changes in both systolic and diastolic blood pressures did not correlate with the changes in weight noted in chapter 3 ($r = 0.25$ and $r = 0.17$, respectively).

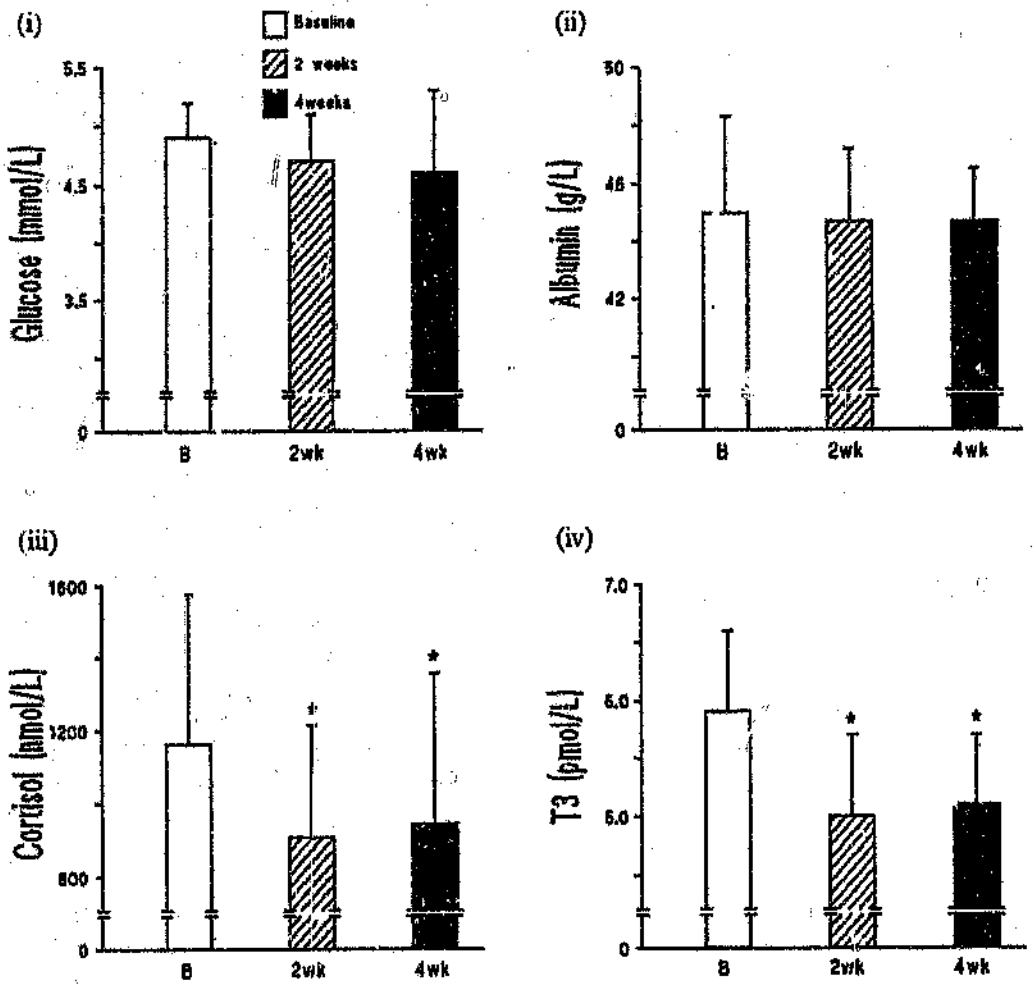



**Figure 4.1** Concentrations of (i) glucose, (ii) albumin, (iii) cortisol and (iv) $T_3$ from nine women before dieting (B), and after two weeks (2 wk) and four weeks (4 wk) of energy restriction. Mean $\pm$ Standard Deviation.

* = significantly different from baseline, $P < 0.05$.

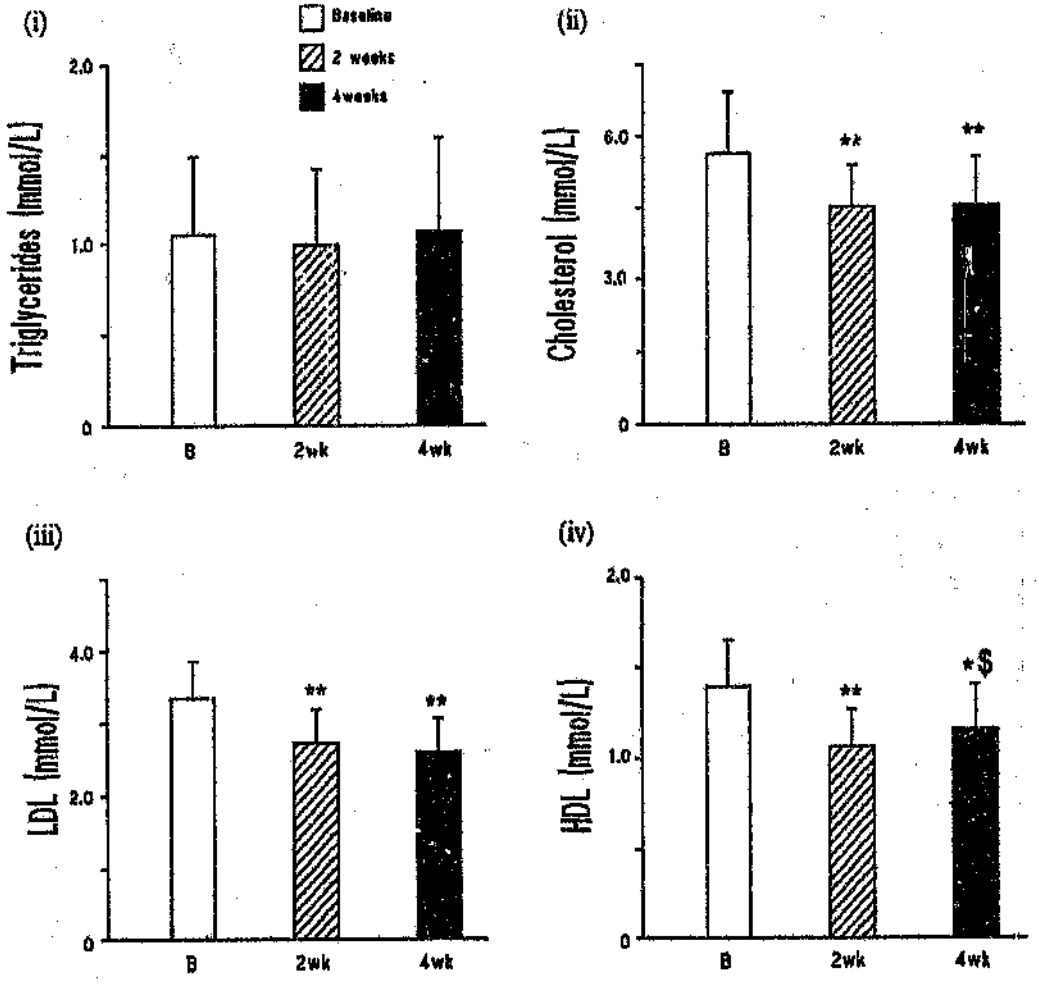



**Figure 4.2** Serum lipoprotein concentrations of triglycerides (i), cholesterol (ii), LDL (iii) and HDL (iv) before dieting (B), and after two weeks (2 wk) and four weeks (4 wk) of energy restriction. Mean ± Standard Deviation.

* = significantly different from baseline, $P < 0.05$.

** = significantly different from baseline, $P < 0.001$.

$ = significantly different from 2 weeks, $P < 0.05$.

## 4.4) Discussion

The very low energy diet employed in this study resulted in alterations in the concentrations of various blood measures and cardiac function.

### 4.4.1) Albumin and Glucose

Blood protein albumin concentrations do not vary significantly during protein and energy restriction (Scafi *et al*, 1990), even anorexic patients do not exhibit hypoalbuminaemia (Passmore & Eastwood, 1986). Despite a significant reduction in protein intake, from 73 ± 17 g pre-diet to 41 ± 15 g during the diet (chapter 3), serum albumin concentration was not altered with energy restriction. Similar results have previously been reported in obese subjects after 20 days on one of four very low calorie diets with an energy intake below 500 kcal/d or a hypocaloric diet of 1200 kcal/d, (Scafi *et al*, 1990). This lack of response was attributed to albumin's long half life (18 days) and large extravascular pool (Scafi *et al*, 1990) and makes it the least sensitive index of change in protein metabolism (Passmore & Eastwood, 1986). Since sex hormone binding globulin is sensitive to changes in dietary composition (Goldin *et al*, 1994), and given the short half life of insulin like growth factor-I (Thissen *et al*, 1994) they are more sensitive measures of protein metabolism.

In general, blood glucose concentration is tightly controlled by a number of feedback mechanisms and fluctuates very little. Data obtained in this study and that obtained in other very low energy diets (Franssila-Kallunki *et al*, 1992 and Katzeff *et al*, 1986), shows that even with marked energy restriction, glucose concentration is tightly regulated and therefore remains unaltered.

4.4.2) **Lipoproteins**

Body fat reserves are the primary energy substrate utilized by the body and the exploitation of fat as a fuel may partly explain the decline in serum lipoprotein concentrations, noted in this study. Triglycerides are the main breakdown product and free form of fats, and it is not surprising that their concentration was maintained while other lipid metabolites were affected. The majority of studies examining energy restriction and lipid profiles however show reductions in triglyceride concentrations with dieting (Datillo and Kris-Etherton, 1992). Most of these studies have examined morbidly obese subjects who display increased baseline concentrations of triglycerides (Bray, 1992). The women in this study, however had baseline serum triglyceride concentrations within the normal range (< 2.3 mmol/L), which were unaltered by the diet. Similarly Follick *et al* (1984) showed no change in triglyceride concentrations after a 10 week weight loss programme undertaken by overweight women with a mean pretreatment weight of 70.3 kg.

The energy restriction regime specified in this study, emphasised that dietary fat and cholesterol were to be specifically avoided. Significant reductions in dietary fat (from 96 ± 23 g to 15 ± 5 g) and cholesterol (from 261 ± 103 mg to 86 ± 47 mg) intakes (Table 3.1) may be responsible for the observed alterations in serum lipoproteins (Figure 4.2). A reduction in dietary cholesterol causes mobilisation of adipose tissue cholesterol stores and may inhibit cholesterol synthesis by the liver (Dattilo and Kris-Etherton, 1992) thus accounting for the significant reduction in serum total cholesterol found in this study. Furthermore, the reduced serum total cholesterol may be attributed to a decrease in ß-hydroxy-ß-methylglutaryl coenzyme AH reductase activity and enhancement of cholesterol excretion in bile for both of these are associated with energy restriction (Dattilo and Kris-

Etherton, 1992).

The reduction in LDL in this study may be attributed to the changes in cholesterol concentration. As cells become cholesterol deficient, the liver increases cholesterol uptake by increasing LDL receptors, which in turn leads to a decrease in LDL remaining in the serum. Significant reductions in cholesterol and LDL concentrations are generally considered consequences of long term dieting (eg. after ten weeks of dieting and after six months of weight maintenance Follick *et al*, 1984). In accordance with Parenti *et al* (1992) and Zimmermann *et al* (1984) the women in this study demonstrated a rapid reduction (after two weeks) in total cholesterol and LDL.

A significant decrease in HDL, evident after two weeks of dieting, was maintained, although at a lower concentration, after four weeks of energy restriction. HDL cholesterol is derived from very low density lipoproteins (VLDL) and chylomicrons, after triglyceride hydrolysis by tissue lipoprotein lipase (Follick *et al*, 1984). During acute energy restriction, tissue concentrations of lipoprotein lipase decrease by 50 - 80 % (Taskinen and Nikkila, 1979) and HDL production is thus reduced and this could be the mechanism responsible for the HDL decrease noted in this study. Since HDL cholesterol is inversely related to coronary heart disease and obesity (Kannel *et al*, 1979), a reduction in HDL with weight loss is unexpected. However, numerous investigators have noted reductions in HDL cholesterol during very low calorie diets (Follick *et al*, 1984; Parenti *et al*, 1992) and during low fat diets (Kasim *et al*, 1993; Staznicky *et al*, 1992). Nevertheless many studies (Dattilo and Kris-Etherton, 1992; Follick *et al*, 1984) show that when weight stabilises, lipoprotein lipase exceeds basal levels which results in an increased transfer of lipids to HDL. The beneficial increase in HDL with energy

restriction is therefore associated with long term, rather than short term dieting. An increase in HDL/LDL ratio would therefore also be associated with long term dieting (Follick *et al*, 1984). In the first two weeks of dieting HDL concentration decreased by 23% and LDL concentration by 18%, which resulted in no change in the HDL/LDL ratio. In the final two weeks, HDL concentrations increased significantly by 9%, however LDL concentrations did not decrease further, again resulting in a no change in HDL/LDL ratio.

The changes in serum lipid profiles noted in this study are all beneficial in the management of coronary heart disease.

### 4.4.3) Cortisol

The higher than normal cortisol concentrations noted throughout this study may reflect that the women were stressed by the blood taking procedure. In addition, higher than normal cortisol levels are noted in women taking oral contraceptives (Kuhl *et al*, 1993; O'Brien *et al*, 1993). Kuhl *et al* (1993) noted that in women treated with a biphasic desogestrel-containing oral contraceptive, serum cortisol concentration increased by 100 %. Since seven out of nine women were taking oral contraceptives, this may have contributed to the high baseline cortisol concentration.

Cortisol secretion can be induced by stressful stimuli and patients with anorexia and bulimia show elevated cortisol concentrations (Crisp, 1980). Increased cortisol concentrations have also been shown in male subjects after 10 days of starvation (Palmblad, 1977). Unlike starving subjects and patients with eating disorders, the women in this study showed a reduction in serum cortisol concentration with energy restriction.

Similar diet induced declines in serum cortisol concentration have previously been reported (Hainer et al, 1992) where cortisol was implicated in the control of android fat distribution.

Much of the pulsatile secretion of cortisol occurs during sleep and secretion is greatest during the latter part of the night (Kupfer *et al*, 1983; Spath-Schwalbe *et al*, 1993). Slow wave sleep (SWS) occurring in the early part of sleep has been shown to have an inhibitory influence on cortisol secretion (Spath-Schwalbe *et al*, 1993). This inhibition is superimposed on the endogenous circadian rhythm (Pietrowsky *et al*, 1994). The observed reduction in cortisol therefore cannot be accounted for by SWS-inhibitory influences, since SWS was also reduced in this study (chapter 6).

#### 4.4.4) Triiodothyronine ($T_3$)

Serum $T_3$ decreased with energy restriction in a similar manner to that previously reported (Davies *et al*, 1989; Katzeff *et al*, 1990; Prentice *et al*, 1991). A clear relationship between the decline in $T_3$ and the severity of an energy restriction regime and/or carbohydrate restriction regime exists (Prentice *et al*, 1991). It is therefore not surprising that a reduction in $T_3$ of 15.3 % after two weeks of dieting (Figure 4.1 iv) was similar to the 12.5 % reduction in $T_3$ observed by Davies *et al* (1989) after two weeks at a similar degree of energy restriction.

Since $T_3$ is the key hormone governing metabolism, the significant reduction in serum $T_3$ noted in this study suggests a concomitant suppression of resting metabolic rate. The 8% fall in heart rate provides further evidence for a decline in metabolic rate. This universal response to energy restriction may be a survival strategy for energy conservation and the

preservation of lean body mass (Osbourne, 1983). Despite this energy-sparing adaptation, restricted energy intake in this study was nevertheless severe enough to facilitate a significant weight loss (see chapter 3).

**4.4.5) Blood pressure and heart rate**

A significant fall in blood pressure is frequently associated with weight reduction (Eliahou *et al*, 1992). The significant decrease in blood pressure noted in this study concurs with results obtained by Cutler (1991) who showed that weight loss, however achieved, lowers blood pressure in overweight, non-hypertensive subjects. While systolic blood pressure and heart rate were significantly decreased in this study, there was no correlation between the changes in blood pressure and weight reduction. It thus appears that other important physiological changes that occur in response to the altered feeding regime are responsible for changes in blood pressure.

The change in blood pressure might be explained by a decline in sodium intake with energy restriction and altered eating habits. The low energy regime resulted in a mean sodium reduction of 810 mg/day. The decrease in sodium intake and it's effects on the renin-angiotensin-aldosterone system may play a part in the reduction of systolic blood pressure. However, reductions in blood pressure with weight loss are shown to occur independently of salt intake (Tuck, 1985).

Although catecholamines were not measured in this study, reductions in norepinephrine and epinephrine concentrations have been shown to accompany energy restriction in both normal weight and obese subjects (Landsberg and Young, 1985; Tuck, 1985) and may have a direct effect on blood pressure and heart rate. Staznicky *et al* (1993) noted that

a low fat, high polyunsaturated:saturated ratio diet results in a selective decrease in noradrenaline cardiovascular reactivity (without apparent changes in noradrenaline release rate or clearance from plasma). The reductions in fat intake (Table 3.1) may therefore have altered cardiovascular responses to noradrenaline (Staznicky *et al*, 1993).

However it is the reduction in $T_3$ that is most likely to account for the observed decline in systolic blood pressure and heart rate: $T_3$ has a direct effect on the excitability of the heart and on the strength of the heart beat. A reduction in $T_3$ may therefore decrease heart rate and stroke volume, thereby decreasing cardiac output and hence blood pressure.

## 4.5) Conclusion

The unchanged serum glucose, triglyceride and albumin concentrations noted in this study provide evidence that the experimental treatment did not constitute a pathophysiological condition such as malnourishment or starvation. The restricted energy intake was sufficiently stringent to induce reductions in weight, $T_3$ and concomitant reductions in metabolism, systolic blood pressure and heart rate. The very low energy diet did not appear to be physiologically stressful as indicated by decreased cortisol concentrations. Furthermore, weight loss appears to produce favourable changes in lipid concentrations and blood pressure profiles in moderately overweight, yet non-obese individuals.

# CHAPTER 5

## 5 Alterations in performance and mood with month long energy restriction

### 5.1) Introduction

Very low energy diets may be viewed as psychologically consequential events since they result in physiological and physical adjustments as well as changes in lifestyle and appetitive behaviour (O'Neil and Jarrell, 1992). Most studies investigating psychological changes with very low energy diets have assessed morbidly obese patients. Psychological and behavioural variables related to weight and eating in these subjects, differ from those of non-obese people (O'Neil and Jarrell, 1992). As such, changes in mood and psychological profiles that occur with weight reduction programmes in obese individuals cannot be extrapolated to normal overweight individuals. This study investigated whether mood and psychological profiles were altered with dieting in non-obese overweight women.

The ability to perform a task with speed and accuracy may be affected by energy intake. Human performance, when measured as a mean reaction time, is not altered by relatively short term (5 or 10 hours) food deprivation (Champion and Field, 1963) however, long term starvation leads to alterations in performance. Both anorexic and bulimic patients display impaired performance on a number of tasks (Fox, 1981; Laessle *et al*, 1990). Cognitive deficits in anorexic and bulimic patients may be attributable to the presence of a primary psychopathology. However studies conducted on non-psychiatric patients have also revealed performance alterations: Green *et al* (1994) showed that dieters display poor performance on a vigilance task and yet they out perform non-dieters on a tapping task. Unlike previous studies, this study assessed changes in long term performance on both

complex and simple tasks, in non-obese subjects before and after a month-long energy restriction regime.

## 5.2) Methods

Mood was assessed before and after two weeks of dieting, using the Profile of Mood States (POMS) questionnaire (section 2.6.2 and . 9) and Paired Student's *t* tests were used to assess changes in mood. Psychological profiles were assessed using visual analogue scales (described in section 2.6.2) completed in the mornings following the nights spent in the sleep laboratory. Baseline and diet visual analogue scale variables were compared using the Wilcoxon signed rank test.

Simple and complex reaction tests described in section 2.6 were undertaken each morning, following the nights spent in the sleep laboratory. Performance alterations were analyzed using paired student's *t* tests.

## 5.3) Results

### 5.3.1) Mood

After two weeks of energy restriction the POMS profile was significantly altered. An example of the altered POMS profile for one women is shown in Appendix 4. All the women showed similar responses. No significant changes in global mood, tension, depression, anger and confusion on the diet were observed. However, mean values for fatigue increased significantly ($P < 0.05$), and that of vigour decreased significantly ($P < 0.05$) with dieting.

Subjective assessment of concentration, temperature sensitivity, irritability, vitality and mood, as measured by visual analogue scales, were not significantly altered on any diet morning. Similarly, subjective need for sleep and subjective sleep quality, assessed in a similar manner, did not change with dieting.

### 5.3.2) Performance

When assessed using the simple reaction test, no significant change in mean reaction time was noted on any of the diet mornings, when compared to baseline (Table 5.1). However, mean reaction times as measured by the complex reaction test, were significantly faster compared to baseline, on all measured diet mornings (Figure 5.1). Despite the unrandomised nature of the study it seems unlikely that this is merely a training effect, since mean reaction times were similar on the first (585 $\pm$ 54 msec) and the last (557 $\pm$ 50 msec) baseline mornings, as were those on the first (529 $\pm$ 42 msec) and last (5[illegible] $\pm$59 msec) diet mornings. Accuracy, as measured by correct hits on the complex reaction test, increased significantly on diet mornings 16, 20 and 28, when compared to corresponding baseline mornings (Figure 5.2). Only on one diet morning (24), was the increase in the mean number of correct hits not significant (Figure 5.2), although there was a trend towards improved accuracy with dieting. Once again, this cannot be simply due to practise or training effects for the number of correct hits was not significantly different between the first (298 $\pm$ 14) and last (302 $\pm$ 18) baseline mornings, nor were the correct hits significantly different between the first (316 $\pm$ 15) and last (314 $\pm$ 20) diet mornings.

**Table 5.1** Mean reaction times (seconds) as measured by the simple reaction test, in nine, healthy women. Measurements were determined in the mornings following corresponding baseline and diet nights, which were matched for menstrual cycle stage. The following nights were matched: (a) baseline 3 and diet 16, (b) baseline 7 and diet 20, (c) baseline 11 and diet 24, and (d) baseline 15 and diet 28. Mean ± Standard Deviation.

| | Baseline | Diet |
|---|---|---|
| a) | 0.31 ± 0.02 | 0.29 ± 0.03 |
| b) | 0.30 ± 0.03 | 0.31 ± 0.04 |
| c) | 0.29 ± 0.02 | 0.31 ± 0.03 |
| d) | 0.31 ± 0.04 | 0.30 ± 0.04 |

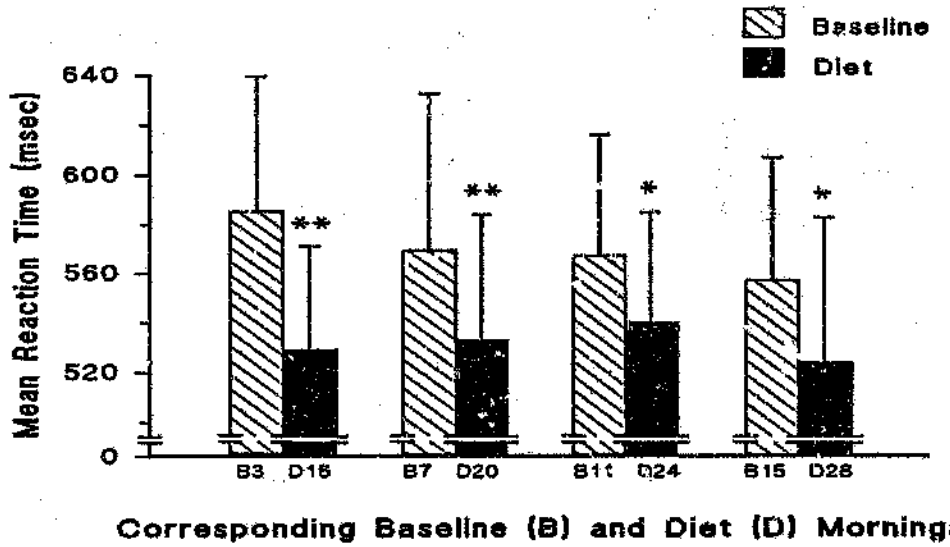



**Figure 5.1** Mean Reaction time, as measured using a complex reaction task, before (baseline) and after a 3347 kJ/d energy restriction regime (diet), on corresponding baseline and diet mornings matched for menstrual cycle phase. Mean ± Standard Deviation. * = $P < 0.05$, ** = $P < 0.01$, ficantly different from baseline.

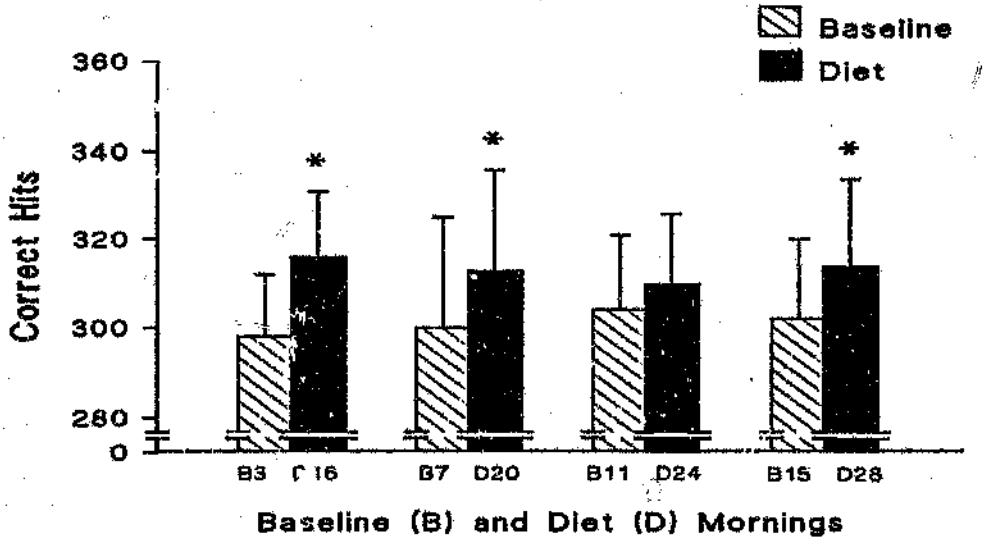



**Figure 5.2** The number of correct hits achieved on a complex reaction task before (baseline) and after a 3347 kJ/d energy restriction regime (diet), on baseline and diet mornings matched for menstrual cycle phase. Mean ± Standard Deviation.

* = $P < 0.05$, significantly different from baseline.

## 5.4) Discussion

### 5.4.1) Mood

While unfavourable emotional responses to dieting have previously been reported (Wadden and Stunkard, 1985), in this study, no global mood changes nor changes in psychological profiles were evident. These results concur with many findings that demonstrate positive or neutral psychological effects with energy restriction. Crisp *et al* (1973) showed that obese individuals undergoing a four month 500 kcal/day diet showed no change in mood and both Foster *et al* (1992) and O'Neil and Jarrell (1992) emphasised that in general, very low energy diets have positive effects on mood, depression, anxiety and hunger in the obese. These results from obese people appear to apply to non-obese individuals undergoing energy restriction.

Despite the neutral effects on mood and psychological profiles noted in this study, a significant increase in fatigue and a decrease in vigour were demonstrated with energy restriction. These results concur with those of Crisp and Stonehill (1970) who noted that a decrease in daytime activity accompanies weight loss in obese patients. Crisp and Stonehill (1970) attributed this finding to very low energy intakes affecting energy resources.

A number of studies have investigated the possibility that dietary components may affect the synthesis of serotonin (5-HT) and thereby alter mood (Deijen *et al*, 1989; Spring *et al*, 1983). A carbohydrate-rich, protein-poor meal is shown to result in an insulin secretion that reduces plasma levels of most amino acids, but not tryptophan. Since tryprophan and the large neutral amino acids compete for a common transport site to gain

access to the central nervous system, the meal induced changes in plasma composition cause brain tryptophan levels to rise (Spring *et al*, 1983). A high carbohydrate/low protein diet is therefore thought to increase the availability of tryptophan to serotonergic neurons which are involved in sleep induction and mood (Spring *et al*, 1983). Spring *et al* (1983) noted an increased sleepiness in female subjects after carbohydrate ingestion when compared to protein ingestion. In this study the % carbohydrate/% protein ratio decreased from 3.2 to 2.4 with dieting (Table 3.1). It is therefore unlikely that the observed increase in fatigue and decrease in vigour noted in this study, are related to changes in 5-HT synthesis in the brain.

It is possible however that the significant reduction in $T_3$ and the corresponding fall in metabolic rate, as well as the decrease in heart rate and systolic blood pressure noted in this study (Chapter 4), could contribute to the women's feelings of fatigue and reduced vigour. However, subjective need for sleep and sleep quality were not altered with dieting.

5.4.2) **Performance**

Keys *et al* (1950) showed that 24 weeks of semi-starvation results in lethargy, tiredness and decreased feelings of energy, however performance on a battery of objective tests was unaffected. However, other studies (Deijen *et al*, 1989; Green *et al*, 1994) demonstrated alterations in performance over a prolonged period (two weeks) of dieting. Neither the increased fatigue nor the change in sleep patterns noted in this study (chapter 6) with energy restriction reduced the women's ability to perform a task, since the reaction times from the simple reaction test were unaltered. Indeed performance assessed by the complex reaction test in this study improved with dieting.

Studies examining performance in anorexic (Fox, 1981), bulimic (Laessle *et al*, 1990) and nonpsychiatric dieting patients (Green *et al*, 1994) have demonstrated impaired cognitive performance. Green *et al* (1994) noted that dieters perform significantly worse on cognitive tasks however they noted that dieters significantly outperform non-dieters on a tapping task requiring motor ability. These authors hypothesise that dieting affects tasks involving cognitive abilities while those involving fine motor ability are improved (Green *et al*, 1994). A dietary dissociation between motor behaviour and higher level cognitive processing has also been demonstrated by Diejen *et al* (1989). It is possible that the complex reaction task used in this study was a better measure of motor behaviour than of cognitive processing and was thus improved by dieting.

The mechanisms by which motor behaviour is enhanced by dieting are unknown. However, it has been shown that dieting alters serotonergic function in women (which may result in sleepiness and fatigue), while adrenergic functions are not modified by weight loss (Goodwin *et al*, 1987). It is therefore possible that dieting alters certain neurotransmitter functions that result in fatigue and listlessness and does not affect others which may result in enhanced motor performance. It is also possible that a decline in physiological stress, as shown by the reduction in cortisol concentrations, may be indicated by faster reaction times on complex tasks. More research will be necessary to determine the precise mechanisms by which performance is altered.

## 5.5) Conclusion

Mood and simple reaction tasks appear to be unaltered by energy restriction in non-obese women, while the hormonal changes associated with energy restriction may be responsible for the increased fatigue, decreased vigour and improved performance noted in this study.

# CHAPTER 6

## 6 Alterations in sleep patterns and nocturnal body temperature with month long energy restriction.

### 6.1) Introduction

Despite the extensive literature examining very low energy diets (Pi-Sunyer, 1992; Prentice *et al*, 1991), the effects of energy restriction on nocturnal body temperature and sleep patterns in healthy normal women, have not been previously documented.

There is evidence that body mass and thermoregulation may be linked. Underweight individuals exhibit impaired thermoregulation: patients who lose weight due to illness, exhibit no increase in thermogenesis on recovery when exposed to cold (Mansell *et al*, 1990). In addition very thin elderly hospital patients show a greater propensity for core temperatures $< 35°C$ than do their well nourished counterparts (Bastow *et al*, 1983). Since a reduction in metabolic rate and hence heat production accompanies energy restriction (Osbourne *et al*, 1983), we hypothesized that a suppression of thermoregulation via thermogenesis will accompany dieting.

Sleep patterns in underweight individuals differ from the norm. Patients with eating disorders such as anorexia nervosa show greatly compromised REM sleep and SWS (Lacey *et al*, 1975). Furthermore, when anorexic patients regain weight their sleep is less disturbed and of longer duration. Evidence that changes in sleep patterns cannot be attributed to body mass per se is gleaned from weight loss in the obese. Here, weight loss is associated with more broken sleep of shorter duration (Crisp *et al*, 1973). The restorative theory of sleep suggests that sleep is a time for tissue growth and repair after

the "wear and tear" of wakefulness (Adam and Oswald, 1983) and that a change in metabolic state affects sleep patterns. Consequently changes in sleep patterns in patients with eating disorders have been linked to alterations in metabolism.

In this chapter I have examined the association between sleep and body temperature changes with weight loss and a reduction in metabolic rate due to restricted energy intake in non-obese women with no history of psychiatric illness.

6.2) Methods

Nine women spent ten non-consecutive nights in the sleep laboratory. Electroencephalogram, electro-oculogram and electromyogram recordings and temperature measurements were determined throughout each night spent in the sleep laboratory.

Sleep recordings from baseline nights 3, 7, 11 and 15, and diet nights 16, 20, 24 and 28 were used for sleep data analysis (section 2.7 and Table 2.1). Data from baseline night 1 and diet night 14 were excluded since these nights acted as adaptation nights. Baseline and diet sleep variables were compared using the Wilcoxon signed-rank test (section 2.9).

All ten nights spent in the laboratory were used for temperature data analysis (see section 2.8). For each subject, temperature variables from the five baseline and diet nights respectively were meaned. Paired Student's *t* tests were used to compare baseline and diet temperature variables as described in section 2.9.

## 6.3) Results

### 6.3.1) Sleep

Awake and movement time did not change significantly in the last two weeks of the very low energy diet (Figure 6.1 vi) when compared to baseline. Slow wave sleep decreased significantly on all the measured nights during the very low energy diet (Figure 6.1 iii). However, most of the variables that changed significantly with dieting did so only towards the end of the month long diet. After 28 days of energy restriction, REM sleep decreased significantly (Figure 6.1 v), while sleep onset latency (SOL) increased significantly (Figure 6.1 i). The SWS ratio (SWS in the first sleep cycle/SWS in the second sleep cycle) decreased significantly from baseline on diet night 24 (Figure 6.1 iv). The change in the SWS ratio indicates that the significant reduction in SWS occurred primarily in the first sleep cycle and, accordingly, ROL decreased significantly on diet night 24 when compared to baseline (Figure 6.1 ii). The significant reductions in SWS ratio and ROL on night 24 were no longer significantly different from baseline on night 28 of the diet (Figures 6.1 ii and iv).

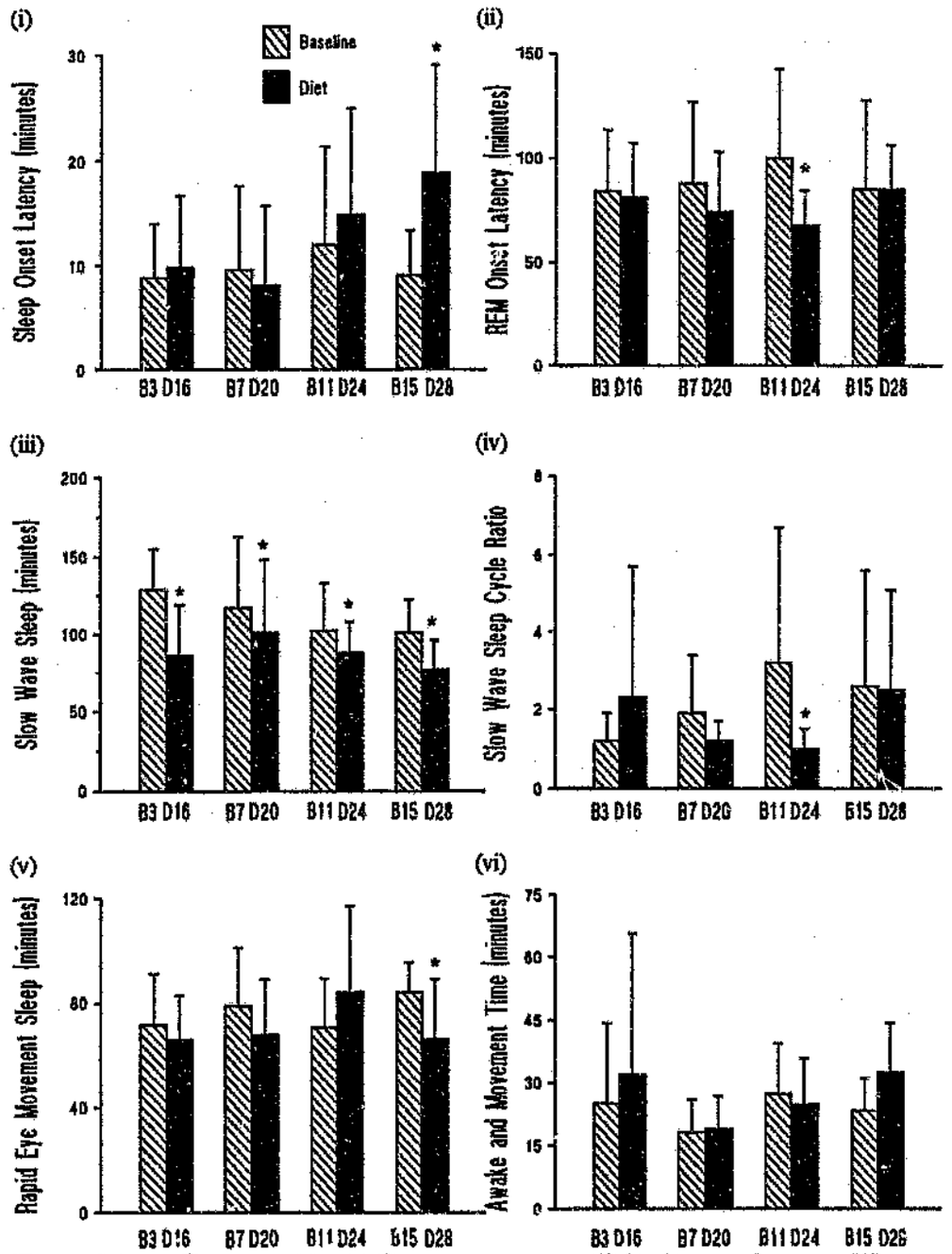



**Figure 6.1** Sleep variables (i) Sleep onset latency, (ii) REM onset latency, (iii) Slow wave sleep, (iv) Slow wave sleep cycle ratio, (v) Rapid eye movement sleep and (vi) Awake and Movement time, calculated over the first 360 minutes after lights out. Sleep variables were measured on baseline (B) nights 3, 7, 11 and 15, and on corresponding diet (D) nights 16, 20, 24 and 28, in nine healthy women.

* = significantly different from the corresponding baseline night, $P < 0.05$.

### 6.3.2) Temperature

Most of the women exhibited a decline in nocturnal body temperature on the diet when compared to baseline. Similarly, a non-significant reduction in the thermal response index occurred with dieting (from 0.1 ± 1.0 to -0.4 ± 1.2 °C/h, n = 7; $P < 0.07$). Minimum nocturnal rectal temperature ($T_{re}$) fell significantly from 36.5 ± 0.3 to 36.3 ± 0.3 °C with dieting ($P < 0.05$). Despite the significant reduction in minimum $T_{re}$ with dieting, the time at which the minimum $T_{re}$ occurred (measured as both clock time and time from lights out) did not change with the diet. Baseline and diet mean waking temperatures did not vary significantly.

## 6.4) Discussion

Altered sleep patterns and a reduction in body temperature were apparent in the final two weeks of a month long diet. These alterations occurred despite the fact that after dieting all the women were within a normal BMI range (see chapter 3). Changes in sleep patterns and body temperature may be due to changes in BMI and weight loss, however they are more likely due to modified nutritional status and consequent changes in metabolism.

The significant decrease in minimum $T_{re}$ may be attributed to the significant reduction in $T_3$ (chapter 4) and the implied associated suppression of metabolic rate, both of which would result in a decrease in heat production. Certain rural human populations, such as the Australian aborigines and the Kalahari bushmen, in situations of limited food and low temperatures, also reduce $T_{re}$ and become torpid at night (Mount, 1979). Australian aborigines save energy by lowering $T_{re}$ by 2 °C at night and by showing no rise in metabolic rate when exposed to the cold (Hammel, 1964). Although the drop in temperature noted in this study was only slight (0.2 °C), the significant fall in $T_{re}$, noted

with energy restriction may be an additional energy sparing mechanism, over and above the energy conserving reduction in $T_3$ discussed in chapter 4.

Reductions in metabolic rate, systemic glucose turnover (Boyle *et al*, 1994) and body temperature occur in many animals during sleep and consequently it is hypothesized that sleep (especially SWS) is an energy conserving mechanism which offsets the high energetic costs of endothermy (Berger and Phillips, 1990). Studies supporting this theory show increases in SWS during times of energy restriction. During energy restriction small mammals and birds allow $T_{re}$ to approximate ambient temperature, their metabolic rate falls, and they enter torpor which is characterised predominantly by SWS (Berger and Phillips, 1988). Large terrestrial birds such as geese and emperor penguins survive fasts lasting several weeks by increasing the time spent in SWS, thereby conserving energy without having to enter into torpor or hibernation (Dewasmes *et al*, 1984; 1989). In this study the reductions in $T_3$ and $T_{re}$ may be energy conserving, however the reductions in SWS with energy restriction (Figure 6.1 iii) do not concur with the energy conservation theory of sleep.

The fall in metabolic rate, implied by the decrease in $T_3$ (chapter 4) and $T_{re}$, may be responsible for the observed reductions in SWS noted throughout this study, (Figure 6.1 iii). During sleep there is a reduction in metabolic rate (Berger and Phillips, 1990), body temperature (Barrett *et al*, 1993) and catabolic hormones. In addition, anabolic hormone concentrations are elevated (Born *et al*, 1988). The restorative theory of sleep therefore suggests that "sleep is a time for restoring that which has been degraded during wa kefulness" (Oswald, 1970). The most restorative period of sleep is thought to be SWS, for it is during this stage that synthetic processes are at their peak (Adam, 1980). The

theory implies that in situations of lowered metabolic activity e.g., hypothyroidism and paraplegia, patients require less restorative SWS (Carpenter and Timiras 1982; Shapiro *et al*, 1990). In this study a restricted energy intake led to weight loss and a reduction in both metabolic rate and SWS, in a similar manner to that previously reported in anorexic patients (Lacey *et al*, 1975) and morbidly obese patients (Crisp *et al*, 1973; Ogilvie and Broughton 1977). This study therefore supports the restorative theory of sleep.

Correlative studies linking body composition or weight with sleep variables have generally been unsuccessful (see section 1.8.2). Nakazawa *et al* (1978) found no correlation between SWS and weight, and Shapiro *et al* (1990) showed no correlation between "altered" lean body mass and sleep in women losing weight. Furthermore, in a group of anorexic women gaining weight and in a group of women on a physical training programme, SWS and lean body mass were positively correlated (Shapiro *et al*, 1990). Indeed, in both these weight gain situations there may also be altered metabolic rates. These studies lend further support to the restorative theory of sleep since they suggest that it is relative metabolic rate and not necessarily anthropometric status, that governs changes in SWS.

In chapter 4, it was proposed that the reductions in cortisol concentrations noted in this study could not be accounted for by SWS inhibitory influences since SWS was also reduced. Despite the findings that sleep, particularly SWS inhibits cortisol secretion, Friess *et al* (1994) showed that pulsatile intravenous infusions of cortisol in normal subjects increases SWS and reduces REM. The reductions in SWS may be consequent on reductions in cortisol in conjunction with reductions in $T_3$ noted in this study.

The reduction in REM sleep noted after 28 days of energy restriction conforms with previous research. On admission anorexics display a gross reduction in REM sleep and, as weight is gained, REM sleep increases (Lacey *et al*, 1975). The results from previous studies have been used in support of a link between REM sleep and metabolism (as opposed to body weight *per se)*. Adam (1980) postulated that REM sleep is associated with brain protein synthesis. Evidence for this was provided by Gillin *et al* (1972) who noted that administering corticosteroids (which penetrate into the brain tissue and promote protein catabolism) resulted in a dose-related reduction in REM. It is possible that in this study certain markers of nutritional status such as hormonal changes and/or changes in the glucostatic, aminostatic or lipostatic feedback mechanisms that occur after long term (28 days) energy restriction may have influenced brain metabolism and REM sleep. This however is speculative since there is no consensus regarding alterations in REM and metabolic processors and other studies have shown that there are no links between REM sleep and cerebral metabolism (Boyle *et al*, 1994; Ramm, 1989).

REM sleep decreases dramatically during the hypothermia that occurs naturally in animals during hibernation and shallow torpor (Glotzbach and Heller, 1994). The fall in REM sleep during hypothermia may be related to reductions in metabolism or it may be associated with alterations in thermoregulatory processors (independently of alterations in metabolic rate) since thermoregulatory responses in humans are markedly inhibited during REM (Glotzbach and Heller, 1994). Similarly, in this study the fall in REM sleep (Figure 6.1 v) may be associated with the observed reduction in $T_m$.

REM sleep has been described as a "fragile state" that is diminished by a wide variety of stressful conditions (Hartmann, 1973). Since REM decreased after 28 days of energy

restriction, it may be possible to assume that the metabolic and/or psychological stressors of energy restriction only became significant after four weeks of dieting. Alternatively, the decrease in REM sleep may indicate sleep disruption since SOL is prolonged and, although not significant, A & M is increased. The interaction between REM sleep, temperature and metabolism is complex and further research into these relationships is required.

Short term dietary manipulations do affect sleep parameters. REM sleep and SOL can be altered during the night following dietary manipulation: intravenous glucose administration increases REM sleep (Lacey *et al*, 1978) and daytime carbohydrate and calorie ingestion increases REM sleep and decreases SOL (Crisp *et al*, 1986). In this study, alterations in these measures occurred after a month of energy restriction and cannot therefore be attributed to dietary manipulation. The increase in SOL after 28 days of energy restriction can be reconciled with the common, though as yet unsubstantiated, belief that dieting induces difficulty falling asleep. The longer SOL may be indicative of a shorter sleep duration. Crisp and Stonehill (1973) noted that obese subjects losing weight, reduce their sleep duration and have a more disturbed sleep. It was not possible to determine whether a reduction in sleep duration occurred on night 28 of this study, since the majority of the women worked and had to be woken up in the mornings. A significant reduction in ROL only occurred after 24 days of energy restriction when the corresponding baseline night 11 displayed the longest ROL (Figure 6.1 ii). Furthermore, SWS cycle ratio decreased significantly between baseline night 11 and diet night 24, indicating that there was more SWS in baseline sleep cycle 1. The significant reduction in SWS therefore occurred primarily in the first sleep cycle when ROL was significantly shorter. It is unclear why the changes in SWS cycle ratio only occurred after 24 days of

energy restriction.

## 6.5) Conclusion

In this study a restricted energy intake altered both nocturnal body temperature and sleep patterns. The reduction in nocturnal rectal temperature may be a consequence of a reduction in heat production, which accompanies a hypometabolic state. In accordance with the restorative theory of sleep, reduced SWS may have resulted from weight loss and decreased metabolism. This reduction in metabolism may be regulated by hormonal changes such as reductions in $T_3$ and cortisol concentrations (Chapter 4). In addition, other changes associated with alterations in nutritional status, such as changes in feedback mechanisms, chemical messengers and other regulators of body and cerebral metabolism and may have been responsible for the modifications in sleep parameters noted in this study. Consequently, the results from this study highlight links between metabolism, temperature and sleep patterns and further examination of these relationships and possible mechanisms are required.

# CHAPTER 7

## 7 Short term (two week) alterations in physiological, psychological and sleep measures in young, healthy women on a very low energy diet.

### 7.1) Introduction

During the month long 3347 kJ/d diet (the results of which are discussed in chapters 2 to 6) the nine women reported that many of the symptoms they experienced during the diet were already apparent prior to laboratory assessment in the second to fourth weeks of the diet. In response to these comments, and given the altered physiological, sleep, temperature and mood profiles discussed in the previous chapters of this dissertation, a second study was undertaken to assess how quickly these modifications occured with dieting.

Previous studies have shown numerous short term physiological and psychological changes within the first two weeks of energy restriction. The most rapid weight losses occur within the first week of energy restriction (Garrow and Webster, 1989). Significant reductions in $T_3$ were noted after three (Palmblad *et al*, 1977) and four days (Loucks *et al*, 1994) of energy restriction. Twenty-four hour energy expenditure is decreased by almost 5% on the first day of energy restriction (de Boer *et al*, 1986). Furthermore, decreases in plasma norepinephrine and blood pressure take place within the first two to three days of a low calorie diet (Eliahou *et al*, 1992). Lipoprotein concentrations such as triglycerides, total cholesterol and LDL cholesterol are all shown to fall significantly within the first 10 days of energy restriction (Weinser *et al*, 1992). In addition, serum proteins, such as insulin like growth factor-I, respond quickly to alterations in energy and protein intake (Thissen *et al*, 1994). Insulin like growth factor-I is significantly reduced

by up to 58% in the first four days of dietary restriction (Loucks *et al*, 1994). Mood profiles are also altered in the first week of dieting (Burley *et al*, 1992) and thermoregulatory function is impaired by a 48 hour fast (Bennet, 1981).

I have therefore, examined the changes in weight, body composition, cardiac function, physiological nutritional status, selected hormone concentrations, psychological variables, sleep and temperature during the first two weeks of an 3347 kJ/d (800 kcal/d) diet.

## 7.2) Methods

### 7.2.1) Protocol

Six premenopausal women aged 21-25 years, with a mean weight of 72.27 ± 10.38 kg and a mean BMI of 26.8 ± 4.0 kg/m$^2$ participated in this study. The women were recruited using the same methods and exclusion criteria as those described in section 2.1.

This study was also conducted during Autumn (maximum temperature 18.7 °C and minimum temperature 7.1 °C). Monitoring of baseline variables began one month before commencing the diet and continued for two weeks. After a two week break, the women were placed on the same 3347 kJ/d (800 kcal/d) diet as that given to the women in the first study (section 2.1 and appendix 3). Monitoring of diet variables occurred throughout the two week diet period (Table 7.1). Menstrual cycle differences were attenuated by scheduling baseline measurements 28 days prior to diet measurements (three out of six women were taking oral contraceptives) and no attempts were made to avoid taking measurements during ovulation or menstruation. Five non-consecutive baseline measurements were made in the first two weeks of the month long baseline period (baseline nights 1, 3, 5, 11 and 15). Baseline night 1 acted as an adaptation night

allowing the women to acclimatise to the laboratory surroundings and procedures. Dieting commenced on the morning following baseline night 28, which served as an adaptation night for the diet phase of the study. Thereafter four non-consecutive diet nights (diet nights 2, 6, 10 and 14) were spent in the sleep laboratory. An identical protocol to that conducted in the long term study was employed. Compliance and energy intake (section 2.2), body composition (section 2.3), blood pressure and heart rate (section 2.4), blood analyses (section 2.5), psychological variables (section 2.6), sleep (section 2.7) and temperature (section 2.8) were assessed.

**Table 7.1** Study design of a two week very low energy diet. Six healthy women visited the sleep laboratory on baseline (B) nights 1, 3, 7, 11, 15 and 28, and on diet (D) nights 2, 6, 10, and 14.

| | Adaptation | | | | |
|---|---|---|---|---|---|
| Baseline (B) | B1 | B3 | B7 | B11 | B15 |
| | Final two baseline weeks | | | | |
| Diet (D) | B28 | D2 | D6 | D10 | D14 |

Diet starts →

- Reaction test practices

**Daily Measurements:**

- Food diary

**Laboratory Measurements:**

- Nocturnal sleep & temperature
- Heart rate and blood pressure (on waking)
- Weights
- Reaction tests
- Visual analogue scales

} (mornings)

**Intermitant Laboratory Measurements:**

- Blood samples (B7, B15, D6, D14)
- Skinfold/Bioelectrical impedance analysis (B28, D6, D14)
- Profile of mood states (B7, B15, D6, D14)

**Figure 7** .

### 7.2.2) Statistical analyses

Energy intake and diet composition data were acquired in exactly the same way as was the data in the first study and details are given in sections 2.2 and 2.9. For each woman, energy intake data from five selected baseline days and five diet days were meaned, and baseline and diet mean values were compared using paired Student's *t* tests. One of the women did not complete her food diary and so mean energy intake and diet composition values were calculated using the information from five women.

Percentage changes in body composition between baseline to one week values, and between baseline and two weeks values, were calculated. Percentage changes were compared using paired Student's *t* tests.

For each woman, blood pressure and heart rate data collected on the five baseline and diet days respectively were meaned to give an average value for the baseline and diet phases. Heart rate and blood pressure data, as well as blood variables and hormone concentrations from the baseline and diet phases were related using paired Student's *t* tests.

The POMS questionnaire factors, determined on corresponding baseline and diet nights B7/D6 and B15/D14, were compared using paired Student's *t* tests. Variations in simple and complex reaction tests and visual analogue scale variables were determined on corresponding baseline and diet days B3/D2, B7/D6, B11/D10 and B15/D14. Paired Student's *t* tests were used to determine alterations in simple and complex tests while Wilcoxon signed-rank tests were used to assess changes in visual analogue scale variables.

Temperature variables from the five baseline and five diet nights respectively were meaned. Mean values were calculated for temperature variables and these values were compared using paired Student's *t* tests. Sleep data from corresponding baseline and diet nights B3/D2, B7/D6, B11/D10 and B15/D14 were compared using the Wilcoxon signed-rank test.

The results obtained during the first two weeks of energy restriction were compared with data obtained during the last two weeks of a month long energy restriction regime discussed in the previous chapters. For these comparisons Student's *t* tests were used.

## 7.3) Results

### 7.3.1) Energy intake

Reported energy intake, macronutrient intakes and dietary cholesterol intake during the baseline and diet phases of the study are shown in Table 7.2. Absolute protein, carbohydrate and fat intakes declined significantly with dieting, but cholesterol intake did not change significantly. Before dieting 18 % of daily energy intake was derived from protein, 45 % from carbohydrates and 37 % from fats. After dieting 22 % of energy was derived from protein, 52 % from carbohydrates and 26 % from fats (Table 7.2). The women reportedly consumed 6641 $\pm$ 665 kJ/d during the baseline phase of the study. A mean value for energy intake:basal metabolic rate$_{expected}$ (EI:BMR$_{expected}$) of 0.99 $\pm$ 0.17 was calculated (Black *et al*, 1991; Goldberg *et al*, 1991, section 2.2.2).

**Table 7.2** Energy intake, macronutrient intakes and dietary cholesterol intake for five women before (Baseline) and during two weeks on an energy restricted diet (Diet). Mean ± Standard Deviation.

| | Baseline | Diet | Change |
|---|---|---|---|
| Energy (KJ/d) | 6441 ± 665 | 3022 ± 308 | 3419 ± 435** |
| Protein (g/d) | 65 ± 8 | 36 ± 10 | 29 ± 12* |
| Carbohydrate (g/d) | 160 ± 20 | 86 ± 19 | 74 ± 9** |
| Fat (g/d) | 65 ± 11 | 21 ± 3 | 44 ± 10** |
| Cholesterol (mg/d) | 447 ± 252 | 198 ± 86 | 249 ± 232 |

* = significantly different from baseline, $P < 0.05$.

** = significantly different from baseline, $P < 0.001$.

### 7.3.2) Weight loss

The women showed stable weights during the month long baseline phase of the study. Their body weight did not change between baseline morning 1 (72.10 ± 11.14 kg) and baseline morning 28 (72.26 ± 10.28 kg). The women significantly reduced their weight from 72.26 ± 10.28 kg at baseline, to 70.55 ± 9.85 ($P < 0.05$) after one week of dieting and to 69.45 ± 9.88 kg ($P < 0.001$) after two weeks of dieting. The women lost a significant amount of weight in the final week of the energy restriction regime ($P < 0.05$). During the two week diet period, the women lost 2.82 ± 0.72 kg (i.e. 4 ± 0.7 % of their initial body mass), which amounts to a loss of 1.41 kg/week. Weight loss was significantly more rapid in the first week (1.72 kg) than in the second week (1.1 kg) of

dieting ($P < 0.05$).

### 7.3.3) Body composition

BMI declined significantly from 26.8 ± 4.0 kg/m$^2$ at baseline, to 26.1 ± 3.8 kg/m$^2$ after one week of dieting ($P < 0.05$), and to 25.7 ± 3.9 kg/m$^2$ measured after two weeks ($P < 0.001$). BMI was significantly reduced after two weeks of energy restriction when compared to that measured after one week ($P < 0.05$). It was noted that none of the methods used to determine percentage changes in body composition, differed significantly with respect to one another, after both one and two weeks of energy restriction (Table 7.3).

**Table 7.3** Percentage changes in weight and body composition for six, healthy, women measured after one week (1 wk) and two weeks (2wk) of dieting. Body composition was measured using body mass index (BMI), skinfold measurements (SM) and bioelectrical impedance analysis (BIA). Mean ± Standard Deviation.

| | Weight | BMI | SM | BIA |
|---|---|---|---|---|
| % Δ 1 wk | 2.4 ± 1.4 | 1.9 ± 1.3 | 2.0 ± 2.7 | 5.4 ± 11.8 |
| % Δ 2 wks | 3.9 ± 0.7 | 3.7 ± 0.9 | 1.0 ± 5.0 | -1.8 ± 6.7 |

### 7.3.4) Cardiac function, nutritional and hormonal status

Systolic blood pressure [(baseline) 107 ± 4 mmHg; (diet) 106 ± 4 mmHg], diastolic blood pressure [(baseline) 73 ± 4 mmHg; (diet) 71 ± 5 mmHg] and heart rate [(baseline) 69 ± 6 beats/minute; (diet) 65 ± 6 beats/minute] were not modified by the energy

restriction regime.

Throughout the duration of this two week study, serum concentrations of glucose, albumin, triglycerides, LDL, HDL and $T_3$ were within normal ranges for young healthy women (Smith and Miles, 1991). The very low energy diet did not alter glucose (Figure 7.1 i), triglyceride (Figure 7.2 i) and LDL (Figure 7.2 iii) concentrations. Neither did the hormone concentrations of $T_3$ (Figure 7.1 iv) and cortisol (Figure 7.1 iii) change with two weeks of dieting. Throughout the study, cortisol values were higher than normal values given for samples taken at 08h00 (Smith and Miles, 1991). Furthermore, cortisol concentration was significantly higher on baseline 15 (920 $\pm$ 330 nmol/L) than that determined on baseline 7 (828 $\pm$ 258 nmol/L, Figure 7.1-iii). Albumin concentration was significantly elevated from baseline (46.1 $\pm$ 2.2 g/L) after one week of energy restriction (43.6 $\pm$ 2.4 g/L, Figure 7.1-ii). However, after two weeks of dieting, albumin was no longer elevated from baseline, nor was albumin concentration significantly different from that measured at one week (Figure 7.1 ii).

Total cholesterol concentration was significantly higher on baseline 15 (5.60 $\pm$ 1.00 mmol/L) compared to that determined on baseline 7 (5.19 $\pm$ 0.87 mmol/L, Figure 7.2 ii). Baseline total cholesterol values fell within the moderate risk range for coronary heart disease, for South African women with a mean age of (23 $\pm$ 1 years), (Rossouw *et al*, 1988). Total cholesterol was significantly reduced from baseline (5.60 $\pm$ 1.00 mmol/L) after two weeks of energy restriction (4.70 $\pm$ 0.73 mmol/L, Figure 7.2 ii). However, the reduced cholesterol value still fell within the moderate risk range for coronary heart disease. HDL cholesterol declined significantly from baseline (1.30 $\pm$ 0.15 mmol/L) after one week of dieting (1.12 $\pm$ 0.12 mmol/L) and remained significantly reduced from baseline (1.40 $\pm$ 0.20 mmol/L) after two weeks of energy restriction (1.02 $\pm$ 0.13 mmol/L, Figure 7.2 iv). HDL cholesterol concentrations did not differ significantly between one and two weeks of dieting (Figure 7.2 iv).

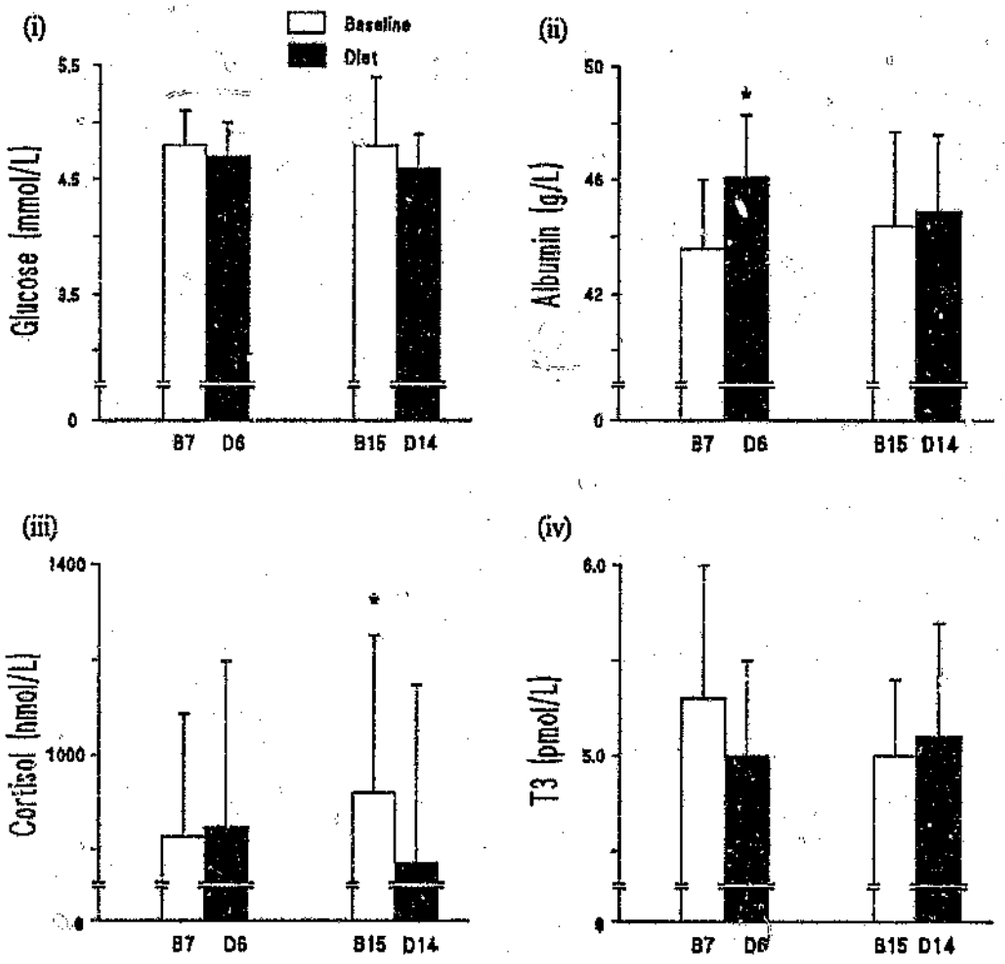



**Figure 7.1** Concentrations of (i) glucose, (ii) albumin, (iii) cortisol and (iv) $T_3$ from six heathy women, determined on baseline (B) mornings 7 and 15, and again after one week (D6) and two weeks (D14) of dieting. Mean ± Standard Deviation. Corresponding days B7 and D6, and B15 and D14 are matched for menstrual cycle stages.

* = significantly different from baseline 7, $P < 0.05$.

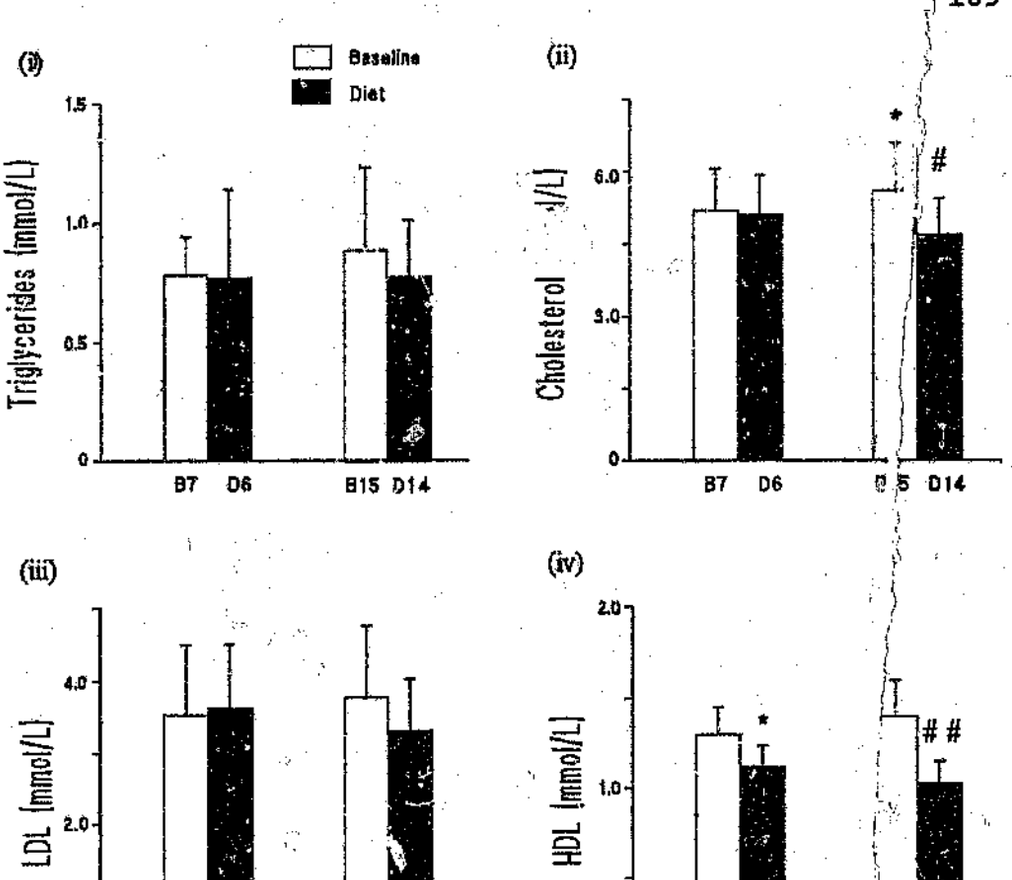



**Figure 7.2** Concentrations of (i) triglycerides, (ii) cholesterol, (iii) LDL and (iv) HDL from six healthy women, determined on baseline (B) mornings 7 and 15 and after one week (D6) and two weeks (D14) of dieting. Mean ± Standard Deviation. Corresponding days B7 and D6, and B15 and D14 are matched for menstrual cycle stages.

* = significantly different from baseline 7, $P < 0.05$.

\# = significantly different from baseline 15, $P < 0.05$.

\## = significantly different from baseline 15, $P < 0.001$.

### 7.3.5) Psychological variables

Performance, as measured using both simple and complex reaction tests, was not altered by short term energy restriction (Table 7.4). Similarly, psychological profiles, as measured using both the POMS and visual analogue scales, were not affected by the two week long diet.

**Table 7.4** Performance in six healthy, women, as measured using simple and complex reaction tasks, during Baseline (B) and Diet (D) phases of the study. Mean ± Standard Deviation. Performance was determined in the mornings following corresponding baseline and diet nights, which were matched for menstrual cycle stage. The following nights were matched: (a) baseline night 3 and diet night 2, (b) baseline 7 and diet 6, (c) baseline 11 and diet 12 and (d) baseline 15 and diet 16.

| | Mean Reaction Times (msec) | | | | Correct Hits | |
|---|---|---|---|---|---|---|
| | Simple Task | | Complex Task | | Complex Task | |
| | B | D | B | D | B | D |
| a) | 0.34 ± 0.01 | 0.36 ± 0.07 | 665 ± 87 | 655 ± 108 | 269 ± 19 | 272 ± 32 |
| b) | 0.32 ± 0.08 | 0.29 ± 0.03 | 681 ± 75 | 651 ± 108 | 270 ± 25 | 276 ± 34 |
| c) | 0.29 ± 0.04 | 0.31 ± 0.04 | 596 ± 55 | 571 ± 14 | 288 ± 8 | 287 ± 5 |
| d) | 0.29 ± 0.04 | 0.30 ± 0.03 | 570 ± 37 | 555 ± 35 | 310 ± 18 | 290 ± 23 |

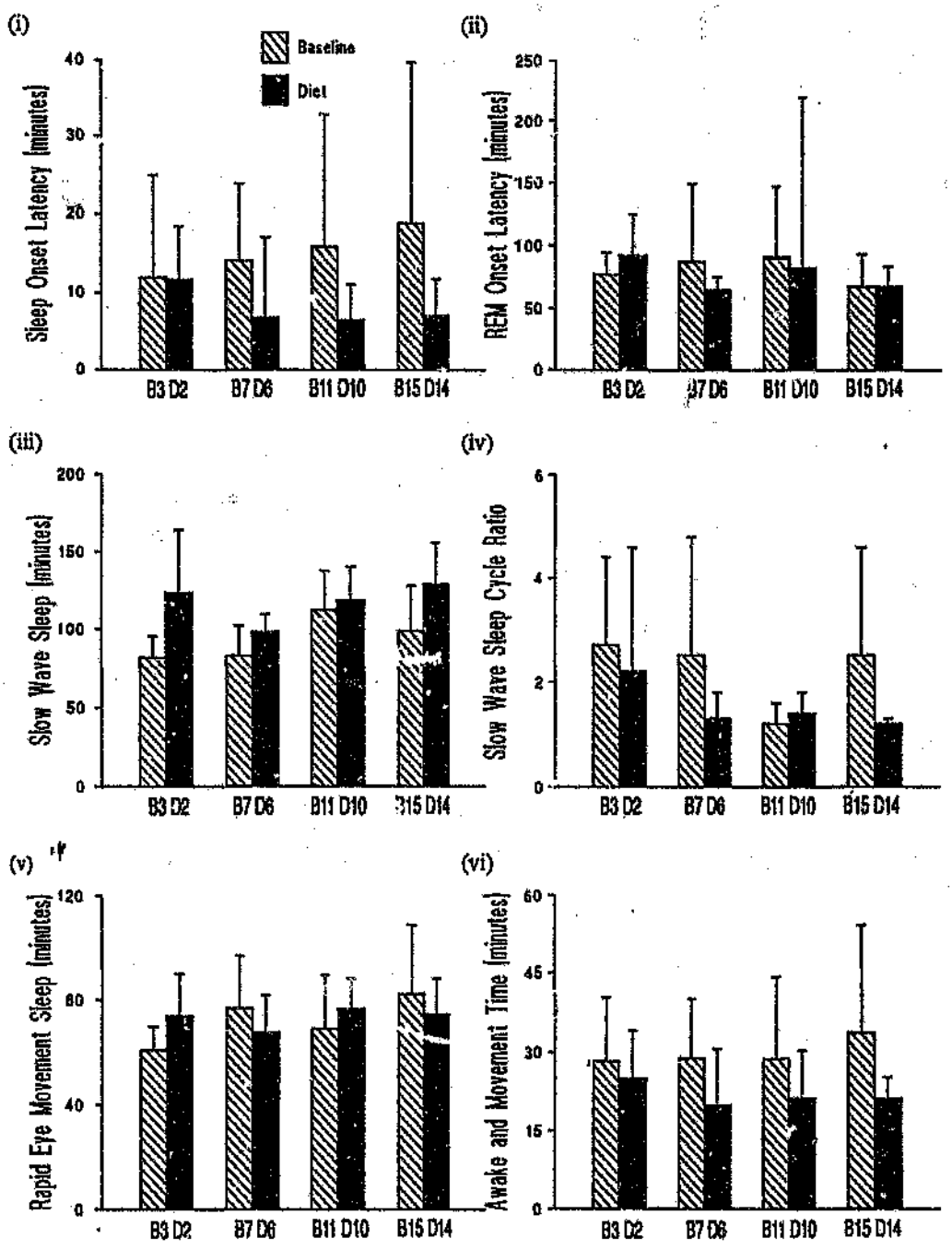



**Figure 7.3** Sleep variables [(i) Sleep onset latency, (ii) REM onset latency, (iii) Slow wave sleep, (iv) Slow wave sleep cycle ratio, (v) Rapid eye movement sleep and (vi) Awake and Movement time], calculated over the first 360 minutes after lights out. Sleep variables were measured on baseline (B) nights 3, 7, 11 and 15, and on corresponding diet (D) nights 2, 6, 10 and 14, in six healthy women.

### 7.3.6) Temperature and sleep

Mean minimum nocturnal rectal temperatures were not altered from baseline (36.4 ± 0.7 ° C) to diet (36.7 ± 0.4 °C). All other temperature variables were unchanged. Sleep variables (Figure 7.3) were also unaltered by short term energy restriction.

### 7.3.7) Comparisons between results from study 1 (month long 3347 kJ/d diet) and study 2 (two week 3347 kJ/d diet)

Comparisons of the baseline variables from both groups of women (Table 7.5) show that mean pre-diet weights and body mass indices were not significantly different between the two groups. However, the women from study 2 reported a significantly lower baseline energy intake (Table 7.5) than did their counterparts in study 1. After two weeks of dieting, the women in the study 2 lost significantly less weight than the women in study 1 (Table 7.6). In addition, % changes in BMI and BIA, measured after two weeks of energy restriction, differed significantly between the two study groups (Table 7.6).

**Table 7.5** Comparison of baseline weights, body mass indices (BMI) and energy intakes, from young, healthy women measured prior to a 3347 kJ/d diet administered over one month (study 1) and over two weeks (study 2). Mean ± Standard Deviation.

| | Study 1 (n = 9) | Study 2 (n = 6) |
|---|---|---|
| Weight (kg) | 71.21 ± 8.06 | 72.26 ± 10.28 |
| BMI (kg/m$^2$) | 26.1 ± 2.9 | 26.8 ± 3.8 |
| Energy intake (kJ/d) | 9240 ± 1670 | 6441 ± 665* |

* = significantly different from study 1, $P < 0.05$

**Table 7.6** Comparison of weight loss and changes in body composition from young, healthy women on a 3347 kJ/d diet administered for one month (study 1) and for two weeks (study 2). Measurements were made after two weeks of dieting, for both groups. Mean ± Standard Deviation.

| | Study 1 (n =9) | Study 2 (n = 6) |
|---|---|---|
| Weight loss (kg) | 3.72 ± 0.89 | 2.82 ± 0.73* |
| Δ BMI ($kg/m_2$) | 1.4 ± 0.5 | 0.8 ± 0.4* |
| Δ SM (% fat) | 1.3 ± 1.3 | 0.4 ± 1.7 |
| Δ BIA (% fat) | 2.6 ± 2.1 | -0.2 ± 1.5* |

* = significantly different from study 1. $P < 0.05$.

7.4) **Discussion**

Prior to comparing the results from the two studies it is important to note that the sample sizes of the two studies differed. The lack of statistically significant results noted in study 2 may have been a consequence of the small number of subjects involved in the study and interpretation of the results is therefore difficult. The work of biostatistician Prof H. Luus, of the University of the Orange Free State, implies that a sample size of eighteen human subjects is preferred in this type of sleep study. However, due to the nature of the study; it's duration, the time and commitment required by the subjects, and the cost of running such a study, it was only possible to examine six individuals. The possibility that the sample size used in this study was too small to detect possible changes, must be considered.

### 7.4.1) Energy intake and compliance

The mean baseline energy intake reported by the women in the two week study was significantly lower than that reported by the women in the month long study. It was established in chapter 3 that the women in the month long study were unlikely to have under-reported dietary intake. Using the fundamental principles of energy physiology a value for EI:BMR $_{(estimated)}$ was calculated in accordance with the methods described by Goldberg *et al* (1991) and Schofield *et al* (1985) (section 2.2.2). The PAL value obtained for the women in the two week study (0.99 ± 0.17) fell below the study specific cut-off limit 2 (1.34) described by Goldberg *et al* (1991). To maintain weight stability a minimum PAL value of 1.27 is required (Goldberg *et al*, 1991) and a value of 0.99 is inconsistent with the weight stability exhibited by the women during the baseline phase of the two week study. It is therefore likely that these women under-reported their energy intake.

The finding that subjects under-report energy intake is not uncommon. Under-reporting has been demonstrated in obese subjects (Bandini *et al* 1990; Prentice *et al* 1986) and individuals of normal weight (Black *et al*, 1993; Johnson *et al*, 1994; Livingston *et al*, 1990). Under-reporting may result because of a lack of motivation, knowingly omitting items from the records because recording is a nuisance and not reporting foods seen as unhealthy (Black *et al*, 1991). In this study a lack of motivation may indeed have been a factor; one subject did not attempt to complete her food diary. Evidence in support of selectively eliminating junk foods from dietary records, may be gleaned from the fact that reported daily fat intake (65 ± 11 g/d, Table 7.2) is lower than daily fat intake typical of a Western diet (100 g/d) (Ganong, 1987). I have assumed that under-reporting during the baseline phase of the experiment implies under-reporting during the diet phase.

### 7.4.2) Weight and body composition

The women in study 2 lost significantly less weight than did their counterparts from study 1 (Table 7.6). A lower weight loss may imply, over and above the established under-reporting, that the women from study 2 did not comply with the prescribed 3347kJ/d diet to the same extent as did the women from study 1 and may have been less motivated. Despite the fact that the women from the two studies may not have reduced their energy intakes by the same degree, the women in the short term study did lose a significant amount of weight (2.82 kg) during the two week study period. The observed rate of weight loss (1.41 kg/week) is in accordance with the "optimum rate of weight loss" as stated by Garrow (1981). This "optimum rate of weight loss" corresponds to an energy deficit of about 4200 kJ/d (1004 kcal/d). The women from study 2 reduced their energy intake, however the level of reduction was unlikely to have reached 3347 kJ/d. Thus, since the degrees of energy restriction achieved by the women in the two studies were different, direct comparisons between the results from the two studies must be treated with caution.

Further support for differences in compliance between the two groups of women is given in Table 7.6. The women from the short term study demonstrated significantly smaller changes in BMI and BIA, measured after two weeks of dieting, compared to the women from the long term study. Since BMI is calculated by weight/height$^2$, the smaller change in BMI demonstrated by the women in the short term study is most likely to be a consequence of the significantly smaller weight loss demonstrated by these women. A negative change in % fat, measured by BIA, after two weeks of dieting in study 2 indicates a reduction in conductivity, which in turn implies a loss of total body water (Section 2.3.3).

**7.4.3) Cardiac function, nutritional and hormonal status, psychological variables, sleep and temperature**

Disturbances in the water balance of the women from the two week study may indeed have occurred. Increased serum albumin concentration after a week of energy restriction (Figure 7.1-ii), provides further evidence for altered hydration. However, serum albumin concentration had returned to baseline levels after two weeks of dieting.

During energy restriction below 4 MJ/d there is a profound decrease in circulating $T_3$ concentrations, since $T_3$ is sensitive to both carbohydrate and energy intake (Prentice *et al*, 1991). After two weeks of energy restriction, $T_3$ was significantly reduced in the month long study but was unaffected in study 2. Since changes in $T_3$ occur within the first few days of energy restriction (Loucks *et al*, 1994; Palmblad *et al*, 1977), it is possible that the reduction in $T_3$ only occurs when energy is restricted to a certain degree. Cortisol was also unaltered by the two week energy restriction regime. The significant difference between the cortisol concentrations on baseline nights 15 and 7 (Figure 7.1-iii) may be due to differences in menstrual cycle stages. Cortisol concentration is shown to be affected by oral contraceptives (Kuhl *et al*, 1993; O'Brien *et al*, 1993) and the higher than normal cortisol concentrations noted throughout the study may reflect that 3 of the 6 women were taking oral contraceptives. The elevated mean cortisol concentrations present throughout the study may also be indicative of increased stress associated with the blood sampling proceedure.

Hormonal alterations (reductions in $T_3$ and cortisol) noted in study 1 were thought to contribute to, and in some cases to result in, the observed alterations in blood pressure and heart rate (section 4.4.5), vigour and fatigue (section 5.4.1), performance (section

5.4.2), sleep and temperature (section 6.4). Since the measured hormones were not altered by the energy restriction regime employed in study 2, it is possible to speculate that a threshold is reached below which restricted energy intake results in the numerous metabolic changes responsible for the alterations in blood pressure, mood, performance, sleep and temperature that were observed in study 1.

Despite the fact that the energy restriction regime employed in study 2 did not result in hormonal changes and the associated changes in numerous physiological, psychological and sleep variables, the reduction in energy intake resulted in reductions in HDL cholesterol and total cholesterol concentrations (Figures 7.2-iv and 7.2-ii). The finding that a week of energy restriction reduces serum HDL cholesterol concentration without affecting other lipoproteins (Figure 7.2) mimics the findings of Taskinen and Nikkila (1979). HDL is derived from VLDL and chylomicrons, after triglyceride hydrolysis by lipoprotein lipase (Follick *et al*, 1984). Short term reductions in HDL concentration are attributed to the 50 - 80% reduction in lipoprotein lipase activity that occurs in the first week of energy restriction (Taskinen and Nikkila, 1979). In accordance with the results from study 1, total cholesterol was significantly reduced after two weeks of energy restriction (Figure 7.2 ii). Similarly, Weinser *et al* (1992) noted that 10 days of energy restriction reduces total cholesterol concentration. Generally, reductions in total cholesterol concentrations have also been noted in long term studies (Follick *et al*, 1984). It is possible that the inhibition of cholesterol synthesis by the liver (Dattilo and Kris-Etherton, 1992) and the onset of other mechanisms responsible for reductions in total cholesterol concentration (section 4.4.2) only occur within the second week of energy restriction. Alternatively, the response time of total cholesterol may be dependant on the level of energy restriction. In contrast to study 1, LDL cholesterol concentration was

unaltered by the energy restriction regime employed in the short term study. We may speculate that the rapid response of LDL cholesterol to energy restriction (Weinser *et al*, 1994) occurs below a certain threshold of energy intake (section 4.4.2). Most studies demonstrating reductions in triglyceride concentrations with dieting, have examined obese subjects with abnormal baseline triglyceride concentrations (Bray, 1992). In this study, (as in study 1 and a study by Follick *et al*, 1984), subjects were not obese, baseline triglyceride concentrations were normal and triglycerides were not altered by energy restriction.

## 7.5) Conclusion

Despite the inconsistencies between this study and the previous investigation, the women on the two week diet showed a significant weight loss, reductions in HDL and total cholesterol concentrations and increased albumin concentration after one week of dieting (Table 7.4). These changes imply that, irrespective of the energy restriction regime employed, there are certain physiological adjustments that occur within the first two weeks of energy restriction. Alterations in cardiac function, hormonal changes, performance, sleep and temperature variables may be associated with long term (after two weeks) energy restriction. However, there may be a threshold of energy restriction below which these changes are initiated within the first two weeks of dieting. Further research into the time course of metabolic adaptations is necessary.

# CHAPTER 8

## 8 Conclusion

The very low energy diets employed in study 1 and study 2 resulted in alterations in selected physiological, psychological and sleep measures in non-obese, premenopausal women, which are summarised in Table 8.1.

**Table 8.1** Summary of significant changes from baseline, noted after a month long very low energy diet in nine, healthy, non-obese women (study 1), and after a two week very low energy diet in six, healthy, non-obese women (study 2).

| Variables | | Study 1 (four week) | Study 2 (two week) |
|---|---|---|---|
| Energy intake | | ↓ 6130 ± 1650 KJ/d | ↓ unknown |
| Weight | | ↓ $P < 0.05$ | ↓ $P < 0.05$ |
| Body Composition | BMI | ↓ $P < 0.001$ | ↓ $P < 0.05$ |
| | SM | ↓ $P < 0.05$ | ↔ |
| | BIA | ↓ $P < 0.001$ | ↔ |
| Cardiac Function | Systolic Blood Pressure | ↓ $P < 0.05$ | ↔ |
| | Heart Rate | ↓ $P < 0.05$ | ↔ |
| Serum Lipoprotein Concentrations | Total cholesterol | ↓ $P < 0.001$ | ↓ $P < 0.05$ |
| | LDL | ↓ $P < 0.001$ | ↔ |
| | HDL | ↓ $P < 0.05$ | ↓ $P < 0.001$ |
| Serum Hormone Concentrations | $T_3$ | ↓ $P < 0.05$ | ↔ |
| | Cortisol | ↓ $P < 0.05$ | ↔ |
| Mood profile | Fatigue | ↑ $P < 0.05$ | ↔ |
| | Vigour | ↓ $P < 0.05$ | ↔ |
| Performance | Mean reaction time | ↓ $P < 0.01$ | ↔ |
| | Correct hits | ↑ $P < 0.01$ | ↔ |
| Sleep variables | SWS | ↓ $P < 0.05_{(\text{all nights})}$ | ↔ |
| | REM | ↓ $P < 0.05_{(B15,\ D28)}$ | ↔ |
| | SOL | ↑ $P < 0.05_{(B15,\ D28)}$ | ↔ |
| | ROL | ↓ $P < 0.05_{(B11,\ D24)}$ | ↔ |
| | SWS ratio | ↓ $P < 0.05_{(B11,\ D24)}$ | ↔ |

**8.1) The month long energy restriction regime (study 1).**

It was shown that the women in the month long study were likely to have correctly reported their energy intakes since their calculated mean physical activity level fell above the cut-off limit described by Goldberg *et al* (1991). The modifications in energy intake achieved by the women resulted in a significant weight loss which concurs with that achieved in previous studies (Davies *et al*, 1989; Foster *et al*, 1992). Furthermore, the energy restriction regime employed resulted in the desired significant changes in body composition, as measured by body mass index, skinfold measurements and bioelectrical impedance analysis.

The month long diet did not resemble a state of starvation since indicators of nutritional status such as serum glucose, albumin and triglycerides, were unaltered. Nor did the very low energy diet appear to be either physiologically (since serum cortisol concentration decreased), or psychologically stressful (since a variety of mood states were unaltered). Indeed beneficial effects were evident: the alterated serum lipoprotein concentrations and reduced blood pressure and heart rate imply that normotensive, overweight women can reduce their risk of cardiovascular disease and hypertension by making use of diet therapy.

The significant reductions in heart rate and serum $T_3$, along with the drop in minimum nocturnal rectal temperature noted with energy restriction were suggestive of reduced metabolic rate. It was argued that the reductions in $T_3$, metabolic rate and cortisol concentration may also have accounted for the noted alterations in sleep architecture. The observed reduction in slow wave sleep was shown to conform to the restorative theory of sleep which implies that in situations of lowered metabolic activity, less restorative

slow wave sleep is required. While similar changes in sleep patterns have previously been recorded in patients with anorexia nervosa (Lacey *et al*, 1975) and in obese patients on weight loss programmes (Crisp *et al*, 1973), the results from this study showed that changes in sleep architecture also occur with alterations in energy intake and metabolism, under normal physiological conditions.

The significant changes in sleep patterns noted with dieting may also increase feelings of lassi The lack of vigour and enhanced fatigue noted in this study, were not reflected in performance results since performance on some tasks were improved with energy restriction.

**8.2) The two week energy restriction regime (study 2)**

The women in the two week study appear to have under-reported their energy intake, since their calculated physical activity levels fell below the cut off limits described by Goldberg *et al* (1991). However, a degree of energy restriction was achieved by the women sufficient for weight loss, a significant increase in serum albumin concentration after a week of dieting, and significant reductions in HDL and total cholesterol concentrations. A reduction in HDL cholesterol occurs soon after the onset of energy restriction (one week) Cardiac function, hormone concentrations, psychological variables, sleep patterns and temperature were unaltered by the two week energy restriction regime.

**8.3) Conclusions**

The degrees of energy restriction and compliance between the women in the two and four week studies differed, making direct comparisons difficult. However, data from the two studies indicate that energy restriction, irrespective of degree, results in a number of

physiological changes (viz. weight loss, alterations in body composition and a modified lipoprotein profile). Very low energy diets (< 3347 kJ/d) resulted in prompt (within two weeks) weight loss and the initiation of improved lipoprotein profiles, in non-obese healthy women.

Alterations in cardiac function, hormonal changes, performance, sleep and temperature variables may be associated with long term (after two weeks) energy restriction. There may be a threshold of energy restriction below which a series of weight dependant, metabolic and hormonal interactions are set in motion resulting in altered mood profiles, performance, sleep patterns and nocturnal body temperature. Previously unreported changes in sleep patterns, minimum nocturnal rectal temperature and performance after a month long low energy diet of 3347 kJ/d are important findings in light of the popularity of these diets and the number of non-obese individuals employing these energy restriction regimes.

# Appendix 1

## 1 General Health Questionnaire (General Practice Research Unit, 1972)

# GENERAL HEALTH QUESTIONNAIRE

GHQ-12

Please read this carefully:

We should like to know if you have had any medical complaints, and how your health has been in general, *over the past few weeks*. Please answer ALL the questions on the following pages simply by underlining the answer which you think most nearly applies to you. Remember that we want to know about present and recent complaints, not those that you had in the past.

It is important that you try to answer ALL the questions.

Thank you very much for your co-operation.

HAVE YOU RECENTLY:

| | | | | |
|---|---|---|---|---|
| 1 – been able to concentrate on whatever you're doing? | Better than usual | Same as usual | Less than usual | Much less than usual |
| 2 – lost much sleep over worry? | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 3 – been having restless, disturbed nights? | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 4 – been managing to keep yourself busy and occupied? | More so than usual | Same as usual | Rather less than usual | Much less than usual |
| 5 – been getting out of the house as much as usual? | More so than usual | Same as usual | Less than usual | Much less than usual |
| 6 – been managing as well as most people would in your shoes? | Better than most | About the same | Rather less well | Much less well |
| 7 – felt on the whole you were doing things well? | Better than usual | About the same | Less well than usual | Much less well |
| 8 – been satisfied with the way you've carried out your task? | More satisfied | About same as usual | Less satisfied than usual | Much less satisfied |
| 9 – been able to feel warmth and affection for those near to you? | Better than usual | About same as usual | Less well than usual | Much less well |
| 10 – been finding it easy to get on with other people? | Better than usual | About same as usual | Less well than usual | Much less well |
| 11 – spent much time chatting with people? | More time than usual | About same as usual | Less time than usual | Much less than usual |
| 12 – felt that you are playing a useful part in things? | More so than usual | Same as usual | Less useful than usual | Much less useful |
| 13 – felt capable of making decisions about things? | More so than usual | Same as usual | Less so than usual | Much less capable |

PLEASE TURN OVER

GROUP 1

HAVE YOU RECENTLY:

| | | | | |
|---|---|---|---|---|
| 14 — felt constantly under strain | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 15 — felt you couldn't overcome your difficulties? | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 16 — been finding life a struggle all the time? | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 17 — been able to enjoy your normal day-to-day activities? | More so than usual | Same as usual | Less so than usual | Much less than usual |
| 18 — been taking things hard? | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 19 — been getting scared or panicky for no good reason? | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 20 — been able to face up to your problems? | More able than usual | Same as usual | Less able than usual | Much less able |
| 21 — found everything getting on top of you? | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 22 — been feeling unhappy and depressed? | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 23 — been losing confidence in yourself? | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 24 — been thinking of yourself as a worthless person? | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 25 — felt that life is entirely hopeless? | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 26 — been feeling hopeful about your own future? | More so than usual | About same as usual | Less so than usual | Much less hopeful |
| 27 — been feeling reasonably happy, all things considered? | More so than usual | About same as usual | Less so than usual | Much less than usual |
| 28 — been feeling nervous and strung-up all the time? | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 29 — felt that life isn't worth living? | Not at all | No more than usual | Rather more than usual | Much more than usual |
| 30 — found at times you couldn't do anything because your nerves were too bad? | Not at all | No more than usual | Rather more than usual | Much more than usual |

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First published 1972, Reprinted June 1981
© General Practice Research Unit 1973.
ISBN 07005 0211 4

Printed in Great Britain.

0981 1075.03.4

## Appendix 2

2 Informed Consent Form

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
EDBLO SLEEP LABORATORY, Brain Function Research Unit

CONSENT TO ACT AS A SUBJECT IN RESEARCH

1. I,.....
being 18 years old or older, consent to participating in a research project entitled
.....
.....
.....
and to allowing the necessary procedures to be performed on me.

2. The procedures have been explain to me by .....
and I understand and appreciate their purpose, any risks involved, and the extent of my involvement.

3. I understand that the procedures form part of a research project, and may not provide any direct benefit to me.

4. I understand that all experimental procedures have been sanctioned by the Committee for Research on Human Subjects of the University of the Witwatersrand, Johannesburg.

5. I understand that my participation is voluntary, and that I am free to withdraw from the project at any time without prejudice.

..... .....
(Subject) (Responsible Scientist)

..... .....
(Witness) (Date)

## Appendix 3

### 3 Very Low Energy Diet (3347 kJ/d) Plan

DIET (800 kcal/day)

WHAT TO EAT:

-You may chose one meal from the Breakfast list, one from the lunch list, one from the supper list and in addition you may eat 4 snacks per day from the snack list.

-Try to include as many fruits in your diet as possible.

-Try to add spices( salt, pepper, curry) to your food. Spicy food speeds up your metabolism

-Try to eat often during the day. This will also increase your metabolism.

WHAT TO DRINK:

-Try to drink as much water as possible.

-You may drink tea or coffee yet no sugar may be added. Any FAT-FREE milk you add must be counted as a snack. Remember coffee creamers are very very fattening ie. they are taboo.

-You can drink as many diet coldrinks as you like.

WHAT NOT TO EAT:

-The most important aspect of this diet is that it is A LOW FAT diet. You may not add any fat to your food eg. butter, margarine, mayonnaise, oil or salad dressings. You should also avoid foods that are high in fats eg. avocado. Please eat only FAT-FREE dairy products eg. skim milk, fat-free cottage cheese (In-shape) fat-free yoghurt (In-shape , Lite or Shape-up). Remember to remove the skin from chicken.

REMEMBER:

-You have been provided with a calorie counter. Please use it and use a scale to weigh your food.

-Weigh yourself everyday, preferably first thing in the morning and preferably with the same scale.

-Don't forget to write down EVERYTHING you eat in your dietary record books.

GOOD LUCK!!!

## BREAKFAST (150 kcal)

1. 30g cereal (Raisin Bran, Weet-bix, Cornflakes, All-bran, Fruitful bran, Pick and Pay sugarless muesli, Woolworths lite cereal.) + 100ml skim milk.

2. Yoghurt (In-shape, Woolworths Shape-up, Lite, or any other that is 100kcal or less) + 1 small fruit.

3. 1 slice of toast + 1 teaspoon low cal jam/marmite + 1 small fruit.

4. 1 scrambled or boiled egg + 1 slice of toast (or 3 provitas) with low cal jam or marmite.

## LUNCH (150 kcal)

1. Fruit salad ( 3 fruits).

2. Tuna (60g) + salad.

3. Sandwich (2 slices slimslice) + cottage cheese 100g
   or salad
   or marmite
   or low cal jam
   or Anchovette

4. Soup (see recipes or Royco lite) + 1 slice of bread.

5. Any of the breakfast options.

## SUPPER (300kcal)

1. 100g grilled chicken or fish + salad.

2. 80g meat + salad

3. Baked potato + any filling that amounts to less than 200kcal eg Tuna, cottage cheese, vegetables or ratatouille.

4. 100g spaghetti or macaroni (cooked) + any sauce that contains no fat and amounts to 200 kcal or less eg. tomato, onion, tuna sauce or Knorr pasta sauces.

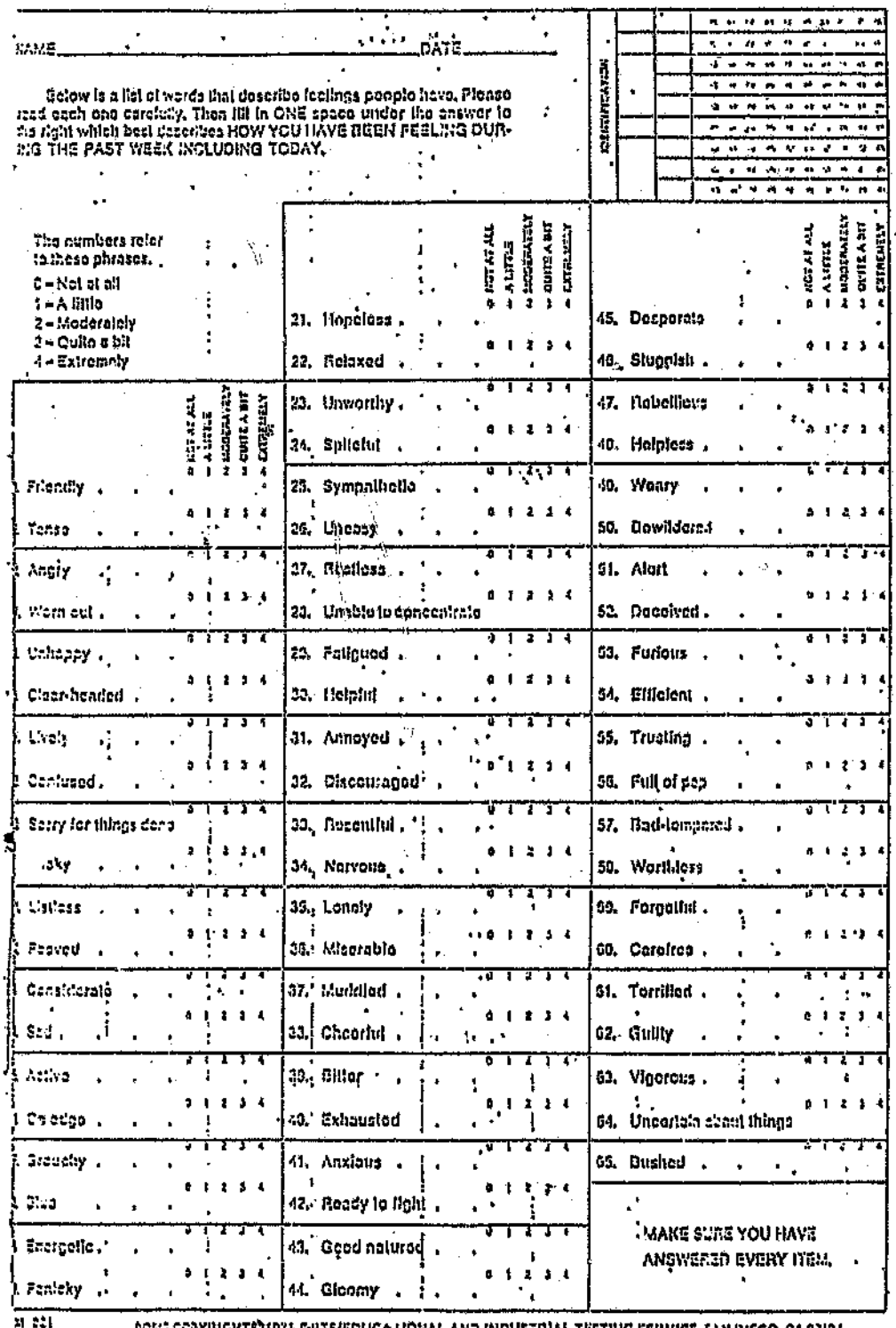
5. Any of the attached recipes. (Please note most of the recipes serve four people and must be divided into four portions).

## SNACK LIST (50kcal)

- 1 small apple
- 75ml wine (not semi sweet)
- 1 medium orange
- 100g Naturalite tinned apricots or peaches
- 1/2 a medium pawpaw
- 100ml Diet Delite ice-cream (Clover)
- 275g of melon
- 75 ml Diet Slim ice-cream (Dairy maid)
- 100g pineapple
- 200g Weigh less free veg mix (Harvestime)
- 75g grapes
- 1 sachet Royco Lite soup
- 4 fresh figs
- 1 sachet Maggie Lunch Time Slim soup
- 2 prunes
- 1 sachet Choc-o-lait
- 1 large grapefruit
- 1 and 1/2 cups of popcorn
- 150ml skim milk.

# Appendix 4

## 4 Profile of Mood States (POMS) Questionnaire (McNair *et al*, 1971)



NAME _____ DATE _____

Below is a list of words that describe feelings people have. Please read each one carefully. Then fill in ONE space under the answer to the right which best describes HOW YOU HAVE BEEN FEELING DURING THE PAST WEEK INCLUDING TODAY.

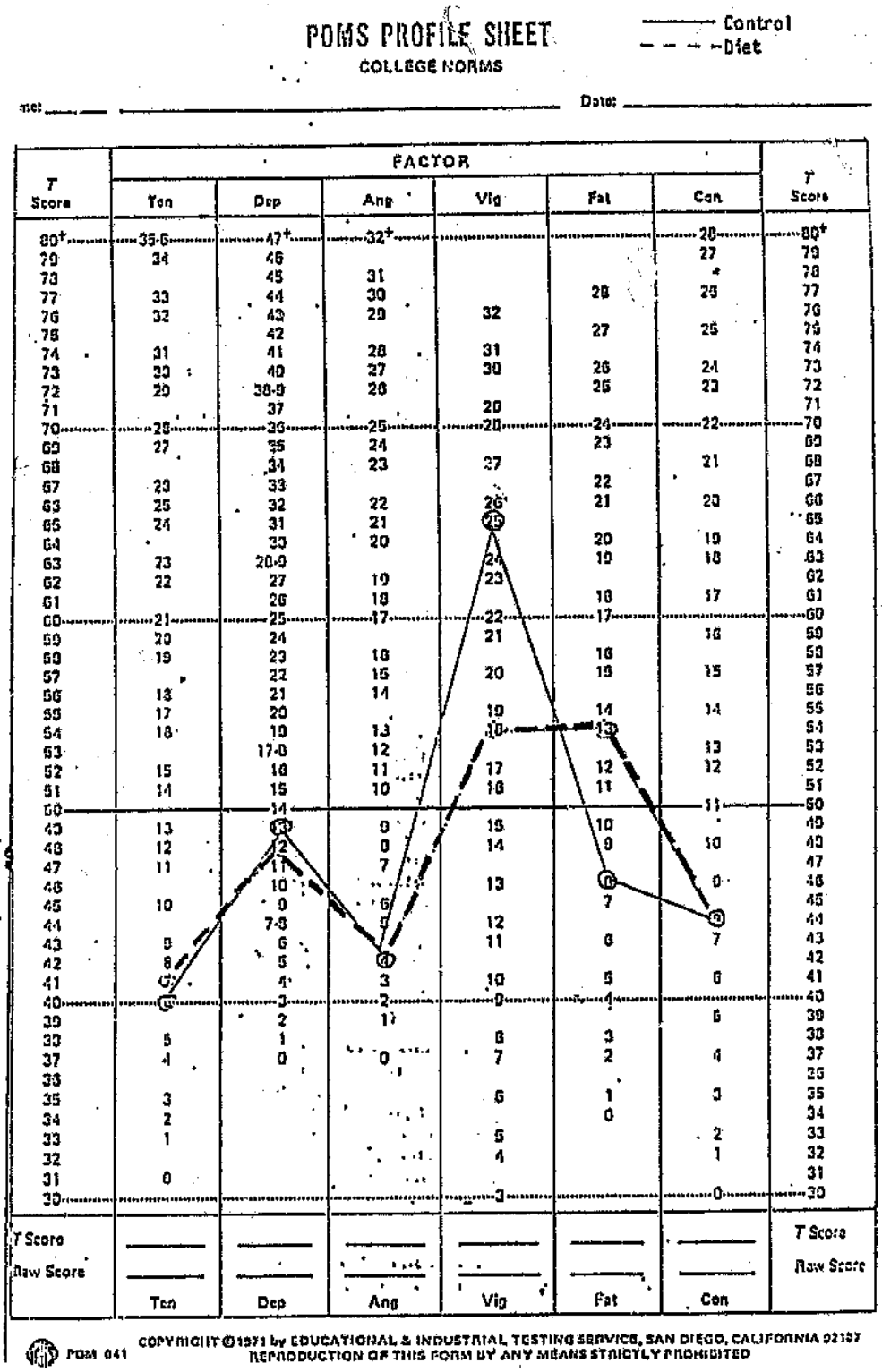
The numbers refer to these phrases.
0 = Not at all
1 = A little
2 = Moderately
3 = Quite a bit
4 = Extremely

| | 0 NOT AT ALL | 1 A LITTLE | 2 MODERATELY | 3 QUITE A BIT | 4 EXTREMELY |
|---|---|---|---|---|---|
| Friendly | 0 | 1 | 2 | 3 | 4 |
| Tense | 0 | 1 | 2 | 3 | 4 |
| Angry | 0 | 1 | 2 | 3 | 4 |
| Worn out | 0 | 1 | 2 | 3 | 4 |
| Unhappy | 0 | 1 | 2 | 3 | 4 |
| Clear-headed | 0 | 1 | 2 | 3 | 4 |
| Lively | 0 | 1 | 2 | 3 | 4 |
| Confused | 0 | 1 | 2 | 3 | 4 |
| Sorry for things done | 0 | 1 | 2 | 3 | 4 |
| Shaky | 0 | 1 | 2 | 3 | 4 |
| Listless | 0 | 1 | 2 | 3 | 4 |
| Peeved | 0 | 1 | 2 | 3 | 4 |
| Considerate | 0 | 1 | 2 | 3 | 4 |
| Sad | 0 | 1 | 2 | 3 | 4 |
| Active | 0 | 1 | 2 | 3 | 4 |
| On edge | 0 | 1 | 2 | 3 | 4 |
| Grouchy | 0 | 1 | 2 | 3 | 4 |
| Blue | 0 | 1 | 2 | 3 | 4 |
| Energetic | 0 | 1 | 2 | 3 | 4 |
| Panicky | 0 | 1 | 2 | 3 | 4 |
| 21. Hopeless | 0 | 1 | 2 | 3 | 4 |
| 22. Relaxed | 0 | 1 | 2 | 3 | 4 |
| 23. Unworthy | 0 | 1 | 2 | 3 | 4 |
| 24. Spiteful | 0 | 1 | 2 | 3 | 4 |
| 25. Sympathetic | 0 | 1 | 2 | 3 | 4 |
| 26. Uneasy | 0 | 1 | 2 | 3 | 4 |
| 27. Restless | 0 | 1 | 2 | 3 | 4 |
| 28. Unable to concentrate | 0 | 1 | 2 | 3 | 4 |
| 29. Fatigued | 0 | 1 | 2 | 3 | 4 |
| 30. Helpful | 0 | 1 | 2 | 3 | 4 |
| 31. Annoyed | 0 | 1 | 2 | 3 | 4 |
| 32. Discouraged | 0 | 1 | 2 | 3 | 4 |
| 33. Resentful | 0 | 1 | 2 | 3 | 4 |
| 34. Nervous | 0 | 1 | 2 | 3 | 4 |
| 35. Lonely | 0 | 1 | 2 | 3 | 4 |
| 36. Miserable | 0 | 1 | 2 | 3 | 4 |
| 37. Muddled | 0 | 1 | 2 | 3 | 4 |
| 38. Cheerful | 0 | 1 | 2 | 3 | 4 |
| 39. Bitter | 0 | 1 | 2 | 3 | 4 |
| 40. Exhausted | 0 | 1 | 2 | 3 | 4 |
| 41. Anxious | 0 | 1 | 2 | 3 | 4 |
| 42. Ready to fight | 0 | 1 | 2 | 3 | 4 |
| 43. Good natured | 0 | 1 | 2 | 3 | 4 |
| 44. Gloomy | 0 | 1 | 2 | 3 | 4 |
| 45. Desperate | 0 | 1 | 2 | 3 | 4 |
| 46. Sluggish | 0 | 1 | 2 | 3 | 4 |
| 47. Rebellious | 0 | 1 | 2 | 3 | 4 |
| 48. Helpless | 0 | 1 | 2 | 3 | 4 |
| 49. Weary | 0 | 1 | 2 | 3 | 4 |
| 50. Bewildered | 0 | 1 | 2 | 3 | 4 |
| 51. Alert | 0 | 1 | 2 | 3 | 4 |
| 52. Deceived | 0 | 1 | 2 | 3 | 4 |
| 53. Furious | 0 | 1 | 2 | 3 | 4 |
| 54. Efficient | 0 | 1 | 2 | 3 | 4 |
| 55. Trusting | 0 | 1 | 2 | 3 | 4 |
| 56. Full of pep | 0 | 1 | 2 | 3 | 4 |
| 57. Bad-tempered | 0 | 1 | 2 | 3 | 4 |
| 58. Worthless | 0 | 1 | 2 | 3 | 4 |
| 59. Forgetful | 0 | 1 | 2 | 3 | 4 |
| 60. Carefree | 0 | 1 | 2 | 3 | 4 |
| 61. Terrified | 0 | 1 | 2 | 3 | 4 |
| 62. Guilty | 0 | 1 | 2 | 3 | 4 |
| 63. Vigorous | 0 | 1 | 2 | 3 | 4 |
| 64. Uncertain about things | 0 | 1 | 2 | 3 | 4 |
| 65. Bushed | 0 | 1 | 2 | 3 | 4 |

MAKE SURE YOU HAVE ANSWERED EVERY ITEM.

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## POMS Profile Sheet from one Subject



# Appendix 5

## 5 Morning Form with Visual Analogue Scales

Person No. _____

Day No: _____

Name: _____

Today's date: day_____ month_____198_

What time did you go to sleep last night? _____hr _____min

How long do you think it took to fall asleep? _____mins

How long did you sleep for? _____hours

Did you sleep well? Yes/No

How many times did you wake up last night? _____times

Can you give a reason/s for waking? _____

_____

What time did you wake up this morning? _____hr _____min

Did you have a nap yesterday? Yes/No
If yes, at what time? _____hr _____min
for how long did you sleep? _____mins

Did you have any alcohol to drink last night? Yes/No
If yes, how much? _____
what did you drink? _____

Did you take any drugs last night? eg. pain killers _____

_____

Did you do any physical exercise yesterday? Yes/No
If yes, what type? _____
at what time? _____hr _____min
for how long? _____mins

Were you more physically tired than usual? Yes/No

Comment if anything unusual happened yesterday,
eg. salary increase, accident etc. _____

_____

_____

Oral temperature on awakening. _____.°C

Oral temperature at noon.

Oral temperature at bedtime.

Person No.____

Day No.____

SELF-RATING SCALE

Name: _____

Today's date: day____ month_____ 198____

In the scales below, please describe your feelings this morning by marking an "x" anywhere along the line. An "x" in the middle of a line would be a response for a "normal" feeling.

| | | |
|---|---|---|
| MOOD | terrible | excellent |
| STRENGTH OF MIND | indecisive | decisive |
| VITALITY | lethargic | energetic |
| IRRITABILITY | increased | decreased |
| CONCENTRATION | decreased | increased |
| APPETITE | decreased | increased |
| SEXUAL INTEREST | decreased | increased |
| TEMPERATURE SENSITIVITY | decreased | increased |
| NEED FOR SLEEP | increased | decreased |
| SLEEP QUALITY | no sleep | excellent sleep |

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**Author: Karklin Amanda.**

**Name of thesis: Very low energy diets: effect on selected physiological, psychological and sleep measures.**

***PUBLISHER:***

**University of the Witwatersrand, Johannesburg**
**©2015**

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