AN ABSTRACT OF THE THESIS OF

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Abstract approved:

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Human satiety and hunger are usually measured by observations of eating behavior or by verbal reports. Neither of these seems to be an objective method of measurement. Some studies have indicated that pupil responses to pictures of food may correspond with interest in food. The objective of this study was to determine the feasibility of using pupil responses to food pictures to measure human satiety.

Pupil sizes of 17 women, mean age 25.3 years, were measured as the women watched slide pictures of food before and after eating a high carbohydrate breakfast. Each subject participated in one to four experiments. Plasma glucose values were measured with the AutoAnalyzer ferricyanide method. Samples were taken during the fasting state and at approximately 30, 45, and 60 minutes after a breakfast which contained one gram of carbohydrate per kilogram of subject's body weight. Pupil sizes were measured with equipment which included an infra-red sensitive television camera. Pupil responses to pictures of food were compared to pupil responses to control pictures of non-food items. The differences of the changes in pupil responses before and about 50 minutes after eating were compared to several variables to determine correlation coefficients.

Plasma glucose values were found to be similar to those in other studies in which subjects ingested glucose solutions. Fasting glucose values were similar for all subjects using oral contrceptives and those who were not. Samples taken at approximately 60 minutes showed a higher plasma glucose level (118.6 mg./100 ml. \pm 30.7) for oral contraceptive users than for non-users (95.2 mg./100 ml. \pm 15.4).

Several significant correlations were found between changes in pupil response to food pictures after eating and some of the considered variables. Blue-eyed subjects had increased pupil responses to pictures of peaches and crackers, and brown-eyed subjects had decreased responses to these pictures (peaches, p < .05; crackers, p < .02). Subjects who usually ate all they wanted had increased responses to pictures of crackers, and subjects who restrained their eating had decreased responses to these pictures (p < .02). Increasing rate of the fall in plasma glucose correlated with smaller or negative changes in response to pictures of eggs and sausage, cookies, and jelly on toast. Decreasing rapidity of the plasma glucose fall was associated with greater responses to these pictures (eggs and sausage, p < .05; cookies, p < .02; jelly on toast, p < .05).

Other significant correlations were also found for changes in pupil responses to various food pictures when the variables of time of day, experiment number, body mass index and percentage of body fat (as determined by skinfold measurements) were considered, but there is some doubt about the validity of these correlations. No correlations were significant when comparisons were made of pupil response changes and the variables of oral contraceptive use, age, plasma glucose value, days before menses, and the time after eating.

Suggestions are given for improvements in the experimental method. The significant correlations of pupil response changes with the rate of plasma glucose decline are in agreement with other reports of significant correlations between verbal ratings of hunger and satiety and capillary-venous differences in blood glucose. With some modifications in techniques, it is suggested that further studies of human satiety and hunger involve pupillometry. Measurements of Pupil Size in Response to Pictures of Food with Changes in the Percentage of Blood Glucose in Underweight, Normal Weight, Overweight, and Obese Women

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TABLE OF CONTENTS

I.	Introduction1
II.	Review of Literature
III.	Experimental Methods and Procedures
IV.	Results
ν.	Discussion

Glucose Load
Timing of Specimans
Patient Behavior
Speciman Processing
Determination of Pupil Responses
Eye Color and the Change in Pupil Response to Food84
Change in Pupil Response to Food and Self-Restraint
on Eating
Change in Pupil Response to Food and Glucose Slope
Change in Response to French Fries and Weight/Height ²
and Percentage Body Fat88
Change in Pupil Response to Peaches and Experiment Number92
A Review of the Significant Correlations with Regard to
Bias by the Elimination MethodBias by the Elimination Method
Other
Summary and Conclusions
Bibliography101
Appendix

•

VI.

LIST OF TABLES

<u>Table</u>	Page
I	Experimental Procedure
II	Stimulus Slides and Controls
III	Description of Subjects
IV	Summary of Results of Glucose Tolerance Tests
V	Mean of Range of Fasting Levels of Plasma Glucose on Different Days Considering Oral Contraceptive Use, Age, and Body Mass Index
VI	Mean of Range of Fasting Levels of Plasma Glucose on the Same Day Considering Oral Contraceptive Use, Age, and Body Mass Index
VII	Fasting Values of Plasma Glucose Considering Oral Contraceptive Use, Age, and Body Mass Index at First Experimental Session
VIII	Significant Correlations of Change in Pupil Response with Other Variables. Fed Condition
А	Pupil Responses, Fed Condition110
В	Pupil Responses, Not Fed Condition114
С	Correlations of Change in Pupil Response with Variables118
D	Anthropometric Values122
Ε	Results of Glucose Tolerance Tests
F	Change in Plasma Glucose Before and After Second Pupil Response Measurement in Fed Condition

LIST OF ILLUSTRATIONS

Figur	Page
1	Pupillometer
2	Pupillogram49
3	Change in pupil response vs. eye color. Fed condition64
4	Change in pupil response vs. restraint on eating. Fed condition
5	Change in pupil response vs. experiment number. Fed condition
6	Change in pupil response vs. glucose slope. Fed condition
7	Pupil response change vs. body mass index. Fed condition69
8	Pupil response change vs. percentage body fat. Fed condition70
9	Change in pupil response vs. time of day. Fed condition71
А	Initial questionnaire128
В	Food intake record129
С	Weight history and control questionnaire

Measurements of Pupil Size in Response to Pictures of Food with Changes in the Percentage of Blood Glucose in Underweight, Normal Weight, Overweight, and Obese Women

I. Introduction

Obesity has been determined to be the primary form of malnutrition in the United States (Karpowitz and Zeis, 1975). Obesity is defined as a weight at least 20 percent above ideal weight for height. This is the standard accepted by most researchers. Several authors have acknowledged the limitations of the definition especially in the case of athletes. For this reason athletes have often been excluded as subjects in obesity studies.

Abundant food has made it possible for most Americans to consume as many calories as they want. The astonishing fact is that less than 10% of Americans are obese (Karpowitz and Zeis, 1975), and this implies that there are mechanisms that prevent normal people from eating more than is physiologically necessary.

Satiety has been defined as "that complex of sensations which impel the organism to stop eating because hunger and appetite have been satisfied, even though food is still available" (Wagner and Hewitt, 1975). The satiety response in some animals has been well defined (Antin <u>et al</u>., 1975), but, in humans, measurements have not been as exact. Not eating or eating small amounts under experimental conditions has been used as a measure of satiety (Schachter, Goldman, and Gordon, 1968); verbal responses and ranking of the state of hunger have also been used (Jordan <u>et al</u>., 1966, Jordan et al., 1968). Humans stop eating for reasons other than satisfaction of hunger and appetite as has been shown by successes in weight control by various types of behavior modification (Paulsen <u>et al.</u>, 1976) and by a study where suspicion of being observed influenced the amounts eaten by obese adolescents (Karpowitz and Zeis, 1975).

Verbal responses are unreliable from subjects who have formed complex psychological responses to food and eating as can be seen in any study of anorexia nervosa (Balagura, 1973). Obese individuals have great difficulty in responding to physiological signals of hunger and satiety (Schachter, 1971b). To study the biochemical and physiological concommitants of hunger and satiety in man it is necessary to have a method of measurement that relies on behavioral or physiological responses that have not been conditioned by past experiences and are not easily manipulated by rational processes. Pupil size has been indicated as a measure of arousal or interest. This somatic response is not easily conditioned and is unlikely to be influenced by past experiences with food.

This experiment was designed to determine whether pupil responses to pictures of food correspond to what is already known of satiety responses and whether or not this would be a useful tool for research in the factors influencing satiety in humans.

Page 3

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II. Review of Literature

Three major areas of study were involved in this experiment: 1) the validity of pupil size measurements as indicators of interest in food, 2) the relationship of blood glucose levels to satiety, and 3) eating behavior in humans as it relates to satiety.

A. Pupil Size as an Indicator of Interest

The pupil has been studied essentially in two aspects. First of all, control of pupil size is essential to vision. Dilation to admit more light in dim conditions and constriction to avoid the entry of too much light into the eye are basic, long-observed phenomena. Second, innervation by the autonomic nervous system results in a classical harmony of the sympathetic and parasympathetic nervous systems. Sympathetic or adrenergic efferent fibers control the dilator muscles of the iris, and parasympathetic or cholinergic fibers innervate the sphincter muscles (Lowenstein and Loewenfeld, 1961). This reciprocal relationship has made observations of unusual pupil responses to light important in understanding neural dysfunction (Loewenfeld and Rosskothen, 1974) and the effects of drugs on the autonomic nervous system.

Studies of pupil dilation as a measurement of responsiveness to sexual attraction, political statements, the taste of foods, and as a measure of the process of cognitive tasks have been stimulated in the last decade by the publications of Eckhard Hess. The validity of many pupillometric (measurement of pupil changes) studies has been a subject of controversy (Goldwater, 1972; Tryon, 1975; Janisse, 1974). C. Westphal, in 1863, was the first to conduct a systematic study of nonvisual sensory stimulation on pupil behavior, and Charles Darwin first remarked about this in 1872.

The equipment available for pupil size measurement has changed during the years, and in many cases the limitations of the equipment have been limitations on the type of subject tested and the type of stimuli used. Early experimenters (Gradle and Ackerman, 1932, and Bender, 1933) used subjects with light-colored irises because they could not achieve enough contrast on their movie film to accurately measure the pupils of subjects with darker irises. There was some concern that the responses of light-colored irises were not the same as those of dark-colored irises. Birren, Casperson, and Botwinick (1950) later found that iris color did not affect pupil responses to light. Hess (1975a) found that blue-eyed subjects showed a greater range of pupil response to emotional stimuli than brown-eyed subjects. He hypothesized that this may have been an important factor in evolution in relation to sexual pair-bonding in blue-eyed people but not important in darker-eyed people where pupil size changes were not as discernible.

An article in the <u>British Medical Journal</u> (1971) related that it took eight minutes longer for normal Africans to reach semimaximal dilation than albino Africans and Europeans. It was suggested that this difference may be explained by the anatomical differences; negroid irises are almost twice as thick as European irises and also have fewer crypts. The adaptive benefit may be to make dilation more difficult.

Spiero (1971) reported that the mydriatic effect of ephedrine eye

drops was inversely proportional to the degree of pigmentation of the iris.

The number of measurements that could be made in a study have been limited by the conventional methods of measuring pupil size. The earliest experiments required the experimenter to sit opposite the subject and observe pupil size through a viewer with calibrations (Gradle and Ackerman, 1932). This required great skill of the observer. This would also have made emotional responses difficult to control because of the proximity of the experimenter to the subject. Chapman, Chapman, and Brelje (1969) determined that the experimenter and his manner can affect responses to sexual stimuli.

Most of the experiments which have been published in the area of pupil size response to stimuli other than light have used photographic records of pupil size. Until recently these required the measurement of each frame of film manually to determine pupil size (Hess, 1965). More recently, photocells (Hess, 1972) and electronic calipers (Fitzgerald <u>et al</u>., 1967) have been used to measure the filmed image of the pupil. Beatty and Kahneman in 1966 used a television monitor to detect the pupil sizes and recorded these with a Kymograph camera. In 1973, Prather and Berry reported experimental results from measurements with a Space Sciences Pupillometer System which records pupil sizes from television images directly on a kymograph.

Sensitivity of film and television tubes has improved in the last two decades, and this has allowed more flexibility in experimental situations with regard to room lighting and illumination of the eyes without affecting pupil size.

Pupil responses to light have been an area of detailed experiments. It seems probable that the major function of the iris is to adjust the amount of light reaching the retina to improve visual acuity and protect the retina from excessive radiation. Autonomic control of pupil size for reasons other than light intensity may or may not have adaptive purposes. Speculations on these purposes have been discussed by Hess (1975a) with regard to inter-personal relationships, but apparently no other discussions have been published. The iris is also affected by supranuclear cortical mechanisms. Common embryonic origins of the brain and the eye in the neuroectodermal tissue may be of importance in explaining some pupil responses (Hess, 1972).

Lowenstein and Loewenfeld (1950a) found in their experiments on cats that the extent of dilation to psychosensory stimuli depended on the initial diameter of the pupil as it reflected the sympatheticparasympathetic equilibrium. Pain and sound were presented as psychosensory stimuli and the resulting dilation was from conduction over cervical sympathetic nerve fibers and from inhibition of parasympathetic activity. Eighty percent of the dilation was effected by the sympathetic pathway and 20% by the parasympathetic. These authors (Lowenstein and Loewenfeld, 1950b) also determined that when excitement inhibited the light reflex this inhibition was not transmitted over the peripheral sympathetic pathways but must have been effected over posterior hypothalamic centers which inhibit activity of the third nerve.

Galvanic skin responses (GSR) have been used as "lie detectors." Pupil size may be a better measure of autonomic activity in experimental

situations because of the greater comfort of the subject. Colman and Paivio (1969) determined that pupillary dilation was more sensitive than the GSR to changes in cognitive activity during an imagery task. Berrien and Huntington (1943) found that pupil responses were a faster and more accurate measure of deceit than blood pressure changes and gave the same percentage of error as pulse records. Hess (1975) has used the percentage of change in response, as measured by the GSR, to subtract the arousal factor from pupillary changes. He considers the net response to relate positive attitude.

Kahneman <u>et al</u>. (1969) reported an experiment in which subjects performed a paced mental task at three levels of difficulty. Similar patterns of sympathetic increase in pupil diameter, heart rate, and skin resistance were observed during information intake and processing, and decreases were observed during the report phase. The peak response in each measurement was ordered as a function of task difficulty.

Hess (1972) has found that dilation and GSR coincide in many cases, but not all, and he contends that the pupil constriction response is present when no GSR changes are observed. The negative aspect of pupil reactions is what Hess considers the primary advantage of pupil measurements over GSR measurements. Pupil constriction is, in his opinion, an avoidance response. Few researchers have reported constriction responses, and this may be the most common point of disagreement with his observations.

Goldwater (1972) suggested that Hess' claims run

"counter to prevailing opinion that all emotional reactions, regardless of their affective quality tend to elicit predominantly sympathetic activity (in this case, therefore, pupil dilation)."

Perhaps they are both right and other nervous mechanisms, e.g., the supranuclear cortical mechanisms, are responsible for pupillary constriction. Goldwater (1972), however, points out that Hess has reported constriction only with visual stimuli and that this may reflect the inherent problems in measuring emotional pupil responses with visual stimuli. Because Hess considers the constriction an avoidance response, perhaps he would consider this avoidance necessary only with visual stimuli that are unpleasant.

Psychologists have made numerous attempts to condition pupil response, and few have been successful. Crasilneck and McCranie (1956) used an electric buzzer as the conditioned stimulus and a light flash as the unconditioned stimulus. After 120 trials they found that pupil behavior was still erratic. Kugelmass <u>et al</u>. (1969) felt that any conditioning of pupil dilation, heart-rate, and GSR were difficult because of the difficulty in avoiding introduction of other unconditioned stimuli. They failed to demonstrate contraction conditioning but did show a possible dilation response where contraction would be expected. Young (1954) determined that he could not support reports of conditioning pupillary contraction to a sound stimulus.

Prather and Berry (1973) were successful with operant conditioning. Operant conditioning is conditioning by reinforcing the proper response after it occurs with a stimulus. In this case, when the subjects' pupils dilated the experimenter said, "Good." Previously it had been considered impossible to condition pupillary responses operantly. Fitzgerald <u>et al</u>. (1967) were able to condition infants' pupillary responses with the combined stimuli of time and sound after 32 conditioning periods. They were not able to elicit conditioning to sound alone. Gerall and Obrist (1962) were able to elicit the pupillary dilation response in cats as a conditioned response with the unconditioned stimulus being an electric shock. When the unconditioned stimulus was only a decrease in illumination the pupillary dilation response could not be elicited. Hilgard and Ohlson (1939) reported that pupillary conditioning to auditory stimuli could not be accomplished when the fixation object was one meter from the eyes, but conditioning was achieved within eight reinforcements when the fixation object was 15 cm. from the eyes.

The difficulties in conditioning pupil response, the sensitivity of the response, and the possibility of a negative response indicate that if light reactions are controlled, pupil responses may be the best method of measuring autonomic responses to emotional stimuli.

The pupil responses to visual material with no apparent emotional impact are well documented, and there appears to be no disagreement among experimenters at this time as to what the reactions are.

Dilation in response to darkness has no constant latent period of dilation, but after a one second period of illumination, a latent period of 0.1875 second is followed by a primary contraction at the rate of 5.48 mm. per second. A secondary contraction of the pupil lasts 0.3125 second at a rate of 1.34 mm. per second (Gradles and Ackerman, 1932).

Pupil sizes can change from day to day, apparently getting larger as the week progresses from Monday to Friday. The pupils also vary in size at different times of the day. They have been observed to be larger in early morning and late evening hours than during the usual working hours of 8:30 a.m. to 4:15 p.m. (Gardner, 1937). Smaller pupils seem to

reflect fatigue (Kumnick, 1956). Tryon (1975) suggested controls for fatigue be incorporated into experimental design by equating time of day, number of hours of sleep the night before, and type of daily activity.

Page 10

A significant moduction in pupil size with age in response to both dark and light was curvilinear rather than rectilinear (Birren, Casperson, and Botwinick, 1950). Bernick (1972) also found less pupillary activity in older subjects under conditions usually employed for psychological assessment. Kumnick (1956) reported no significant differences in rate of pupillary change because of age. Age was also not a significant factor in the mean maximal and minimal diameters and the extent of constriction. McCawley <u>et al</u>. (1966) found that age classifications were important in determining pupillary reactivity.

Different lighting conditions alter the extent and shape of the pupillary reflexes (Lowenstein and Loewenfeld, 1961). With constant lumens, pupillary constriction increases with shorter wavelengths (Bouma, 1962).

Pupil constriction can occur with constant brightness when viewing near objects for any length of time. This accomodation response varies among subjects and is more common with older subjects (Janisse, 1974). Barlow (1969) originally tried his experiments with a distance of 18 feet between the subject and the viewing screen. At this distance he found no pupillary variations. When he shortened the distance to four feet and shielded the subject from viewing the rest of the room he obtained results which corresponded to stated political preferences (dilation to similar thinking politicians and constriction to those on the opposite side). Barlow attributed the differences to distractions rather than viewing distance. Janisse (1974) suggested that distances can be lengthened without distractions by using mirrors.

Retinal distribution of visual images may alter pupil size. Hess (1972) found that brightness contrasts elicited pupil responses that were not correlated with overall brightness of the visual stimulus. For this reason he advocates minimizing contrast brightness. In 1975, Hess <u>et al</u>. published a study of changes in pupil size while looking at different areas on a slide. The areas were of light intensities varying from six to eighteen footcandles at the screen. The range of pupil variation amounted to 2.7% of the mean of the pupil diameters. The range in brightness was greater than Hess allows in his experimental stimuli.

Stimulation of one eye affects both eyes equally (Lowenstein and Loewenfeld, 1950a).

Nunally <u>et al</u>. (1967) suggested that background noise from equipment could affect pupil size.

Hess (1975) reported a greater range of pupil responses to words by men than women. This was supported by Beck's studies of responses to auditory clicking. The sexes of the experimenters were not reported.

Pupil sizes have been good indicators of mental processing. Bradshaw (1967) found pupillary dilation until problems were solved or stopped. More difficult problems produced greater dilations. Verbalization of a stored response resulted in greater pupil dilation than other verbalizations. Bradshaw (1968a) reported that arousal also played a part in increasing the pupil response to cognitive loads. He suggested that this was the reason for obtaining smaller diameters in the second half of his experiment. Not only did the act of verbalization contribute to pupillary dilation, but pushing a button at the time of solution also raised the peak of the response. Bradshaw (1968b) found in reaction-time tasks that at the highest levels of stimulus uncertainty there was an overall flattening of pupillary response peaks and a rise in the baseline levels of pupil size.

Bartlett (1967) found, in a hypnosis experiment, that alertness instructions produced a significant increase in pupil size relative to relaxing suggestions.

Fitzgerald (1968) found that, of all stimuli presented, the greatest response was elicited from one-month old and four-month old infants by face stimuli. The greatest pupillary response from fourmonth olds was to strangers' faces.

Hutt and Anderson (1967) determined that pupil size in response to emotional words was significantly and negatively related to recognition threshold. They suggested that this is a significant relationship if autonomic pupil response is the basis of perceptual defense and vigilance. Goldwater (1972) reported a study by L.M. Krueger which found a correlation of 0.85 between pupil size and the difficulty of recognition of visual stimuli.

The degree of mental processing elicited by different stimuli may be a variable that is difficult to control with any type of stimulus. Whether emotional responses can be separated from mental processing is a subject that is beyond the scope of this paper and this writer.

Measurement of pupil responses to food is relatively unexplored.

Hess and Polt (1966) measured differences in pupillary responses to different orange-flavored beverages. These responses were significantly different from responses to water.

Hess (1965) reported a stronger response to food pictures in late morning or late afternoon. With controlled food deprivation he reported subjects' pupil responses $2\frac{1}{2}$ times larger than those of subjects who had had a meal within an hour before. He later reported (1975) that when the pupil reaction to food did not agree with the verbal response in some cases, the person was on a diet and probably was trying to tell himself that he was not hungry.

Hess (1972) reported an experiment by Allan Seltzer with hypnotized subjects. Pupil response to food pictures was moderate. After the suggestion that they were very hungry, subjects responded to food pictures with a greater pupil dilation than to other pictures. The subjects were then led hypnotically through a meal and told that they were satiated. The response to food pictures was now pupillary constriction. Beijk and deJong (1971) reported that pupil responses to pictures of food by hungry subjects were significantly larger than those by fed subjects.

Beaver's studies on pupillary response to stimuli provided by pictures of food showed that the responses of hungry non-obese subjects were significantly different from those of fed non-obese subjects, but obese subjects had pupil responses to food pictures that did not change from the hungry to the fed state. He also found that food-deprived subjects had a smaller pupil response to pictures of desserts than to pictures of more complete meals (Beaver, 1976).

If dilation of pupils indicates a responsiveness to stimuli in the absence of the light-dark reflexes, then hungry people should have a greater dilation response to food stimuli than non-hungry people. If visual stimuli are used, it is necessary to control the factors that elicit adjustments for visual factors such as light intensity, color, and distance. With any type of stimuli it is necessary to control mental processing, fatigue, age, time of day, and the day of the week.

B. Blood Glucose Levels and Satiety

The rise in blood glucose after ingestion of carbohydrates has been universally observed. Measurement of the changes in glucose in the blood is the basis for glucose tolerance tests which are commonly used to detect errors in carbohydrate metabolism, such as diabetes. Another universally-observed normal reaction to food ingestion is loss of hunger. The possibility that the changes in blood glucose and loss of hunger are related has been investigated by many experimenters.

Bilateral lesions in the region of the ventromedial nuclei of the hypothalamus regularly result in an increase in food intake, hypothalamic hyperphagia. No extra energy is expended by the animal and the consequent condition is obesity. These effects have been produced in the rat, cat, dog, and monkey. This also is one of the effects of basal brain tumors in man (Froelich's syndrome, or dystrophia adioposogenitalis) and of spontaneous degeneration of the ventromedial nuclei in the mouse (Miller et al., 1950)

The role of the ventromedial nuclei in the control of food intake was intensively studied. One possibility that was explored was the

sensitivity of this area to blood glucose. Glucoreceptors in the ventromedial hypothalamus of the rat were confirmed by destruction of this area by gold thioglucose. Cerebral glucoreceptors were also indicated by hyperphagic reactions to cerebral infusions of phloridzin, an inhibitor of glucose uptake (Glick and Mayer, 1968).

The glucostat theory that has been developed from many rat studies has been a model for many hypotheses on satiety. The glucostat theory is based on the sensitivity of the ventromedial hypothalamus to blood glucose levels. It calls for initiation of satiety responses when the "satiety center" in the hypothalamus detects a certain level of glucose in the blood. The lack of glucose then "turns off" the satiety center, and mechanisms that initiate eating can operate (Mayer, 1973).

Brobeck (1975) suggests that satiety signals may be influenced by fat stores. The nature of the signals may be multiple, involving glucostasis, lipostasis, thermostasis and other factors that are not related to the energy value of the diet. If adipose store are full, the hyperglycemic stage of glucose tolerance may be high and prolonged. The satiety and hunger signals may not be related to the blood glucose level <u>per se</u> but to its direction and rate of change.

Wilson and Heller (1975) administered intragastric and intraperitoneal injections of varying concentrations of glucose and mannitol to rats. Their conclusions were that blood glucose level <u>per se</u> is not an important feedback parameter in long-term control of food intake. They observed depression of food intake after intraperitoneal injections of 16, 20, and 25 percent glucose and mannitol solutions but attributed this to abnormal physiological conditions. Rats with diabetes induced by alloxan showed a preference for *%* glucose concentrations, and controls preferred 3*%* solutions of glucose when no other food or liquid was available. Resulting hyperphagic activity in the diabetic rats led to a larger gross caloric intake, but when glucose losses in urine were subtracted from the intake, the net intake of calories was less than that of controls. Loss of weight by the diabetic animals during a two day period of exposure to only these two sources of food and other experiments which elicited suppression of food intake with glucose infusions in the ventromedial hypothalamus indicated that lateral hunger or satiety signals may be dependent on the presence of insulin, but short term glucostat responses may not require insulin in the presence of a hyperglycemic state (Panksepp and Meeker, 1976).

Peripheral glucoreceptors may also have a role in the regulation of food intake. Novin, VanderWeele, and Rezek (1973), after experiments on rabbits, reported that injections of 2-deoxy glucose into the hepaticportal system elicited more eating and a shorter latency than similar injections into the jugular vein or into the hepatic-portal system of vagotomized rabbits. From this they suggest the existence of vagally mediated peripheral glucoreceptors that are important in the initiation of food intake.

Other studies have concentrated on the possibility of intestinal mediation in the satiety response. Experiments on rhesus monkeys by McHugh <u>et al.</u> (1975) have shown that these animals have an amazing ability to regulate caloric intake. Infusions through gastric cannulas of preloads varying in volume, caloric concentration, and nature of nutrients resulted in accurate control of caloric intake during a four

hour feeding period even though some of the preload remained in the stomach. Plasma glucose did not always vary in the same manner, and after gastric infusion with medium chain triglyceride oil, the plasma glucose fell to about half of the baseline level.

In a review of published experiments on gastric emptying time, Hunt and Stubbs (1975) discussed the variations and performed mathematical analyses. Their conclusion was that the rate of emptying was dependent on nutritive density and independent of meal volume. Nutritive density was defined as kcal/ml. Some of the studies analyzed had used mixed meals and others had used fat only or carbohydrate only.

Rezek, et al. (1975) observed feeding behavior in rabbits after small and large glucose infusions in the hepatic-portal vein and in the duodenum. In comparison to animals with saline infusion of the same volume, there was no significant change in food intake with portal infusions of 10 and 30ml. of 5% glucose. Duodenal infusions of 10 ml. glucose resulted in a 21.9% delay and a 24.5% reduction in food intake during the first post-infusion hour. Duodenal infusion of 30 ml. of glucose solution, however, resulted in an increased first hour post infusion food intake and this was the only situation in which the animals started eating before the infusion was completed. The hunger reaction apparently extended into the third hour. Blood glucose and hormone levels were not measured in this experiment.

VanderWeele <u>et al</u>., (1974) infused physiological concentrations of glucose into the hepatic-portal win and duodenum of rabbits. They determined that first hour food intakes were suppressed after duodenal infusion in intact animals but were not affected with portal infusions and with duodenal infusions in vagotomized animals. Although glucose concentrations were physiological, it should be mentioned that the duodenal cannulas were inserted surgically into the stomach and threaded through the pyloric sphincter.

The possibility of enteric hormones signaling satiety or causing the release of satiety signals was confirmed by experiments by Antin <u>et al.</u> (1975). They found that injections of cholecystokinin could elicit a satiety response from rats.

VanItallie and Hashim (1960) observed changes in non-esterified fatty acids (NEFA) in the blood and capillary-venous differences in glucose after meals. They found the NEFA changes paralleled the pattern of hunger, i.e. lower NEFA values were present with lower hunger intensity, and conversely the rise in NEFA values occurred at the time of rising hunger intensity. Glucose changes did not correlate with satiety in carbohydrate free diets. This study was conducted on human males.

DeFronze <u>et al</u>. (1977) tested hormonal response in five normal male humans after an hour of sustained hyperglycemia (presumably by venous infusion). There was no increase in plasma growth hormone, cortisol, or catecholamines as long as the blood glucose concentration remained above fasting levels; these hormones were each released when the mean blood glucose reached, respectively, 28, 39, and 39 mg./100 ml. below the fasting level. Plasma glucagon was not released until the blood glucose concentration fell below basal levels. A progressive increase in glucagon occured, but returned to fasting values when the nadir of glucose concentration was reached. Plasma insulin was the only hormone which showed any change during the period of rapid decline in glucose levels, and its response lagged behind the decline in blood glucose.

Conditioned responses may also have a role in feeding behavior. LeMagnen (1969), through various conditioning experiments, was able to show that the stimulation of oral receptors in rats by food at the beginning of food intake could elicit a facilitatory or an inhibitory action on eating reflexes. The end of feeding or satiety could thus be an adaptation to the caloric content of a meal by conditioning. The post-prandial effects of previous, similar meals would have reinforced the stimulation of oral and gastric receptors.

Moskowitz <u>et al</u>. (1976) found that subjects considered 1<u>M</u> glucose solutions more pleasant tasting than 2<u>M</u> solutions or solutions of concentrations less than 1<u>M</u> after an overnight fast, just after breakfast, and just after lunch. Another group, after an oral glucose load (1.5 grams glucose/kg. body weight), rated increasing glucose concentrations as increasingly pleasant. They rated the 2<u>M</u> glucose solutions more pleasant than the 1<u>M</u> solutions. These were normal weight male medical students. Contents of the meals were not described. These results agreed with Cabanac's (1971) finding that glucose loads transformed pleasantness ratings of glucose concentration dramatically from previous ratings. Moskowitz <u>et al</u>. suggested that the glucose load is an abnormal physiological state that disturbs normal hedonic responses and may be similar to the condition of obesity which also seems to eliminate a hedonic monitor.

The change in hedonic responses with obesity is not as universally accepted as these authors indicated. Rodin (1975) found that hedonic preferences for sweetened milkshakes did not differ among normal, overweight and obese undergraduates. The overweight individuals, however, expended more effort to drink the preferred milkshake than did normal or obese subjects.

Woods and Kulkowsky (1976) reviewed published attempts to alter blood glucose levels with classical conditioning. It was determined that the central nervous system (CNS) has the capacity to alter the secretion rates of all the hormones that alter blood glucose, i.e. insulin, glucagon, epinephrine, glucocorticoids, and growth hormone. Administration of insulin with a set of stimuli results in a hypoglycemic condition. Subsequently the stimuli alone elicit hypoglycemia, apparently because of the CNS-mediated release of pancreatic insulin in response to the conditioned stimulus. The experiments reported had mixed results depending on dosage, but the authors concluded that glucose and glucagon could elicit similar conditioned responses. The authors suggested that the hypoglycemic response occurs when sufficient insulin is transported into the cerebrospinal fluid. The increases in insulin facilitate glucose uptake by insulin-sensitive glucoreceptors in the brain. These cells respond to the increased glucose uptake and elicit pancreatic insulin release via a reflex which involves the vagus nerves. This conditioning provides some explanation for the observations of insulin release in response to sweet tastes and to seeing food which were also reviewed in this article.

In a detailed review of studies of food intake regulation, Mayer

and Thomas (1967) elaborated some conclusions about the mechanisms of regulation. They examined the roles of oropharyngeal sensations, the glucostatic mechanism, and peripheral chemoreceptors in food intake regulation. From animal studies on the hyperphagia resulting from damage to the ventromedial hypothalamic nuclei, they concluded that oropharyngeal sensations in the absence of satiety determine the rate and duration of overeating and are necessary for development of maximum obesity levels. The lateral hypothalamic area seems to link the neural correlates of hunger and appetite with the feeding response system.

The glucostatic mechanism appears to regulate day-to-day food intake, but long-term food intake regulation may depend on a lipostatic mechanism that is affected by mobilization of surplus body fat.

Central mechanisms regulating daily food intake may be supplemented by peripheral chemoreceptors in determining the amount of food consumed in a meal. This may explain the occurence of satiety before significant absorption of the meal's nutrients. The initial rise in blood glucose with ingestion is caused by the release of endogenous hepatic stores of glucose. From these conclusions, Mayer and Thomas proposed three stages of regulation of food intake operating through the same mechanism. Peripheral feedback of the nutritive (or caloric) value of ingested foods may be relayed to the hypothalamus regulator by neural and/or humoral means. This added to other information such as glucose availability would determine the operation of feeding or satiety responses to regulate the length of the meal. Intermeal intervals could be determined by post-absorptive cues, and long-term intake would be regulated lipostatically.

A discussion of the complexities of obesity and the various causes and resulting physiological and behavioral differences preceded these authors' conclusion that obesity is a reflection of the failure of the energy balance mechanism from some combination of many possible neurological, endocrinological, enzymatic, and psychological disorders.

As satiety responses are studied in humans it is important to determine the biochemical correlates. Extrapolation from animal models may or may not be valid.

One of the most common biochemical measurements on the changes after ingestion by humans has been the glucose tolerance test (GTT).

Factors that affect the results of glucose tolerance tests may give some insight into post-prandial changes in man but more importantly must be considered when the results of different tests are compared. Some of the conditions that may affect the results of glucose tolerance tests in humans are; previous diet, time since last meal, racial differences, menstrual cycle variations, and diurnal variations.

i) Previous diet

Permutt, <u>et al</u>. (1976) found that subjects who had been on a low carbohydrate diet for three days previous to testing exhibited a lower nadir in plasma glucose as well as a later and higher peak in glucose tolerance tests than they had in previous tests preceded by a three day intake of at least 300 grams of carbohydrate. Insulin response was lower and later after the low carbohydrate diet, and glucagon levels were higher in the second through fifth hours of testing.

ii) Time since last meal

Parker (1976) determined that the time since last eating has a relatively marginal effect on the glucose tolerance test.

iii) Racial Differences

Dales <u>et al</u>. (1974) concluded on analysis of over 7000 GTT's on women from age 15 to 79 that the serum glucose response one hour after 75 grams of glucose was lower in blacks than whites and orientals. The differences between whites and orientals were not significant but the means were lower in whites than orientals. Weights of the subjects were not considered. This, in my opinion, could be a factor because Stunkard (1968) has determined that obesity in American women has a strong negative correlation with socioeconomic status and mobility.

iv) Menstrual cycle variations

Intravenous glucose tolerance tests given throughout the menstrual cycle resulted in no difference in mean blood glucose values or plasma insulin levels during the proliferative and secretory phases of the cycle. There were also no significant changes in weight during the cycle. Basal temperature records confirmed ovulation in the subjects who also exhibited normal menstrual histories and glucose tolerance (Spellacy et al., 1967).

Jarrett and Graver (1968) reported that random variations in many women masked any differences in responses to oral glucose tolerance tests during different phases of the menstrual cycle. In others, variations, primarily in the level of the peak of blood glucose, resulted in the tolerance test area being least at the beginning of the cycle.

Macdonald and Crossley (1970) found that oral glucose tolerance tests administered weekly showed a greater variation in 13 women as compared to six men. They suggested that the variation may be secondary to the influences of hormones on the gastro-intestinal tract.

v) Diurnal variation

Zimmet <u>et al</u>. (1974) determined that blood sugar levels were higher in the afternoon than in the morning from the 60 minute sample on. They also found less diurnal variation in glucose levels with obese subjects.

C. Eating Behavior in Humans as it Relates to Satiety

The satiety response in rats has been well defined (Antin <u>et al</u>., 1975). From this response it has been possible to measure many of the biological concomitants of satiety in these animals. Feeding behavior in animals is assumed to be instinctive behavior and thus satiety causes the cessation of eating and hunger initiates eating.

Human eating behavior reflects not only hunger and satiety but conditioned responses to reward and punishment, social behavior, and cultural aspects of meal feeding. Some of the ways in which we can get closer to understanding what satiety is and how closely the physiological mechanisms of satiety in humans parallel those in animals are; 1) understanding what human eating behavior is, 2) determining what aspects of it are conditioned, and 3) observing the differences in behavior between normal weight people who apparently have effective mechanisms regulating food intake and obese people who apparently have ineffective mechanisms.

Stunkard and Koch (1964) asked male and female, obese and non-obese

subjects to swallow tubes which permitted measurement of pressure changes in the stomach. Pressure changes reflected gastric motility. Several aspects of gastric motility and perception of hunger were explored. The results indicate that; 1) there was no relation between gastric motility and percent overweight, 2) non-obese women showed a high correlation of simultaneous gastric motility and reports of hunger and conversely no gastric motility and no hunger, 3) most of the obese women showed a much lower correlation between gastric motility and reported hunger, 4) non-obese men did not show as high an association between gastric motility and reports of hunger as non-obese women, 5) non-obese subjects did not show the bias of reporting hunger that was present in obese subjects, 6) obese men showed a bias in reporting hunger most or all of the time, and 7) obese women showed a bias by rarely or never reporting hunger. Half of the obese women suffered from the night-eating syndrome and, as a group, their bias was greater than the other half of the obese women. (These tests were conducted in the morning) The authors suggested that these biases parallel the clinical axioms that obese women frequently underestimate their food intake and that obese men rarely underestimate the intake and often boast about it.

In a subsequent study, Griggs and Stunkard (1964) investigated the perception of gastric motility by attempting to influence the perception of two male subjects, one obese and one non-obese. The obese subject was able to develop a high degree of sensitivity to gastric motility. The non-obese subject was more sensitive, however, without training, and his responses could not be substantially altered. Unfortunately, the obese person was unable to improve control of his weight as a result of

his increased ability to perceive gastric motility.

Schachter, Goldman, and Gordon (1968) found that after a preload of sandwiches, normal weight subjects ate less of a test food than did normal weight subjects who had not had a preload of sandwiches. Obese subjects ate similar amounts of the test food in the pre-loaded condition and in the condition without a preload.

Suspicion of being observed in a situation where they could eat resulted in differences in the amount that obese adolescents ate. Those subjects who had previously participated in a weight control program ate less than those who had not tried to lose weight (Karpowitz and Zeis, 1975). This and other personality variables may explain some of the conflicting reports on the eating behavior of obese individuals.

Many studies of the eating behavior of obese, overweight, and normal weight people have shown that people in these groups have similar reactions to hunger. The major difference appears to be a lack of appropriate satiety responses in the overweight and/or obese individual rather than abnormal hunger (Mayer, 1973).

Judith Rodin (1975) found that overweight (16.2-38.2% over normal) subjects were more inclined to drink a good tasting milkshake and less inclined to drink a bad tasting one than obese(60% or more overweight) or normal ($\frac{+}{-}$ 10%) subjects.

Lesions of the ventromedial hypothalamus in the rat produce hyperphagia (excessive eating) and consequent obesity. During the dynamic stage of obesity, i.e. when they are gaining weight, they display an exaggerated positive attitude to good tasting food and only a slightly negative response to adulterated food. When they are obese, however,
they display an exaggerated negative response to quinine adulterated food and stop eating. Normal rats eat for the calories in the food and don't seem to be as sensitive to the stimulus characteristics of the diet (Teitelbaum, 1955). If this hyperresponsiveness to taste occurs mainly in the static phase of the ventromedially lesioned rat, then this is apparently not the cause of obesity but a correlate.

In an amusing article by Schachter (1971a) similarities were drawn between hypothalamic lesioned rats in the static phase and obese humans. He pointed out that the rats "have been abused by a variety of people named Epstein, and Teitelbaum, and Stellar, and Miller, and so on." Many of the reported experiments on humans were performed in his laboratory and the subjects were "mostly Columbia College students, nice boys who go home every Friday night, where, I suppose they too are abused by a variety of people named Epstein, and Teitelbaum, and Stellar, and Miller." The points of parallel eating behavior in the lesioned rats and the obese humans were: 1) obese eat less of quinine-adulterated food than normals, 2) obese eat slightly, but not considerably, more than normals daily, 3) obese eat fewer meals than normals, 4) obese eat more per meal than normals, and 5) the obese eat more rapidly than normals. Other behavior comparisons were that the obese seem to react more emotionally than normals and are also less active.

Schachter reported that the lesioned rats did not work as hard to get their food as the normal rats did. To determine if obese humans are similar to the lesioned rats in not working hard to get their food, Schachter and his colleagues determined that obese subjects were more likely to eat shelled peanuts than unshelled but normal subjects showed little variation in preference. Confirmation of this aspect of parallel behavior was obtained in Chinese and Japanese restaurants. Normal occidentals were more likely to eat with chopsticks than obese occidentals.

Schachter also reported that obese humans, like the rats, do not regulate food consumption when preloaded with solids but they do with liquid preloads.

Because genetically obese mice who behave similarly to the lesioned rats have no structural difference from normals in the hypothalamus Schachter presented an explanation by Mrosovsky that the ventromedial hypothalamus of the obese mice and obese humans is "functionally guiescent."

To determine other behavior characteristics, Schachter and his colleagues experimented with obese humans and found that they 1) have better recall to visual stimuli, 2) have a faster and more accurate complex reaction time, 3) are more accurate at proof-reading when undistracted but less with medium and high levels of distraction. From these characteristics he speculated that the obese are more stimulus-bound in their behavior. [I would suggest that his college students were poor subjects for this without controls for intelligence and grades. Obese college students may be brighter than normal weight students. Eden (1975) reported a study by the Harvard School of Public Health that indicated that with similar grades, I.Q.'s, aptitude test scores and health records, one third more non-obese girls and two thirds more non-obese boys were admitted into the college of their choice than were obese girls and boys.]

Schachter cited experiments with humans that confirmed his

Page 28

hypothesis that obese humans will work harder for food when food cues are compelling and prominent. Normal subjects work as hard if the food is remote or prominent.

Schachter's parallels are interesting, but he assumed that all obese humans are at a static phase. Humans, unlike rats, often attempt to control their weight, and he had not differentiated between subjects who were attempting control and those who were not. The dynamic stage of the hypothalamic lesioned rats might be a more appropriate stage of comparison for some subjects. The youth of the subjects may also be a factor in determining what stage of obesity they are in.

Colby, Misovich and Kasouf (1974) tested Schachter's proposal that the human response to external food cues in the obese state is similar to the rat's and thus may show a common physiological basis. They tested the response of ventromedially lesioned rats in the dynamic phase of obesity and found that they did not eat more when the food was in plain view than when it was hidden away in tubes. The normal rats also did not show any differences in the amount eaten when food was hidden and when it was in plain view. (The dynamic stage was not the basis for Schachter's hypothesis) This is not what Nisbett (1968) observed in human subjects. Nisbett's subjects were deprived of lunch and put in a situation where they were presented with roast beef sandwiches. They were told that they could have as many sandwiches as they wanted for there were many more in an adjacent refrigerator. There were either one or three sandwiches on the table. Obese subjects ate more sandwiches than normal weight subjects in the three sandwich situation and less in the one sandwich situation. (Nisbett also did not differentiate between those

who were attempting weight control and those who were not.)

In two of Schachter's publications (1968, 1971b) he has described several studies that indicate the overweight or obese person is more likely to respond to external cues for eating than the normal weight person who, although somewhat responsive to external cues, responds mainly to physiological cues for initiating eating and for determining the number of calories consumed.

Schachter's own studies and others that he reported indicated a variety of external cues that apparently stimulate obese people to eat. When the time shown on a clock was later than it actually was, obese people ate more than normal weight people. Studies of pilots who flew the Atlantic showed that normal weight pilots had more difficulties in adjusting to the drastic change in meal schedules than did obese pilots. The obese pilots could easily adjust their food intake to the customary meal times of their new location even though it would require a longer time between meals. Non-obese pilots found that the time between meals was more important than the time when other people were eating for experiencing hunger. Obese men who observed fasting on Yom Kippur had little problem with the fasting if they spent the day in the synagogue. If they spent most of the day outside the synagogue where they were exposed to food and eating cues, they had a difficult time fasting. Normal weight men had similar difficulties with the fast no matter where they were. These studies seem to indicate that eating behavior in the normal weight people is a response to internal cues and obese people base their eating behavior on external cues.

An experiment by Hashim and VanItallie (1965) supported the

previously observed differences in eating behavior. Two subjects, one normal weight and the other obese, were hospitalized and given a bland liquid diet. Both had an initial drop in caloric intake with the change from usual hospital fare. The normal weight subject soon adapted to an intake that maintained his weight. The obese subject, however, continued her decline in caloric intake and soon was ingesting a very small amount although she was allowed to have as much of the bland diet as she wanted.

As indicated by the Schachter studies, normal weight individuals seem to have internal clocks that stimulate hunger, whereas the obese individuals rely on external cues. Stevenson and Fierstein (1976) found that rats under constant illumination with <u>ad libitum</u> feeding have circadian rhythms of the digestive enzyme sucrase and the absorptive transport system for glucose. With controlled feedings at 1400-1800 hr. or 200-600 hr. EST the rhythms shifted with time and there was an enhancement of the general level of these activities. Peak sucrase activity occurred before feeding and transport activity peaks occurred during feeding. The shifted rhythms were synchronized by the previous days' feeding pattern.

Stanton (1975) described his effective method of weight control using hypnosis. He felt that resulting behavioral changes were effective in large part because the therapist and patient believed the method would work.

Garrow and Stalley (1975) reported a case study which indicates that weight may be maintained at plateaus which have a "buffer" system that resists weight loss and gain. This plateauing or maintenance of a set point resembles the plateauing of weight in the hypothalamic hyperphagic rat.

Cabanac (1971) reported experiments on lean subjects who reduced their body weight by ten percent. During the reduced state, ingestion of 50 grams of glucose did not make certain sweet tasting solutions unpleasant to taste. When these subjects returned to their normal body weight the ingestion of 50 grams of glucose resulted in the same sweet solutions tasting unpleasant. Obese subjects responded the same as the reduced normal subjects. The author suggests that many obese people combat their obesity and are thus below their "set" point.

Rats compensate with changes in volume of food ingested within 24 hours to changes in the caloric density of the food if water dilution is used, but they do not seem to respond to changes in caloric density when inert solids replace calories in the diet. Adjustments in food intake after solid dilution of calories seem to be more dependent on weight loss than the caloric density of the diet (Brobeck 1974).

Warner and Balgura (1975) found that obese and normal weight subjects did not differ significantly in number of bites of food or bites per minute, but they did find that obese subjects' meals had a significantly longer duration. The amounts of food were not measured but each subject apparently ate as much as he or she wanted. Although the differences in the two experiments reported were not significant, the obese subjects took more bites per minute. The exception was that non-obese men took more bites per minute than obese men in a college lunchroom. The necessity for eating rapidly was not considered by the author.

Support for the indications that obese people eat more rapidly than non-obese people was given by results of other studies. Gaul et al.(1975) found that obese subjects spent less time chewing and took more bites in a five-minute observation than non-obese subjects. Thus the obese were more rapid eaters.

Hospitalized obese and non-obese subjects were observed during mealtimes. Observations were made in such a manner that subjects were not aware that their eating behavior was being observed. Obese subjects ate faster with less time spent chewing each mouthful. The authors, Wagner and Hewitt (1975), interpreted the results to demonstrate that obese subjects do not sense oral satiety, this aspect of satiety can be overridden, or that oral satiety, if present, is a relatively weak component of overall satiety.

Human subjects who received a liquid breakfast orally or intragastrically by activating a pump attained the same level of intake by either method if the pump rate was not varied for several days. The subjects could not accurately estimate the amount ingested. Oral and intragastric feedings were similar in preventing subjects from feeling hungry before the next meal, and intakes in both situations were depressed by emotional stress and illness. After intragastric feedings they felt more need for oral stimulation and their hunger ratings did not fall as low as they did after similar oral feedings (Jordan et al. 1968).

Support for the importance of oral satiety cues was demonstrated in a recent experiment by Booth <u>et al.</u> (1976). Conditioning of satiety responses to flavor was attained in normal weight adults. During training, 100 ml.of a 65% starch solution was given before lunches which included a yogurt-based dessert of one flavor and 100 ml. of a 5% starch solution was given before a meal with a different flavored dessert. Subjects who initially ate lunches of similar size following the two drinks altered, after several pairings, their intake to consume larger lunches after the dilute solution than after the concentrated one. During extinction tests, identical 35% starch solutions were given before the meals and subjects continued to eat less of lunches containing the dessert with the flavor that had been paired with the concentrated solution and more of the other meal. The authors concluded that one type of feeding control is the association of a food with past relationships between its sensory qualities and after-effects of ingestion.

Glucose (50 mg. in 100 ml. water) taken 20 minutes before lunch depressed calorie intake at lunch and in a snack three hours later for male and female subjects (relative weights not given). The control was a saccharine-cyclamate drink. If the glucose was taken just before lunch, caloric intake was also less than under control conditions but the depression was half as great as it was with the 20-minute interval. The snack three hours after lunch was not affected by glucose loading just before or after lunch (Booth et al., 1970).

Jordan <u>et al</u>., (1966) described a device which allowed subjects to drink liquids without being able to see how much they were drinking. Ingestion of milk or Metrecal with this device resulted in a high correlation between subjective hunger ratings and the amount ingested in the next five minutes. Correlations were not as high when initial hunger ratings before a meal were compared to the total amount ingested. Experiments in which subjects were preloaded with 235 cc. of the liquid from a tumbler resulted in depression of intake during the test meal. Maximum depression of intake resulted from varying time intervals between

Page 34

preloads and meals but this time was consistent in a given subject over several trials. Of eight subjects, four showed maximum depression at 15-30 minutes, three at 1-5 minutes, and one at one hour. Preloads of water caused depressions of intake which paralleled the effect of Metrecal preloads, but the effect was not as marked or long-lasting. Subjects reported that these experimental meals were adequate substitutes for their regular breakfast or lunch.

III. Experimental Methods and Procedures

A. Recruitment of Subjects

Subjects were recruited by various means. These included notices on bulletin boards around the campus, classified advertisements in the campus newspaper, an article in a local extension publication, announcements in large undergraduate nutrition classes, and word of mouth. A detailed article was written by a journalism student and was published in the campus and community newspapers.

It was requested that subjects be women 20-45 years old, able to see at three to six feet without correction, not be diabetic, and not be pregnant.

The purpose and procedures of the experiment were explained to all the subjects; their duties were explained (e.g. how to keep dietary diaries and how long a fast to observe before the experiment); and they were told they would receive no monetary compensation but would be furnished breakfast and the results of their glucose tolerance tests.

Three potential subjects never came for experimentation, but nineteen subjects who agreed to participate fulfilled their agreement with the exception of one who became pregnant. The subjects were well motivated for various reasons. Generally the motivation was participation in an experiment that would produce information in an area that interested them personally.

The subjects were interesting and enjoyable, and their enthusiasm was very helpful to the experimenter.

Page 37

B. Scheduling

Subjects usually agreed to participate in four experiments at least a week apart. At the initial interview the average length of the subject's menstrual cycle was determined. Three experiments were scheduled to coincide with three different weeks of the menstrual cycle, and the fourth experiment was scheduled to duplicate a week of the cycle in which a previous experiment had been conducted. No attempt was made to schedule experiments during any specific weeks of the cycle.

No experiments were scheduled on Mondays to avoid deviations in food intake, activity, and fatigue on the day before the experiment. Times chosen for experimentation ranged from 7 a.m. to 11:45 a.m. at the convenience of the subject and experimenter. Schedules of food preparation in nearby rooms were ascertained to avoid influences from food odors.

In most cases experiments with any one subject were at the same time of day and on the same day of the week.

C. Pre-experimental Conditions

For at least three days before each experiment each subject kept a record of food intake (kind, amount, and time of intake), drugs taken, sleeping times, and any unusual activity or condition (Appendix, Figure B).

When the experiment was scheduled for early morning the subject was asked to limit oral intake from midnight for all except water, decaffeinated coffee, and oral contraceptives (if this was the usual time for taking them). For experiments scheduled after 10:30 a.m., subjects were allowed a breakfast of one piece of bread, one egg, four ounces of juice and whatever fat was necessary for preparation. This breakfast was to be consumed at least four hours before the experiment and was optional.

D. Experimental Procedure

For an outline of the procedure followed for each experiment, see Table I. The subject was admitted to the room and welcomed. She was seated at the pupillometer (see Figure 1) and the chair height was adjusted. The pupillometer used was a Space Sciences Pupillometer, model 800.3X (manufactured by the Space Sciences Division of Whitaker Corporation, 335 Bear Hill Road, Waltham, Massachusetts 02154). This instrument contains a head harness, an infra-red light source, a television camera, a visual monitor, and a control unit with a graph and a stylus. The slides were shown in a Caramate Projector (manufactured by Singer, Education Division, Education Systems, Rochester, New York 14603). This is a rear screen slide viewer that can be programmed to advance slides at a given rate. Room lights were turned off and she was asked to look at a non-food picture while the pupillometer was focused and aligned.

She was then given a bottle or beaker and asked to make a urine collection at a nearby toilet. When she returned, the door to the room was closed and she was seated at the pupillometer. After determining that the subject was comfortable and the pupillometer was in focus, the subject was instructed to look at the middle of each slide and not to be concerned if some of the slides were blank. Pupillometer readings

TABLE I. Experimental Procedure

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		1.	Focus and adjust pupillometer
		2.	Collection of urine sample
		3.	First pupillometer reading
		4.	Fasting blood sample drawn
Time =	0	5.	Eat breakfast or water only
		6.	Anthropometric measurements
Time =	30 min.	7.	Blood sample drawn
Time =	45 min.	8.	Blood sample drawn
		9.	Urine sample collected
Time =	50 min.	10.	Second pupillometer reading
Time =	60 min.	11.	Blood sample drawn



Figure 1. Pupillometer

were made as she watched 32 slides.

To get subjective responses to the slides, the subject was asked if any of the slides struck her as especially appetizing or unappetizing. She was then seated at another chair for drawing the fasting blood sample. As the technician took the blood sample, the experimenter prepared the breakfast. In two cases the subjects were anxious about the blood drawing and were taken to a nearby room to lie down during the sampling.

When the subject started eating at a third place in the experiment room, the timer was started; thus, commencement of eating was time zero. For most subjects, during one experiment no food was served. When the subject was seated at the table where eating was normally performed, this was also considered time zero. Water was always available to all subjects and they were instructed to drink whenever they were thirsty.

After the subject had eaten she was questioned about her food diary and when her last menstrual cycle had begun. She was weighed and her height was measured without shoes or heavy outer garments. Skinfold measurements at the triceps muscle and one inch above the suprailiac crest were made with Lange calipers (Cambridge Scientific Industries, 101 Virginia Ave., Cambridge, MD). These measurements were made in the manner described by Sloan and Weir (1970).

Except for these activities, the subject was seated and read the morning newspaper or was involved in conversation with the experimenter or technician. (An attempt was made to avoid discussion about specific foods, but this was not always achieved.)

Second and third blood samples were drawn as close to 30 and 45 minutes after zero time as could be managed. After the third blood drawing, the subject was again asked to make a urine collection. On her return to the darkened room, she was seated at the pupillometer. The same slide sequence was shown again and recall of subjective impressions was ascertained. The final blood sample was then taken. This was about 60 minutes from zero time.

The subject was thanked, and the next experiment time was confirmed. If she had not been fed during the experiment, whe was offered the breakfast at this time.

E. Processing of Samples

Urine samples were tested for glucose and ketones as soon as possible. Measurements were made with Keto Diastix (Ames Company, Miles Laboratories, Elkhart, Ia.) according to directions on the label. This is a semi-quantitative test to detect the possibility of a diabetic condition.

Five to ten milliliters of blood were drawn for each sample into heparinized Vacutainers from the antecubital vein. Blood samples were refrigerated immediately and centrifuged within an hour of drawing. The plasma was aspirated, placed in tubes, and frozen. The samples were held at -20°C. until analysis. All blood samples were analyzed in a three day period at the end of testing by ferricyanide technique with a Technicon AutoAnalyzer (Technicon Instruments Corporation, Tarrytown, New York 10591) (Hoffman, 1937).

F. Techniques for Measurement of Food

Approximate weight was requested of each subject on an initial questionnaire (Appendix, Figure A). This weight was used to determine the amount of food the subject would ingest at each experiment.

The food was adjusted to provide each subject with one gram of

Page 43

carbohydrate per kilogram of body weight. The amount of carbohydrate in

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the food was estimated by values from <u>Handbook 8</u> (Watt and Merrill, 1963).

Orange juice -- Each meal contained six ounces of unsweetened, canned orange juice. The brand was Western Family (Western Family Inc., San Francisco, Calif.). The orange juice was not weighed but came from individual six ounce cans.

Toast -- Sandwich slices of white enriched bread were toasted immediately before service. These were presented as whole slices and were weighed before the experiment day and stored frozen. Subjects weighing less than 125 pounds received one slice of bread, those weighing 125-145 pounds received two slices of bread, and those weighing more than 145 pounds received three slices.

Jelly -- The jelly was blackberry jelly which had been prepared by OSU foods classes. The amount given was that necessary to bring the carbohydrate amount to one gram per kilogram of body weight. The jelly was spread on the toast before service.

Estimated energy values of the food were: Orange juice, 81.8 kcal. per six ounce portion; bread 64.8 kcal. per 24 gram slice; jelly, 2.7 kcal. per gram (Watt and Merrill, 1963).

G. Slide Preparation

Control and stimulus slides were photographed from the same distance (18 inches) and angle under the same lighting. Three levels of exposure were used during photography to give a range of intensities from which to choose. One group of slides was duplicated so control slides could be presented before and after the stimulus. The second processing of the slides resulted in different intensities of light so the duplicates did not match the originals in light intensity. All slides were in full color.

The stimulus and control slides are described in Table II. The light intensities indicated were measured in foot-candles at one foot from the center of the screen. The room light was at zero foot-candles. Light intensity measurements were made with a Light Meter (General Electric, Cleveland, Ohio).

TABLE II. Stimulus Slides and Controls

<u>Slide #</u>	Stimulus	f/c^{a}	Control	f/c ^a
1,2	Two canned peach halves	4	Two rolls of yellow tape	4,2 ^b
3,4	Carrot Sticks	4,5	Orange napkin cut with jagged edges	3,2
5,6	Handful of cheese crackers on woven plat	4 ce	Orange napkin folded on a woven plate	1,2
7,8	One slice of toast with a slice of cheese melted on it	4	White paper square colored with brown and orange crayons	2,2
9,10	Two eggs, sunny side up, four link sausages	3	Two white flowers with a yellow centers and a horseshoe	1,1
11,12	One egg, sunny side up, one pancake with a pat of melting butter, and four link sausages.	5,7 1	One white flower with a yellow center, one brown flower, and a horse- shoe.	4,5
13,14	Two pancakes with butter and four link sausages	c 2	Two brown flowers and a horseshoe.	3,1
15,16	Two plain cookies with holes in the center	4	Two wooden drapery rings	3,4
17,18	One slice of toast with blackberry jelly sprea on it	9 ad	A square of white paper colored with violet and red crayons	5,3
19	A cream puff with chocolate icing	3	A ball of beige yarn and a cotton puff on a dark brown napkin	3
20	A sticky bun	2	A small brown bag folded do	wn 2
21	Chocolate cake - a slice from a roll with pink filling	e 1	A round box wrapped as a gi with dark brown paper and a pink ribbon	ft 1 d
22	The above cake slice cut	. 1	Same slide as above	1
23	A T-bone steak	5	A clothesbrush	5
24	French fries	5	Clothespins	5
25	Fruit cocktail	2	Assorted buttons	2

^aLight intensity as measured in foot-candles at one foot from viewing screen.

^bWhere two values are presented under "f/c" this indicates more than one copy of the slide was used.

Control slides for slides 1 to 18 were darker than the stimulus slides, as used to avoid bias in experiments by Beijk and deJong (1971). This would prevent any dilation to the stimulus slide from the light response. Other slides were similar to their controls in brightness, as used by most experimenters. In no case was the control slide brighter than the stimulus slide.

Stimulus slides were pictures of food on a plate or in a dish. The background was grey, the dishes were plain white or brown, and no garnishes were added to the food to make it more attractive. To enhance the photographic presentation, foods were occasionally plastic food models or natural foods which were prepared cosmetically. The subjects were not told of these procedures.

Control slides were designed to mimic the shape, color, texture, placement, and volume of the food without appearing to be food. They were usually easily identifiable common objects and were presented on a circle of paper which was the size and color of the plate used for presentation of the food.

H. Presentation of Slides

A Caramate projector was set so the screen was slightly above eye level. The size of the screen was 22 x 22 cm. The screen was 81.3 cm. from the subject. After an initial focusing slide, thirty-two slides of 10-second duration were presented. In the first experiments, all the slides had a pictorial content. Later, to avoid pupil fatigue, blanks were left in the sequence. These blanks were dispersed throughout the sequence but were never presented between a stimulus and its control The first five or six slides in the presentation were nonexperimental, i.e. landscapes, children, flowers. During the first experiments each stimulus slide was presented with control slides before and after. Later the sequence pattern was changed to present a stimulus slide with controls before and after, a dark blank, two stimulus slides each preceded by a control, a dark blank, a stimulus with controls before and after, etc.

The order of presentation of stimuli was randomized. These sequences were changed each week so no subject saw exactly the same sequence twice although she saw many of the slides at more than one experiment.

I. Measurement of Responses

An infrared light was reflected off the subject's left eye, and this image was transferred by the television camera to the viewing screen. The change in brightness from the pupil to the iris caused a line to appear in the viewing screen. This line was measured electronically and the length of the line represented the diameter of the pupil. In turn, the electronic impulse moved a stylus on a graph and this was calibrated so that the placement on the graph represented the diameter of the pupil. When the stylus movements did not reflect pupil measurements the experimenter noted this on the graph.

The graph was marked during the measurement to indicate which slide was being presented to the subject.

J. Readings of Pupil Size and Determination of Percentage Change in Pupil Diameter

A representation of the graph produced by the pupillometer is shown

in Figure 2.



Figure 2. Pupillogram

Vertical background lines indicate seconds, horizontal background lines indicate millimeters of pupil diameter (zero at the bottom, 10 at the top).

The heavy line indicates the tracking of the stylus. The abrupt vertical movements, A_1 and A_2 , are artificial and indicate the change in slides. The slow rise after A_1 usually indicated adjustments of the equipment to measure a new pupil size. The pupil itself would adjust in the first second of the presentation of the slide. The usual reaction to darkness was continued dilation for the full 10 seconds. The abrupt vertical movement, B, indicates a blink.

To determine the measurement of the pupil for this slide there was a potential of ten readings, one at each intersection of the stylus track with the vertical time line. In this case, however, each intersection would not have been counted. The first two intersections represented adjustments and would be disregarded. All intersections that for this slide. If less than five were counted, the measurement was not recorded and was indicated as "no reading."

The reading represented in Fig. 2 was smooth and had little variance. Many readings were notthis smooth, and a standard deviation was determined for each slide by taking the square root of the variance of the measurements.

The percentage change in pupil size from control to stimulus was determined by subtracting the mean pupil size of the control from the mean pupil size of the stimulus, dividing by the control mean and multiplying by 100.

$$\frac{\overline{x}_{st} - \overline{x}_{c}}{\overline{x}_{c}}$$
 x 100 = percentage change in pupil size or pupil response

This value was considered to be "significant"^a when $\left| \bar{\mathbf{x}}_{st} - \bar{\mathbf{x}}_{c} \right|$ was greater than the standard deviation of measurements of both the control and the stimulus. All pupil responses that showed a percentage change greater than 5% and were not "significant" were omitted from the data. [Hess <u>et al</u>. (1975) determined that a 2.7% change in pupil size could be evoked from intra-stimulus brightness differences. The choice of 5% as an arbitrary demarcation was a generous inclusion of possible experimental variations as a zero change in response. Consideration of these small "insignificant" changes with regard to correlation sig-

nificance is discussed under Data Analysis.]

^aSignificance as used here is not the usual statistical definition. Here it was considered to be a measurement that did not reflect experimental error because it was greater than the standard deviations of the measurements considered.

K. Glucose Determination

From a pilot study on healthy young women it was determined that the food as given elicited glucose tolerance reactions similar to those achieved with conventional glucose solutions in a similar group of women with one gram of glucose per kg. body weight (conditions of testing were similar and plasma glucose was measured in the same manner.)

The food used was chosen because of its 1) high carbohydrate content, 2) low fiber content, 3) general acceptibility, 4) convenience, and 5) similarity to a breakfast meal.

The plasma glucose level at the beginning of each pupillometric measurement period was determined by extrapolation from the glucose percentages of the samples taken closest in time to the pupillometric measurement. Fasting glucose was considered to remain stable and was used for the plasma glucose value for the first pupillometric reading. The rate of change of glucose, or slope, was considered to be zero. Glucose values for samples taken before and after the second pupillometric reading were used for determining the slope of glucose change rate, i.e.:

slope =
$$\frac{\text{Glucose}_2 - \text{Glucose}_1}{\text{time interval}}$$
.

The level of the glucose at the beginning of the second pupillometric reading was determined by multiplying the time from the Glucose₁ sample to the beginning of the pupillometric reading by the slope and adding this value to that of Glucose₁, i.e.:

adding this value to that of $Glucose_1$, i.e.: $Glucose \ level \ at \ p_2 = \begin{pmatrix} time \ from \\ Glucose_1 \ to \ p_2 \ x \ slope \ + \ Glucose_1 \end{pmatrix}$

L. Skinfolds

Skinfold measurements at the triceps and suprailiac crest were taken three times at each place. The means of these measurements were used to determine the percentage of body fat with the nomograph and formula developed by Sloan and Weir (1970) for use with young Caucasian women. The formula is based on correlations between skinfold measurements and body density as determined by underwater weighing.

M. Definitions

The following definitions were used to categorize subjects. Breakfast eater determination:

Information from the food intake records was used to determine whether subjects were accustomed to eating breakfast. Breakfast eaters were those who had had some caloric intake within 2 hours of arising for two of the three days preceding the experiment.

Eats all she wants or not:

Subjects were given a questionnaire (Appendix, Figure C) during the final experiment to determine whether they were accustomed to eating all they wanted to eat. They were specifically asked if they ate everything they wanted to. Answers to other questions in this questionnaire substantiated the validity of this response.

N. Analysis of Data

Data were analyzed in the Statistical Interactive Programming system (*SIPS) at Oregon State University.

Because readings were not obtained on all the slides at any one

experimental session and because a subject may have had readings on the same slide at more than one experimental session it was necessary to eliminate some data. Comparisons were made on the responses before and after feeding, so it was necessary to have acceptable readings on pupil responses to a particular slide twice in an experimental session. To avoid having readings from the same subject in the data more than once, only the readings before and after feeding at the experimental session in which the first acceptable readings were obtained were left in the data, e.g., if good measurements on a particular slide were made at the second and third sessions, only the measurements from the second session were retained.

Because all the subjects had no more than one session where they were not fed, it was not necessary to eliminate duplicate data for the "not fed" condition.

Correlation coefficients were determined by comparing the changes in pupil responses (second response - first response) to the values of the variables. The variables considered (and the numbers assigned for analysis) were: eye color (blue=2, brown=1); eating all she wants (yes=2, no=1); the experimental session number for that subject; the change in glucose level (glucose at second reading - glucose at first reading); the change in glucose slope (because the slope at the first reading was considered zero, this was the slope at the second reading); the days before the onset of the next menstrual cycle; weight/height²; the percentage of body fat (as determined from skinfold measurements); the time of day the first reading was taken; the day of the week (Monday=1); the elapsed time between ingestion and the second pupillometry; and whether the subject was a breakfast eater at that session (yes=2, no=1).

The pupillary response data that were analyzed are listed in Tables A and B, Appendix. In several cases, the significance was determined to be caused by artifact and the corresponding correlation was eliminated from further consideration. The correlations that were obtained before subjective elimination are found in Table C, Appendix. Some of the situations that warranted elimination of statistically significant correlations were; all changes in glucose levels and slopes in the "notfed" condition were within the range of experimental error of glucose determination, the correlations were obtained on pupil changes which were determined by "insignificant" responses before and after feeding, the sample number was so small that the variables associated with the largest pupil change determined the correlation, extreme responses resulted in invalid correlations, the sample group was not representative of the group as a whole with respect to the variables considered, and considerations of breakfast eating habits had so few non-breakfast eaters that this variable could not be considered.

Page 55

IV. Results

A. Subjects

Eighteen women of mean age 25.3 years participated in one to four experiments. Most (13) of the subjects did not use oral contraceptives, and the group was well divided in eye color (blue=10, brown=8). The study was originally designed to provide classifications based on obesity, normal weight, and underweight, but the subjects recruited did not make the groups large enough for classifications, so body mass index (weight/height²) and percentage of fat were used as variables. Table III gives a description of the subjects. All subjects were Caucasian, and all but three of the subjects were students at Oregon State.

Although most of the subjects regularly ate breakfast, the group was evenly divided in the area of eating to appetite. Nine of the subjects imposed no restraints on what they ate, but eight indicated some restraint was necessary to maintain their weight were it was. Restraint of eating did not follow any clear cut pattern in relationship to body mass index, r=0.1438, or to percentage of fat in the body, r=0.1888.

B. Anthropometric Measurements

Weight measurements did not vary much from session to session, and height was measured only once. Thus, the weight/height² value showed little variation for any one subject (the mean standard deviation was $0.274 \text{ kg.}/\text{m}^2 \pm 0.199$).

Skinfold measurements on some subjects were very difficult to duplicate. (The mean standard deviation was $1.653\% \pm 1.398$ with a range of

Subject Number	Oral Contra- ceptive user	Eye color	Age	Eats all she wants	Breakfast eater	^{Mean} wt/ht ² (kg/m ²)	Mean % fat
1	no	blue	35	yes	yes	23.6	24.2
2	yes	blue	22	yes	yes	20.4	17.8
3	no	blue	21		yes	19.2	19.4
4	no	blue	23	yes	yes	21.8	21.9
5	yes	blue	21	yes	no	19.0	21.0
6	no	blue	24	no	yes	41.0	41.2
7	no	brown	20	no	yes	19.5	19.5
8	no	brown	45	no	yes	24.9	29.8
9	no	blue	23	yes	yes	22.0	22.9
10	yes	brown	23	no	yes	19.4	20.2
11	no	brown	31	yes	yes	24.0	27.2
12	no	blue	19	yes	yes	23.2	24.6
13	no	blue	30	yes	yes & no	34.8	37.4
14	yes	blue	24	yes	yes	22.0	23.3
15	no	brown	24	no	yes	20.1	23.5
16	no	brown	25	no	yes & no	24.1	26.5
17	no	brown	22	no	yes	28.6	34.4
18	yes	brown	23	no	yes	21.2	20.6
Total or	Yes 5	Blue 10	19-45	Yes 9	Yes 15	19.2-	17.8-
Range	No 13	Brown 8		No 8	no 1 yes/no 2	41.0	41.2
Mean			25.3			23.8	25.3

.

Table III: Description of Subjects

0.100 to 4.725%.) The triceps measurements in some cases became a subjective assessment. In most women the triceps muscle is separated from the subcutaneous fat, and it is easy to lift the fat away from the muscle to measure it with the calipers. In the few exceptional women the fat seems to be incorporated into the muscle itself, and the subjectivity comes into play when a decision must be made on how far into the fold the calipers should be placed. Table D, Appendix, shows the results of height, weight, and skinfold measurements.

In spite of the variations in some skinfold measurements, correlations between body mass index and percentage of body fat were significant, r = 0.9324, (p < 0.001).

C. Plasma Glucose Determinations

The results from the glucose measurements are presented in Tables IV-VII. A more detailed table of fasting and 60 minute values is presented in Table E, Appendix.

The range of experimental error was determined to be 8.7 mg/100 ml. or 10%. This was determined by processing samples of the same plasma at different times.

Table IV indicates that all of the subjects had plasma glucose responses within the normal range. Subject five had a high 60 minute response (203 mg/100 ml) on the first experiment. She had ingested less than 150 gm. of carbohydrate on each of the three days preceeding the test (76 gms., 41 gms., 64 gms.). She did not show glucose or ketones in her urine. Apparently this high response reflected inadequate carbohydrates in her diet rather than a diabetic condition. Her pupil responses on that day were not included in any of the significant correlations.

			Mean mg. Glucose/	Mean mg. Glucose/
Subject	Number of	Grams	100 ml. plasma	100 ml. plasma
Number	tests	СНО	Fasting	60 minutes
1	3	66.8	93	88
2	2	54.5	93	118
3	1	51.4	101	113
4	3	56.8	92	93
5	3	55.4	94	156
6	3	82	89	96
7	2	63.6	81	69
8	2	63.6	83	130
9	3	57.3	108	78
10	3	61.4	89	142
11	3	61.4	79	86
12	3	65.9	88	96
13	3	92	93	97
14	3	63.6	91	86
15	3	47.3	80	87
16	2	63.6	110	103
17	3	86.4	100	102
18	3	66	96	91
	Totol 48			
	10021 40			
Mean		65.2	92 + 9	102 + 22

Table IV: Summary of Results of Glucose Tolerance Tests

Table V indicates that variations in fasting levels of glucose from day to day were not different when oral contraceptive use, age, and body mass index were considered. The means of the ranges were, however, all greater than the experimental error of glucose determination (8.7 mg./100 ml.).

Table VI indicates that the means of variations in fasting levels of glucose on the same day were somewhat less for oral contraceptive users and subjects age 30 and above, but all variations were within the range of experimental error of glucose determination (8.7 mg./100 ml.).

TABLE V												
Mean	of	Range	of	Fasting	Levels	of	Plasma	a Gluo	cose	On D	iffere	ent
Days	Cor	nsideri	ing	Oral Co	ntracep [.]	tive	Use,	Age,	and	Body	Mass	Index.

	Number of Subjects	Mean $(\Delta mg/100ml)$	Std. Dev.
Oral Contraceptive Users	6	18	+ 12
Non-users	11	17	$\frac{+}{-}$ 7
Age \geq 30	4	19	$\frac{+}{-}$ 4
Age < 30	13	17	+ 10
wt/ht ² > 25	3	18	+ 6
wt/ht ² \langle 25	14	17	+ 9

TABLE VI

Mean of Range of Fasting Levels of Plasma Glucose On the Same^a Day Considering Oral Contraceptive Use, Age, and Body Mass Index.

	Number of Subjects	Mean (Δmg/100ml)	Std. Dev.
Oral Contraceptive Users	5	4	± 3
Non-users	9	7	+ 5
Age≥30	3	3	+ 5
Age <30	11	7	+ 4
$wt/ht^2 > 25$	3	6	+ 5
wt/ht ² \leq 25	14	6	+ 5

^aDetermined by measurements during the experiment when no food was given.

The mean fasting levels of all subjects at the first experimental sessions are shown in Table VII. When the fasting levels are considered with respect to oral contraceptive use, age, and body mass index only age appears to be a possible factor in differences of fasting glucose values. The difference here, however, is less than the range of experimental error of glucose determination and the standard deviation of both groups of data.

	Number of Subjects	Mean (mg/100 ml)	Std. Dev.
All subjects	18	90	+ 12
Oral Contraceptive users	6	91	+ 13
Non-users	12	90	<u>+</u> 12
Age_230	4	84	+ 18
Age < 30	14	92	+ 10
$wt/ht^2 > 25$	4	89	$\frac{+}{-14}$
wt/ht ² \langle 25	14	91	+ 12

TABLE VII

Fasting Values of Plasma Glucose Considering Oral Contraceptive Use, Age, and Body Mass Index at First Experimental Session.

Comparisons of values of plasma glucose other than fasting were difficult because of variations in timing. When 60 minute values are listed these are from the samples taken closest to 60 minutes. When the means of the 60 minute values of plasma glucose are compared for oral contraceptive users and non-users the differences are much greater than was seen in fasting values. Sixty percent of the oral contraceptive users had mean plasma glucose values greater than 100mg/100ml. The mean of all 60 minute values for oral contraceptive users was

Page 61
119 mg/100ml \pm 31 and for non-users was 95 mg/100ml \pm 15.

D. Pupil Measurements

Pupil responses as determined by percentage change of stimulus response from control response are presented in Tables A and B, Appendix. Correlation coefficients for the changes in response to the different slides with respect to the variables considered are presented in Table C, Appendix. Correlation coefficients that were found to be significant for the changes in response to certain slides and the corresponding variables are listed in Table VIII.

Pupil response changes are the pupil response (percent of pupil change from the control to the stimulus slide) for the second pupil measurements during an experimental session less the pupil response for the first measurements in the same session.

Eye color and pupil response change:

Because blue eyes were assigned the higher value, a positive correlation indicates an increase in pupil response for blue-eyed subjects and a decreased response for brown-eyed subjects. A negative correlation indicates an increase in pupil response for brown-eyed subjects and a decrease in pupil response for blue-eyed subjects.

Positive correlations were obtained between eye color and pupillary responses to peaches when the stimulus slide preceded the control slide, $r=0.6860 \ (p < .05)$, and to crackers when the stimulus slide preceded the control slide, $r=0.7213 \ (p < .02)$. Graphs of these relationships are presented in Figure 3. Both of these correlations occured in the fed condition. Thus, significant increases in pupil response from blue-eyed

Page 63

TABLE VIII. Significant Correlations of Change in Pupil Response with Other Variables. Fed Condition.

Slides: Peaches Crackers Carrots French Fries (control 2nd) (control 2nd) (control 1st) (control 1st) Variables Eye color r=0.6144* r=0.7213** (Blue = 2, brown = 1) Eats all r=0.7010** (2) Not (1) Time of a r=0.7135* dav Experiment r=0.7210* number wt./ht² r=0.6452* % Fatb r=0.6329* Slides Eggs, Sausage Cookies Jelly on toast (control 1st) (control 2nd) (control 1st) Variables Difference r=0.7539r=0.9892** r=0.8806* in glucose slope ^aAll times considered are a.m. ^bAs determined from skinfold measurement ^CThis value equals the slope of glucose change rate at second pupil measurement, i.e.: ** p**<**0.02 Glucose₂ - Glucose₁ *p**<**0.05 time interval

subjects and decreases in pupil response from brown-eyed subjects occured for pictures of peaches and crackers after the subjects had eaten.



Figure 3. Change in pupil response vs. eye color. Fed condition.

Restraint on eating behavior and pupil response change:

The subject's ability to control weight without self-imposed limits on food intake (eats all she wants) was given the higher value. Positive correlations indicate an increase in pupillary response for subjects who eat all they want and a decrease (or a smaller increase) in response for subjects who do not eat all they want.

There was a positive correlation, $r=0.7010 \ (p <.02)$, for the crackers when the stimulus preceded the control in the fed condition. A graph of this relationship is shown in Figure 4. This indicates that those subjects who did not restrict eating had a greater pupillary response to crackers after eating and the subjects who restricted their eating had a decreased response.



Correlation between changes in pupil response and experiment number:

A positive correlation indicates a larger pupil response change in later experiments and a smaller change in earlier experiments. A negative correlation indicates a smaller change in pupil response atlater experiments and a larger change for earlier experiments.

In this case experiment one always showed a negative change in pupil responses to peaches when the stimulus preceded the control and experiments two, three, and four usually resulted in positive changes in pupil responses in the fed condition, r=0.7210 (p $\langle 0.05$).

A graph of this relationship is seen in Figure 5.





Change in glucose slope and change in pupil response:

A positive correlation indicates a decreasing pupil response and a more negative slope or an increasing response and a slightly negative or a positive slope. (The range of the slopes in the fed condition was -3.05 to 0.36. These values are presented in Table F, Appendix.)

A negative correlation would indicate pairings of increased pupil responses and more negative slopes and/or pairings of decreased pupil responses and less negative or positive slopes.

The correlations here were positive for glucose slope and pupil responses to eggs and sausage (stimulus preceded the control) by fed subjects, r=0.739 (p(0.05), for cookies (control preceded the stimulus) by fed subjects, r=0.989 (p(0.02), and for jelly on toast (control preceded the stimulus) by fed subjects, r=0.881 (p(0.05). Graphs of these relationships are presented in Figure 6.



Subjects' body mass index (weight/height²) and change in pupil response:

A positive correlation between these values indicates that a greater body mass index (BMI) corresponds with a greater increase in pupil response and a smaller body mass index corresponds with a decrease in pupil response or a smaller increase. A negative correlation here indicates a decreased response (or slightly increased) for subjects with a greater BMI and a greater increase in response for subjects with a smaller BMI. In this case a positive correlation, r=0.6302 (p<0.05), was found for the picture of french fries in subjects who were fed. A graph of this relationship is seen in Figure 7.



Figure 7. Pupil response change vs. body mass index. Fed condition.

Subject's percentage of fat and pupil response changes:

The correlations here are similar to those for body mass index. The determination of percentage fat was made from skinfold measurements. In this case, also, a positive correlation, r=0.6030 (p $\lt 0.05$) was obtained for fed subjects between percentage body fat and the response to pictures of french fries. A graph of this relationship is seen in Figure 8.





Time of day and change in pupil response:

A positive correlation indicates an increasing pupil response later in the day and a decreasing response earlier in the day. A negative correlation indicates a decreasing response later in the day and an increasing response earlier in the day.

The significant correlation in this study was found between pupil response changes to carrots (stimulus preceded by control) and the time of day, r=0.7135, (p< 0.02) for the fed condition. The relationship of these factors is shown in the graph in Figure 9.



Other variables and pupil response changes:

There were no significant correlations between pupil response changes and age, between pupil response changes and glucose level change, between pupil response change and the days before the next menstrual cycle, between pupil response change and the day of the week and between pupil response change and the time between eating and pupil measurement.

Lack of adequate numbers of non-breakfast eaters led to no meaningful correlations with respect to this variable.

All of the above considerations were with respect to the fed condition. Absence of significant correlations of the variables considered and change in pupil response in the not fed condition may be attributed to insufficient data.

V. Discussion

A. Anthropometric Determinations

The study was designed to use equal groups of underweight, normal weight, overweight, and obese subjects. It was harder to recruit subjects than was expected and relative weights were considered on a continuum as a variable rather than as criteria for classification. Skinfold measurements would have been important in classification because weight and height parameters have their limitations in determination of the fatness-leaness component of body structure. Using the classifications of Thomas <u>et al.(1976)</u> based on Metropolitan Life Insurance Company Statistics the range of normal Body Mass Index (wt/ht²) for women is 18.8-23.8. Overweight is 23.8-28.6, and underweight is 15-18.8. Obesity is the classification for a BMI greater than 20% above normal (28.6). Standards have not been determined for percentage fat using the method of Sloan and Weir (1970). Subjective estimates by this author would place the normal range between 20 and 25%, overweight 25-30%, obese greater than 30% and underweight less than 20%.

Using the mean values of wt/ht² and % fat as reported in Table III, page 56, this would result in discrepancies in classification, for subjects 2, 3, and 7. Subject 17 who would be on the line between overweight and obese by BMI would definitely be in the obese category by % fat determinations.

Muscular development, age, and bone structure can cause deviations from the wt/ht² categories for amount of body fat. Skinfold determinations by different observers with different calipers can cause variation in determination of body fat of up to 5% body fat (Burkinshaw et al., 1973 and Womersly and Durnin, 1973). Standard deviations of as high as 4.75% were found in this study. To avoid not using subjects who subjectively do not fit into wt/ht² classifications, skinfold measurements provide an alternative method of classification. Ward <u>et al</u>. (1975) found that five skinfold measurements in different areas of the body could account for up to 90% of the fat in females as determined by D_2^0 dilution.

Repeatability in measurements would be improved if the subjects were tatooed. This would assure measurement of the subject in the same spot each time. This would be an especially appropriate technique if a long term observation of weight loss were studied. Burkinshaw <u>et al</u>. (1973) found that marking the sites of measurements resulted in close inter-observer agreement. This agreement was significantly less with the same observers and subjects when the sites were not marked.

The measurements used in this study were easily done and did not require the subject to remove clothing, with the exception of shoes, heavy sweaters, and coats.

B. Plasma Glucose Determinations

Comparisons of glucose values obtained here with the glucose tolerance data of other authors are difficult because of the timing of the samples. Samples were obtained to determine the values of plasma glucose and the rates of change at the time of the pupil measurements, not to study the glucose tolerance of the subjects.

Several factors that should be considered to make reliable comparisons of glucose tolerance tests have been listed by Meinert (1972). These factors will be discussed point by point to indicate the controls which were observed.

1) Pre-test diet. Meinert suggests an intake of at least 150 grams of carbohydrate on each of the three days preceding the test.

Because of the nature of this study, no instructions were given on the pre-experimental diet. Subjects were asked to keep diaries of food intake for the three days prior to testing. Statistical analysis of these diaries has not been made to determine if at least 150 grams of carbohydrate had been ingested each day, but with the exception of subject six, none of the diaries indicated that the subjects normally chose diets low in carbohydrates. It is not difficult to ingest 150 grams of carbohydrate in one day. For example, if the subject had four slices of bread, six ounces of fruit juice or cola, two cookies, a one cup serving of pasta and twelve ounces of skim milk in one day, she would ingest at least 150 grams of carbohydrate (Church and Church, 1975). Most of the subjects either drank beer, ate candy or desserts, or were on vegetarian diets, and these all elevated the carbohydrate intake. Most of the subjects were students and did not choose to spend their food money on the large amounts of meat or cheese which would be necessary to maintain weight on a low carbohydrate diet.

Two measurements that would indicate inadequate carbohydrate intake would be (a) the presence of ketone bodies in the urine and (b) elevated plasma glucose values at 60 minutes. Ketones were detected in the urine of subject six only. Analysis of her diet previous to experiments one, two, and four indicated that her carbohydrate intake was lower than 150 grams on at least two of the three days prior to each of these experiments.

Page 76

Subject five was the only subject who had a 60 minute plasma glucose level higher than 150 mg/100ml (Table E, Appendix). As discussed previously, her carbohydrate intake was much lower than 150 grams for each of the three days prior to testing.

A third factor which would indicate a low carbohydrate diet would be a hypoglycemic response after two hours of a glucose tolerance test (Permutt <u>et al.</u>, 1976). Because glucose values were not measured more than 75 minutes after ingestion, this would not be a factor in these results.

2) Acute illness. Meinert suggests waiting two weeks after an acute illness to perform glucose tolerance tests.

None of the subjects suffered from an acute illness during the experimental period. The subjects were requested to not come for testing if they were not feeling well. All subjects complied with this request.

3) Medication. It is suggested that all medications that have been shown to influence glucose tolerance be discontinued three days before testing.

With the exception of oral contraceptives, no subjects were taking any medication which has been shown to influence glucose tolerance. The fasting levels of plasma glucose of subjects who were taking oral contraceptives did not differ in this study from those of subjects who were not taking oral contraceptives. The mean of the sixty minute values of plasma glucose was higher for oral contraceptive users (non-users, 95 mg/100ml \pm 15, 0C users,119 mg/100ml \pm 31). Other authors have discussed the impaired tolerance of glucose by oral contraceptive users (Doar and Wynn, 1970, Phillips and Duffy, 1973). In a review of the effects of oral contraceptives and other sex steroids on carbohydrate metabolism by Kalkhoff (1972), it is suggested that changes in glucose tolerance may involve interactions of the steroids with insulin and endogenous glucocorticoids. None of the subjects changed her use of oral contraceptives during the study.

4) Fasting period. Meinert suggests that all subjects fast at least eight hours and no more than sixteen hours before testing.

All subjects fasted for at least four hours before testing, and most fasted for at least eight hours. The meal that was allowed four hours before testing was restricted in carbohydrates to 35 grams. Parker (1976) found that fasting times beyond four hours have only a marginal effect on the glucose tolerance.

5) Miscellaneous restrictions. Meinert suggests subjects refrain from the use of tobacco and coffee for eight hours before testing.

Subjects did not ingest coffee for eight hours before the test and were requested to not smoke for an hour before the test. Restricting smoking longer than that time may have caused abnormal pupil responses to the food by a habitual smoker. Very few of the subjects smoked and those who did did not usually smoke in the morning, so there was probably little effect from smoking.

6) Testing time. It is suggested that fasting specimens be drawn between seven and nine a.m. and that all testing be done between seven a.m. and noon.

These hours were not always observed. Diurnal variations can affect the 60 minute value of glucose (Zimmet et al., 1974). Because of

the variability of the times of glucose samples, 60 minute samples could not be compared in this study. For the purposes of this study, time of day was considered as a variable in pupil responses and was not a significant variable when glucose values appeared to have significance. 7) Glucose load. Meinert suggests that 40 grams of glucose per square meter of body surface, diluted to 300 ml., be the load for testing.

The amount of carbohydrate given was determined by weight (one gram of carbohydrate per kilogram). This seems better than giving each subject a standard load, but whether this load should be determined by lean mass, usual meal size, or some other factor is not known. Under these experimental conditions where the first load was prepared before many variables were known about the subject, weight reported by the subject was used to determine the load. The same load was given at each experimental session. The use of one gram of glucose per kilogram body weight seems to be the most commonly used dose if standard doses such as 50 grams, 75 grams, 100 grams, or 150 grams are not used.

8) Timing of specimens.

The timing was not standard in these experiments because the pupillometric studies took precedence and because the technician also had other priorities.

9) Patient behavior. Meinert suggests the patient avoid physical exertion, emotional stress and stimulants.

The subjects were kept quiet and not allowed to stand or move around any more than was necessary. They had no stimulants during the testing period. Any walking that was done was on the same level and for a distance not greater than 100 meters.

10) Specimen processing. Meinert suggests centrifugation of samples within 30 minutes and preservation by freezing or the addition of sodium EDTA and sodium fluoride.

Page 78a

Separation of plasma was performed within sixty minutes and all samples were refrigerated until centrifugation. Plasma was stored frozen until analysis.

The methods of analysis suggested are glucose oxidase, Nelson-Somogyi and Hoffman's ferricyanide (AutoAnalyzer) methods.

The Hoffman ferricyanide method in an AutoAnalyzer is one of the methods suggested by the Committee on Statistics of the American Diabetes Association (Meinert, 1972). This was the method used. This method relies on reduction of potassium ferricyanide to ferrocyanide by glucose (Hoffman, 1937). Proteins that have reducing properties are removed from the plasma by dialysis, but other reducing agents that might be present are not accounted for. Using plasma rather than whole blood lowers the possibility of interference by other reducing agents. Results of ferricyanide analysis are usually about 7% higher than results from glucose oxidase measurements (Pileggi and Szustkiewicz, 1974).

The mean values for fasting glucose and the glucose measured closest to 60 minutes were 92 mg/100 ml. and 102 mg/100 ml., respectively. These values were within the range found by other researchers. Using the AutoAnalyzer technique with ferricyanide, DeFronzo <u>et al.</u> (1977) determined the mean fasting glucose value of males, ages 24-37 years to be 96 $\stackrel{+}{-}$ 2 mg./100 ml. Parker (1976) using the Bittner and Manning technique which involves reduction of a copperneocuproine complex, determined the plasma glucose one hour after ingestion of 75 grams of glucose to be 120.9 $\stackrel{+}{-}$ 40.7 for subjects between 20 and 30 years of age and 128.7 $\stackrel{+}{-}$ 40.7 for subjects 30 to 40 years old. Using an AutoAnalyzer glucose oxidase method, Permutt <u>et al</u>. (1976) determined the fasting plasma glucose of subjects on a normal diet to be 83 $\frac{+}{-}$ 2 mg/100 ml. Subjects were male and female and their ages were 21-28 years.

C. Determination of Pupil Responses

Although visual stimuli present many problems in pupillometry it was decided that the easiest presentation of food stimuli was colored pictures of the food.

The slides of the stimuli were the same as the slides of the controls in every case with respect to background, color, shape, and distance. The overall brightness of the control slides was always the same as or darker than the food slides so that any increase in pupillary dilation to the food would not be influenced by the light intensity.

Because there are several problems in comparing the pupillary dilations of one subject to another, the actual pupil sizes were not compared. Comparisons were made on pupil size changes in the same subject and of the difference in the changes of pupil response between subjects. To elaborate -- For a given subject the response (i.e. pupil size) to the stimulus slide was compared to the response to the control slide to generate the figure which was defined as percentage change in pupil response and which has been shortened to the term "pupil response." To compare this subject's responses to other subjects' responses, changes in pupillary response were determined by subtracting the "before" response from the "after" response. Thus the comparisons between subjects were not of the pupil dilations, <u>per se</u>, but of the changes in the "percentage change in pupil response."

This method should eliminate many of the problems involved with determining the baseline of pupil size and comparing the control to

the stimulus. As far as I can determine, no one else has used exactly this procedure. Beijk and deJong (1971) used controls before and after the stimulus to determine the baseline, but they measured the responses to the food in the "hungry" and "not-hungry" conditions on different days to determine the effects of feeding on responses to food.

Most authors have used black and white visual stimuli. They have done this to avoid responses of the pupil to colors. Longer wavelengths elicit greater pupil dilation (Bouma, 1962). If, however, the colors elicit a response to the stimuli, the colors in the controls should also elicit a response. If these colors are not changed from the control to the stimulus, the response to the stimulus would not be determined by the color. Black and white stimuli are appropriate if the stimuli are normally seen in black and white, e.g. printed words or newspaper photographs. Food, however, is never presented for eating in black and white, and to present food stimuli achromatically would not elicit natural responses.

Pictures of food may not elicit as natural a response as the food itself, but to present food itself so that it appears the same at each experiment would be very difficult.

Most authors have not had controls which resembled the stimulus. Usually they were numerals (Hess, 1972) or symbols such as asterisks (Barlow, 1969, and Janisse, 1974). Simms stopped using numerals as a control when he found that the subjects were trying to add the numbers (Janisse, 1974), Changes observed with this type of control may reflect a response to the shape or form of the stimulus. For this reason the control pictures in this experiment had the same general shape as the stimulus pictures.

One problem, however, did develop from having the controls resemble the stimuli. Many of the subjects realized there was a connection between the control slides and the stimulus slides and they began to try to guess what food would be presented next. Because mental activity increases pupil size (Beatty and Kahneman, 1966, Elshtain and Schaefer, 1968, and Simpson and Hale, 1969) this could account in some cases for a larger response to a control during the first measurement on that slide. The significant correlations, however, are found in the difference between the stimulus with the control following as often as in the difference between the stimulus with the control preceding. There is also the possibility that the variations in pupil size that occur with thinking would make the standard deviation on the reading large enough that the results would have been eliminated from the data. Also, it seems unlikely that the tendency to guess the content of the next slide would correlate with any of the variables considered.

Background light can affect the pupil response (Lowenstein and Loewenfeld, 1961). This was not completely controlled in this study. Some of the early morning experiments started before dawn and were completed after sun-up. Weather changes could also change the background light from the beginning of an experiment to its end. The subject never viewed the slides in bright light because the room lights were turned off, the shade was drawn, and there were opaque shields between the subject and the window. Only one significant correlation, however, was found with the time of day and change in pupil response. The earliest time that entered into this correlation was 7:30; the rest of the experiments began and ended after sun-up.

Background noises can cause pupil dilations (Nunnally <u>et al</u>. 1967). The experimental room was quiet, but occasionally the scintillation counter in this room would go through changes that were very audible. This was noted on the measurements, but it never affected the pupil size. If it had, the reading would have been eliminated. The clicking of the Caramate as the slides changed may have caused some pupil response, but there was also a light response elicited and the pupil changes at this point were not included in the measurements.

The experimenter can cause some differences in response (Chapman, Chapman, and Brelje, 1969). Because the experimenter sat so close to the subject and because the experimenter was female, this factor was considered by using all female subjects. The experimenter also always wore a lab coat over the usual student clothing to convey a casual but professional manner.

Because blood sampling is a traumatic experience for some people, the sampling was not done immediately before pupil measurements. Blood was always collected very soon after the pupil measurements. One of the reasons for urine collection before each pupil measurement period was to separate, with another activity, the blood sampling before the second measurement from that measurement. The urine collection also relieved the subject of any bladder discomfort she might have been reluctant to report. This was not mentioned in any of the papers on pupillometry, but it seems logical that the need to urinate could affect responses to many stimuli.

It is because of these precautions and using each subject as her

own control that the significant correlations can be considered as involving responses to the food aspect of the slides rather than the slide itself.

D. Eye Color and the Change in Pupil Response to Food

Increased pupil responses to peaches and crackers after eating by blue eyed subjects and decreased responses to these stimuli by brown eyed subjects resulted in significant correlations between these stimuli and eye color. Because the correlation was significant for pictures of peaches and cheese crackers, the first impression is that the correlations have something to do with color. Both of these stimuli were similar in being orange in color. The carrots and cheese stimuli, however, were also orange, and there were no good correlations with these stimuli and eye color. Other similarities having to do with the food properties are that they are primarily carbohydrates and that they are usually considered snack-type foods.

Greater variations in pupil response are found in blue-eyed people (Janisse, 1974), but in this case greater variations in response from the blue-eyed subjects should have occurred before and after eating and thus cancel out any correlations.

Perhaps the eye color reflects other genetic differences in food responses that have not been observed, and these interesting results are offered here because they occurred, not because they can be explained.

E. Change in Pupil Response to Food and Self Restraint on Eating.

All those who eat all they want had an increased response to crackers after eating, and all those who don't eat all they want had a decreased response to crackers after eating. This suggests that crackers are a tempting food to people who do not try to limit food intake, and that they do not tempt those who try to control their weight. Some subjects who were placed into the "doesn't eat all" category mentioned which foods they avoided, and all these subjects mentioned avoiding sweets. No other types of foods were mentioned. No one mentioned crackers although three of the eight indicated that they avoided between-meal snacks. A rating by the subjects of preference for certain foods before experimentation would, perhaps, have been helpful in understanding this and other responses.

Schachter (1968) found contrasts in the eating behavior of obese and non-obese subjects with crackers as the experimental food. He found that normal subjects ate fewer crackers when their stomachs were full than when they were empty, but the obese subjects ate slightly more crackers when their stomachs were full than when they were hungry. Five types of crackers were available and no information was given about which crackers were eaten. Schachter (1968) described another of his studies on obese and non-obese subjects using crackers. In this experiment, time was manipulated. The obese subjects ate almost twice as many crackers when they thought the time was 6:05 as when they thought the time was 5:20. The normal subjects had the opposite reaction, and they apparently refused the crackers at the supposedly later time because they didn't want to "spoil their dinners." Schachter's experiments indicate that crackers are an appealing food to obese subjects at all times and to normal weight people some of the time.

In the present study, the variable being considered in this

correlation is not obesity, but self limitation of food intake. In the subjects in this study the correlations between eating all and weight/ height² and percentage body fat are 0.1438 and 0.1888, respectively. For this reason it is expected that the pupil response changes with the variable "eats all" would not align with Schachter's observations on the obese--non-obese continuum.

The results here suggest that different foods may have different degrees of temptations to those who "watch their weight."

F. Change in Pupil Response to Food and Glucose Slope

With a more rapid fall in plasma glucose, there is a decreasing response to eggs and sausage, cookies, and toast with jelly. The response to the eggs and sausage was a progressive increase in pupil response change with a less rapid fall in plasma glucose. The response to the cookies was increasingly negative with the increasingly faster fall in the glucose. The jelly on toast elicited a mixed response with slight decreases and somewhat large increases in pupil responses changes as the glucose drop became less rapid.

Because most of the subjects had an increasing response to the eggs and sausage, it could be that the carbohydrate breakfast they had eaten did not fulfill what they considered to be a complete meal. (A question that should have been asked would be one that ascertained the subject's concepts of an ideal breakfast.) The negative responses to the cookies would follow from this idea. Probably cookies would not seem to be an appropriate food for breakfast. Also, most of the subjective impressions to the cookies were negative or neutral before and after eating. These responses also fit with Beaver's (1976) observations that hungry subjects showed a greater response to full meals than to desserts. These subjects had been fed, however, and Beaver did not indicate that there were differences in responses to the types of foods by fed subjects. The jelly on toast may fall between the response classifications of full meal and dessert. This may be especially true because the subjects had recently eaten a "meal" that was composed mainly of jelly on toast.

The rapidity of the fall in blood glucose that is drawn from the ante-cubital vein reflects uptake of glucose in the body tissues. Capillary-venous differences in plasma glucose reflect extra-hepatic glucose uptake (Foster, 1923). Because the peak plasma glucose level had already been reached in these subjects, the rate of fall of venous plasma glucose would parallel, in reciprocal fashion, the capillaryvenous differences.

Van Itallie <u>et al</u>. (1953) reported a correlation between a desire for food and the capillary-venous differences in blood glucose. When the differences in glucose were more than 15 mg. per 100 ml., hunger was never reported. In normal (non-diabetic) subjects on a diet that was not restricted in carbohydrates, if the glucose differences were low for a period of time or if they were negative, hunger was always reported. Van Itallie and Hashim (1960) measured capillary-venous differences in subjects after a self-selected breakfast meal. The capillary-venous differences changed at similar rates (but the opposite direction) as the plasma levels of non-esterified fatty acids (NEFA) when the subjects had self-selected diets previous to testing. The NEFA levels paralleled the hunger-satiety pattern with more hunger being experienced when the percentage of NEFA was low, and conversely, less hunger being experienced when the percentage of NEFA was high.

Because the subjects in this study reported mixed diets previous to testing and exhibited glucose tolerances in the normal range, it appears that the degrees of response to food pictures paralleled the hungersatiety responses in the VanItallie <u>et al</u>. and the VanItallie and Hashim studies. Their subjects rated their hunger intensity on a four-point scale: "1. No desire to eat; 2. Could eat but don't want to; 3. Moderate desire to eat; and 4. Strong desire to eat." It appears that pupil responses to pictures of food would be more sensitive to degrees of hunger with a virtually infinite number of points on the scale.

The falling plasma glucose may not be responsible for the hungersatiety response, as indicated by VanItallie and Hashim, but may indicate some other physiological change that was not measured. Because oral contraceptive users had higher plasma glucose levels at 60 minutes, this may have had some influence on the results. Determination of the correlations of glucose slope and changes in pupil response in the fed condition for non-users of oral contraceptives resulted in correlation coefficients similar to those of the whole group. The glucose slope for oral contraceptive users was similar to that for non-users (mean slope for all subjects, $-1.460^{\pm}.593$; OC users, $-1.522^{\pm}.539$; non-users, $-1.434^{\pm}.635$).

G. Change in Response to French Fries and Weight/height² and Percentage Body Fat

The correlation of weight/height² or percentage body fat and pupil response change to french fries is very weak and negative, r=-0.2566 and

Page 89

r=-0.0715, in the normal weight range (wt/ht²= 18.8-23.4, % fat= 20-25), but when the overweight and obese subjects are included, the correlation is much better, r=0.6452 (p<0.05) and r=0.6329 (p<0.05). The indication here is that the responses of the obese subjects differed from those of the normal weight subjects. The small number of obese subjects here does not confirm the hypothesis that the response of obese subjects differs from that of normal weight subjects in the fed condition, but it does indicate that this might be the case for french fries.

Several observers have indicated that obese people have similar reactions to food before and after eating, whereas normal weight people have a decreased interest in food (Schachter, 1971b). The data on the non-fed condition in the present study are insufficient for comparison.

If a decreased interest in food is indicated by a negative change in pupil responses, then all but three subjects showed a decreased interest in french fries. The two obese subjects (as defined by weight/ height² and percentage body fat measurements) showed an increase in response to french fries after being fed. Both of these subjects had indicated in conversations that once they started eating meals high in carbohydrates, they craved more carbohydrates. In reviewing these subjects' responses to all foods other than french fries after eating a high carbohydrate meal, the following was observed:

Subject Number	To CHO	Foods	To Other	Foods
-	+ P.R.	- P.R.	+ P.R	- P.R.
6	8	5	3	1
17	0	11	3	3

Thus it is not the carbohydrate quality of the food that elicited this

response. Both subjects had seen the french fries at other experimental sessions. (These data were eliminated from the statistical analysis because the measurements had been made at succeeding experiments.) Their other response changes to french fries in the fed condition indicated that subject six showed a negative change and a positive change and subject 17 showed a negative change at these experimental sessions.

From these results the conclusion is that obese subjects may show an increased response to french fries after eating and normal weight subjects show a decreased response. In any experiments studying eating behavior and food attitudes in obese and non-obese subjects it would be advisable to include french fries as one of the foods.

H. Change in Pupil Response to Carrots and Time of Day

Most of the pupil response changes were negative and they were more negative early in the day.

American dietary patterns rarely include vegetables as a morning food. (I am told this is not the case in other countries.) Because carrots are not usually eaten early in the day it is not surprising that in fed subjects there would be less response to carrots at breakfast time than there was closer to lunch.

The change in pupil response correlated well with carrots and not to other non-breakfast foods. This finding may be related to the relatively bland taste of carrots. (Slides of other vegetables were not presented because of photographic difficulties with green materials.) Goetzl <u>et al</u>. (1950) have demonstrated differences in acuity for sweetness that are related either to diurnal variations or having eaten a meal. Their subjects could detect lower concentrations of sucrose at noon than at 10:00 a.m. The threshold for sweetness rose, however, after subjects had lunch, and the threshold continued to decline if the subjects did not have lunch. Because the subjects ate breakfast before coming to work at 9:00 a.m., the lower threshold for sweetness at noon may have been dependent on the time since their last meal rather than diurnal variation.

Moskowitz <u>et al</u>. (1976) found that satiety with food didn't change preferences for sweetness but that satiety with a glucose load did. All subjects showed increasing preferences for glucose solutions as the concentrations were doubled until the concentration was 1<u>M</u>. The subjects who were tested after breakfast, after lunch, and after an overnight fast had decreased preferences for 2<u>M</u> glucose solutions as compared to 1<u>M</u> solutions. The subjects who were tested after a glucose load, however, indicated a greater preference for 2<u>M</u> solutions than 1<u>M</u> solutions. Having breakfast did not significantly change the subjects' ability to detect sweetness or their preference for all of the tested concentrations of glucose. The range of concentrations was greater than those used by Goetzl <u>et al</u>.(1950) and indicate that the threshold of taste is not affected by meals.

Goetzl <u>et al</u>. (1950) and Moskowitz <u>et al</u>. (1976) have observed conflicting results and the discussion by Moskowitz <u>et al</u>. indicates that there is quite a bit of conflict in this area. Moskowitz <u>et al</u>. studied subjects in India and Goetzl <u>et al</u>. studied Americans. Perhaps the cultural aspects of the diet of the subjects affect the taste sensitivity.

Stevenson and Fierstein (1976) found in the rat that circadian rhythms for intestinal sucrase and glucose transport could be influenced by the times of feeding on previous days. Perhaps a more important factor to consider in this study would have been the time at which the subjects had breakfast the day before rather than the time of day.

The relationship between changes in pupil response to carrots and the time of day possibly reflects the local dietary habits.

I. Change in Pupil Response to Peaches and Experiment Number

Changes in pupil response to peaches were negative when responses were measured in the first experiment and mostly positive when the responses were measured in later experiments. This correlation has importance because the results of the first good reading obtained for a subject were the results entered for analysis. Because the first good readings would be more likely to occur on the first experimental session than at succeeding ones, the implications of this correlation are that the data were biased toward negative changes in pupil response after feeding.

There were no duplicate data on responses to this slide, so these results were not biased by the method of duplicate elimination. Analysis of data eliminated indicates that the significance and nonsignificance of some correlations may have been changed if another method of elimination had been chosen. The problem was, however, the choice of a method of elimination that would not bias the results. Because every time there were good readings for a subject's responses to a particular slide there was always a first good reading but not always a second or a third good reading, it seemed that this method would

conserve as much data as possible. Averaging of responses may have been useful when certain unchanging variables such as eye color were concerned, but this would not have been useful when considering changing variables such as glucose slope. In analyzing data that were eliminated as compared to the data that were considered it does not appear that the bias shown for experiment number and change in response to peaches would be present when the experiment number is considered for the responses by any one subject to any particular slides. The eliminated data were mixed in respect to being smaller or larger than the data retained.

J. A Review of the Significant Correlations with Regard to Bias by the Elimination Method

The results with french fries and body mass index and percentage fat have been discussed under that topic. The choice of which results to use would, in these cases, change the already shaky correlations. The significant correlation between pupil response changes and the time of day with the carrot slide would not be as high but would still be a very positive correlation. The correlations involving the crackers, i.e. eye color and restraint on eating, would not be appreciably changed if eliminated data were considered. Only the response changes to eggs and sausage would have a poorer correlation with glucose slope.

K. Other

The absence of significant correlations with any of the sweet foods (cake, sticky roll, and cream puff) and steak may indicate the appeal of these foods is mixed in the morning. Their appeal may override satiety in some individuals and not in others and the variables considered may not have accounted for these differences.

The responses to the sticky bun, the fruit cocktail, and the steak may have been different if there had been different controls. The controls used seemed to stimulate the most curiosity about what the stimulus would be, and because in all cases the controls preceded the stimuli, this would mean a larger pupil response to the control because of mental activity and also a large pupil response when hungry for these usually tempting foods. The curiosity would not have been present when the subjects saw the controls again after being fed. Pupil response to the food may have been mixed at this second reading with the temptations overriding satiety in some subjects. As mentioned before, there is no obvious reason for curiosity about the control being related to any of the variables considered. The other factor is that although the first experiment where good readings were obtained on a slide was the experiment from which data were used, this does not mean this was the first time the subject saw the slides. Her curiosity may have caused deviations on the first response to the control that ruled out using the data from that response.

The purposes of this study were to determine whether pupil responses to food agreed with what is known of satiety responses in man and whether pupillometry would be a useful tool in studying satiety.

The correlations which were found with the glucose slope agreed with what is already known about satiety (Van Itallie <u>et al.</u>, 1953, and Van Itallie and Hashim, 1960), The relationships between pupil response and eye color, time of day, eating all one wants, and experiment number have not been studied in the literature this author has reviewed. The

Page 95

correlations of pupil response and obesity seem to agree with the findings of other authors, but as has been indicated the correlations seen are questionable. Larger sample sizes and more subjective questioning of the subjects may have made some correlations more meaningful. In some respects the number of subjects was adequate but the same slides should have been shown at each experimental session to insure a measurable response for each slide from each subject. A larger number of subjects in the overweight and obese classification would have provided a better measure of how well the pupil response changes fit with the observations on satiety responses in obese persons.

The absence of a correlation between food intake restraint and obesity indicates that in turn it may be necessary to make classifications within a group of obese people and this would require a larger sample size. People who are overweight or obese are apparently difficult to recruit for experiments relating to obesity. Other experimenters have found that they can be interested in an experiment if it offers some possibility of helping them lose weight. This might be the key to design of future experiments. If pupillometry studies were one aspect of a larger weight reduction experiment this might produce a larger sample group. The group, however, may not be representative of obese people because only those desirous of and optimistic about losing weight would be included.

Most of Schachter's experiments were done under the guise of another type of experiment, and working out of a psychology department he would have little trouble maintaining credence for such a guise.

The usefulness of pupil measurements is the second aspect of this

study. With the equipment used here I would recommend further refinement of the methodology and additional equipment before a large scale experiment is undertaken.

Reading the graphs of each pupil response and entering the data into a calculator was a long process and only two experimental session responses could be processed in an hour if there were readable responses to each of the slides. Determining which pupil measurements were real and which were the result of equipment adjustment required subjective judgements which eliminated random sampling of measurements. It would be difficult to program a computer to make these judgements unless the pupillometer were more responsive to pupil size changes and would automatically adjust to a new pupil size. There is some skill required of the experimenter to make these adjustments quickly. An improvement on the present set-up would be a direct read-out of numbers in addition to stylus markings. Better yet would be a recording on perforated tapes that could be easily edited by the experimenter to remove values that do not reflect pupil size.

Acquisition of skills by the experimenter involved not only developing the ability to quickly adjust the pupillometer to changes in pupil size, but easily lining up the subject, the light source and the camera also required some practice. It was determined toward the end of the experimentation that subjects with contact lenses could be used. The reflections from the lenses could be easily controlled once the experimenter had developed skill in changing the position of the light source.

Even after skill in handling the pupillometer had been developed some subjects did not adapt easily to the experimental situation. This
did not happen often, but if two experimental sessions do not produce readable measurements on a subject it is probably best to not continue with that subject. On the whole, subjects were extremely patient and did all they could to cooperate.

Some changes were made early in the experimental period. These changes improved the possibility of getting good pupillometric readings.

It had been suggested that the light source, because it emitted infra-red light, should be one foot from the subjects' eyes to avoid burning. The instrument had to be modified to do this and none of the literature on pupillometry gave this warning, but the modification was made. The light at that distance made it impossible to get readings with many subjects. A conference with Dr. Andrew Harris of Salem, an opthalmologist, gave me the assurance that the distance of an infra-red light source is harmful only when it has the intensity of a blast furnace. Repositioning the light source as the manufacturer intended resulted in proper reflections from all subjects.

The position of the viewing screen was important with some subjects. Looking straight ahead often meant that eyelashes and eyelids interrupted a complete image of the pupil. Raising the viewing screen slightly above eye level relieved this problem and caused no discomfort to the subjects.

Another change in the experimental procedure which was unrelated to the pupillometry was the manner of urine collection. Urine collections are a common procedure for Foods and Nutrition students, but subjects from other departments were embarrassed to carry bottles of urine down the hall from the rest room. Tote bags disguised the bottles and this relieved the subjects of embarrassment. In January, however, another group of experimenters needed the urine collection bottles and another method of urine collection was necessary. Discovery of a toilet in a closet in the room next door meant that collection into and transport of beakers was possible. This also cut down on the walking done during the experiment by the subjects.

Experimental design improvements would decrease the number of measurements made, e.g. present the same slides at each experimental session and have the subjects come for only two sessions. (In this case a pilot study on a very few slides at different times of the menstrual cycle would have determined the effects of the cycle on pupil responses.) Experimenter skill development would increase the probability of usable readings.

Probably most of the problems that detracted from the ease of experimentation are present when anyone uses a new method. The apparent sensitivity and reliability of pupil measurements make pupillometry a potentially useful tool in studying responses to food.

Justification for the expense of additional equipment, however, will require many more experiments with stylus readings entered into a calculator by a human.

The possibility of using pupil responses to evaluate biochemical agents for weight reduction, to improve acceptibility of foods by cancer patients, to enhance hedonic evaluations of new food products, and to understand factors influencing food choices in general makes it important to continue development of methodology employing pupillometry in the area of foods and nutrition.

VI. Summary and Conclusions

The conventional methods of measuring hunger and satiety in humans have been based on verbal responses from the subjects. An objective method of measuring these states could be helpful in studies of eating behavior and the treatment of obesity. Pupillometrics, the use of pupil dilations as indicators of interest, has been applied to studying many aspects of human behavior and seems to be an objective method of measuring interest under well controlled conditions.

To determine the feasibility of using pupil measurements as a method of assessing satiety, 17 female subjects, mean age 25.3 years, were shown a series of colored pictures of food and similar pictures of nonfood items, used as controls. These pictures were viewed by the subjects before and after eating. The subjects participated in one to four experimental sessions. Pupil diameters were measured with a Space Sciences Pupillometer as the women looked at the pictures. The differences between pupil responses to the food pictures and control pictures. were compared for the fasted and fed conditions. Correlations of the changes in pupil responses and several variables were determined.

Two of the variables considered were body mass index (kg/m^2) and $-VA\ell$ percentage body fat (from skinfold measurements of the triceps and supra-iliac regions). Venous blood samples were analyzed for plasma glucose concentrations by the ferricyanide method in an AutoAnalyzer. Plasma glucose levels and the rates of plasma glucose change were determined and considered as variables. Other variables considered were: experiment number, age, eye color, time of day, days before menses, VACtime since eating, oral contraceptive use, the need to restrain eating to control weight, and habitual breakfast eating. _____ V Ai-

Page 100

Although skinfold measurements showed greater variations than weight measurements there was a good correlation between weight/height² and percentage body fat as determined from measurements of skinfold thickness at the triceps and supra-iliac crest.

Plasma glucose responses after ingestion of a high carbohydrate meal were similar to those obtained in other studies after ingestion of glucose solutions. Fasting values of plasma glucose were similar in all subjects, but 60 minute values were higher in subjects using oral contraceptives than in non-users.

Pupil responses to slides of food were measured before and after eating. Subjects participated in one to four experiments, but they did not see the same combination of slides in more than one experimental session. To avoid duplication of data from a subject, only the first measurements of pupil responses to a particular food slide were considered. This required measurable responses to the control and stimulus slides before and after eating. Significant correlations were found, with subjects who had been fed, between pupil response changes and eyecolor, restraint on eating behavior, and the change in glucose slope. The correlations indicated that in the fed condition blue-eyed - 1.04women had an increased pupil response to peaches and crackers and brown-eyed women had a decreased response to peaches and crackers; those who usually eat all they want had an increased response to crackers; and increasing steepness of the glucose slope meant a smaller or negative response to eggs and sausage, cookies, and jelly on toast whereas a decreasing steepness corresponded with a greater response

to these foods.

Significant correlations were seen for other variables; time of day, experiment number, body mass index, and percentage fat. There is some doubt about the validity of these correlations.

No significant correlations were found between pupil response changes and the variables of oral contraceptive use, age, plasma glucose value, days before menses, and the time after eating.

Improvements in the experimental technique have been suggested to decrease the time spent on determining pupil responses and to increase the number of useful data. These include presenting the same slides at each experimental session, eliminating slides that may give ambiguous results, determining subjective responses to the foods at the time of day of testing, use of computer analysis of pupil sizes, and having each subject participate in only two experimental sessions.

The correlations of pupil response changes and the rate of plasma glucose decline indicate that pupil measurements may provide a sensitive and objective method of determining hunger and satiety in experiments where physiological and biochemical conditions are being monitored. This could be useful for determining the effects of biochemical and behavior manipulations which are employed to control obesity. At this point it would appear to be more useful in experimental than clinical situations. Other possibilities for the use of pupil responses to food are in improving food acceptance by patients suffering from cancer or anorexia nervosa and in expansion of hedonic ratings of new food products. It is recommended that pupillometry be incorporated into future studies of human hunger and satiety.

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Slide	Peaches 1st co	Peaches 1st control		Peaches 2nd control		Carrots 1st control		s ontrol	Crackers 1st control		Crackers 2nd control	
Subject ^b	1 ^{°C}	2	1	2	1	2	1	2	1	2	1	2
1			-23.9	-32.7	29.9	0.7	24.5	34.9	4.7	-2.1	-26.5	-24.0
2	-6.3	2.4	-9.8	-2.7				-			_	
4	-16.5	12.1			-14.6	-16.1					-10.6	0.9
5	14.3	-0.3	-10.1	-5.8	-10.6	-0.1						
6	-8.1	-4.4	-9.7	3.0	-				-13.4	-3.6		
7			-			- - -					11.1	-7.1
8				-	-0.4	0.3			-11.5	-3.2	0.7	1.2
9	-2.8	-5.7	-8.4	-3.7					0.1	9.2	-10.1	-6.6
10	-2.7	-4.5	6.3	1.8	2.5	0.2	-13.8	-21.5	-17.8	-17.3	-8.4	-15.0
11					4.2	-10.8			-4.7	-0.6	-0.2	-1.4
1.2												
13				_	1.6	-6.6		-		_	-4.3	-2.4
14					-23.1	-29.7					-2.1	6.4
15									<u> </u>			
16	-9.8	-10.3	-5.8	-7.8	-1.8	-13.3		_	-4.2	-3.7	-4.4	-8.0
17	17.6	-3.6		- - - -							-0.3	-3.1
18			-10.0	-20.4	_	- 						
a Percentage	e change :	= <u>x</u> sti <u>x</u> sti x	mulus -	X contro	<u>1</u> x 100).		 1=first	reading	2=2nd	reading	Page 110

TABLE A. Pupil Responses. Fed Condition.^a

b No pupil readings were valid for subject three. Data was considered for analysis of other parameters only.

Slide:	Che	Cheese		Cheese		Eggs, Sausage		Eggs, Sausage		akes, Eg	gs, Sausage	
	1s	t control	2nd	2nd control		ontrol	2nd	control	1st co	ontrol	2nd control	
Subject	1	2	1	2	1	2	1	2	1.	2	1	2
1	2.6	-3.9	-7.1	-7.8	-22.4	-20.6	5.6	2.1	_			
2			-20.6	-43.9								
4			-11.9	-7.8								
5	-4.0	-8.8	-1.5	-1.0	-1.9	-9.1						
6			-22.1	-17.3	-14.3	-7.7	-4.1	-2.7	-15.4	-3.4		
7	-7.7	-11.8	0.9	-2.2								
8		_ _ _				—— —	-9.4	-8.5			_	- - -
9	1.2	-2.3	-0.7	1.5					11.8	-3.2		
10	-6.8	-9.2	-12.6	-8.7	-6.7	2.9	-7.9	-1.8	2.5	3.6		
11	-0.4	-6.0	-1.5	0.8	-2.9	-0.1	0.7	11.9	-1.1	-3.1		
12		_										
13			-13.2	-12.2	-1.2	-4.6					-14.0	12.7
14	-11.9	2.1			-0.4	40.4			-3.9	3.6		
15					0.6	1.9						
16			-11.0	3.4	-15.1	-7.4	-11.1	2.2				
17	-7.7	8.2	-3.0	-2.6	-12.5	-13.3	-16.1	-10.1				-
18	-9.2	-11.9			-1.4	-10.4			-7.3	-12.2		

TABLE A Continued

Slide:	Slide: Pancakes 1st control		Pancakes 2nd control		Cookies 1st control		Cookies 1 2nd control		Jel 1st	ly on toa control	st Jell 2nd	Jelly on toast 2nd control	
Subject	1	2	1	2	1	2	1	2	1	2	1	2	
1	4.3	6.9	-4.2	2.3	4.8	18.4	·		7.7	11.6	-21.9	-18.9	
2	1.9	-5.3	0.0	-1.3	40.4	-36.2	-1.5	8.7					
4	3.0	0.0			28.7	-20.1	-10.8	-4.9			-44.9	-53.2	
5	-2.0	-10.2	-2.6	-4.3									
6	1.3	1.7	-3.8	-1.2	-3.7	-10.5	4.5	-2.6	-1.6	-2.3			
7	4.8	2.0	-1.9	-0.3									
8	1.4	-19.0	-1.6	-1.7									
9	-0.2	3.6	-3.8	-4.2									
10	-0.7	11.6			3.3	-0.4	-2.3	2.9			-5.1	5.7	
11	16.5	-1.9	-8.4	-12.3			8.7	-4.2					
12							-		_			-	
13	15.2	-0.8	2.6	-15.1				_	-16.1	3.8	-41.0	16.2	
14							-4.8	-25.9					
15	-26.1	15.0	-8.9	-3.5			-13.2	14.2	-2.9	-5.1			
16	-1.9	-6.2											
17	9.0	-21.2	-2.8	-13.5	_		12.8	-5.9					
18									-16.5	-24.0			

TABLE A Continued

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Slide:	Cream Puff		Sticky bun			Cake		ke cut	Ste	eak	Frenc	h fries	Fr	uit
Subject	1	2	1	2	1	2	_ 1	2	1	2	1	2	1	2
1	52.4	-15.8	1.6	-4.3	1.2	0.2			5.1	2.9	7.8	-2.0	3.6	-4.2
2	-7.6	3.2									-4.9	-11.8	-2.3	-6.0
4			-7.0	-15.8										
5	-9.4	0.3	-4.1	-6.5	7.0	-1.0			6.2	-3.3	-3.9	-1.0	3.9	3.7
6	3.6	-6.5			-1.5	-0.7	-0.5	-10.3	10.3	0.9	23.4	32.1	-6.5	-2.3
7	-3.0	-1.1	-0.4	5.8							-1.6	-8.9	-	
8	-4.0	-0.7	-6.9	2.8	5.7	-10.9					-2.0	-5.7	2.8	-3.3
9	2.6	4.8	-0.4	-6.4	-4.2	12.2	_		-14.2	-11.6	-1.2	-4.1	3.9	1.6
10			-4.9	-0.5	2.2	-3.7	6.8	-14.1			0.3	-4.1	4.3	1.4
11					8.6	-4.7	8.2	-7.2	4.4	-2.6	-4.5	-8.7		
12	_												16.4	-1.6
13	1.4	-2.6	0.5	3.7	7.3	0.6							-	
14					0.9	-5.7	0.7	-12.6	11.6	3.6		_	_	
15	-2.1	-0.8			6.3	15.9							1.2	-2.6
16	2.0	0.4	-6.1	-15.3	9.5	-20.3					-5.5	-10.4	-3.5	-3.2
17			11.0	-6.3	11.0	3.7	3.9	-6.2	0.0	2.9	-1.4	11.2		
18						<u> </u>								_

Page 113

Slide: Peaches 1st control		Peach 2nd	Peaches 2nd control		Carrots 1st control		Carrots 2nd control		cers control	Crackers 2nd control		
b Subject	c 1	2	1	2	1	2	1	2	1	2	1	2
1												 _
2				-								
4						·	-17.9	-2.4	-2.3	-0.7		
5	-0.2	0.0	3.9	4.5								
6	-23.1	-4.0	-9.0	8.4								
7			5.4	-13.6					-14.3	-4.4		
8		_										
9			_									
10		 -										
11	-3.6	-3.0	-0.5	-0.6								
12												
13	-3.9	-11.0	-5.0	-16.4					-8.7	-9.8	-6.5	2.0
14					14.7	-11.7	-7.9	-8.3	-19.3	-12.2		
15			-8.2	-7.1	2.8	3.2						-
16												
17												
18												
a Percenta	ge chan	$ge = \frac{\tilde{x}}{st}$	imulus X contr	x control	x 100			c _{l=fi:}	rst read	ing 2=2	2nd reading	Page 114

					а
TABLE B.	Pupil	Responses.	Not	Fed	Condition.

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^bNo pupil readings were valid for subject three. Data was considered for analysis of other parameters only.

TABLE	В	Continued	

Slide:	Chees 1st	Cheese 1st control		Cheese 2nd control		Eggs, Sausage 1st control		Sausage control	Pancakes, Eggs, 1st control		Sausage 2nd control	
Subject	1	2	1	2	1	2	1	2	1	2	1	2
1			2.3	-5.3	-6.7	-4.7						
2										<u></u>		
3								-				
4	-							· ·				
5												
6								<u> </u>				
7												
8					<u></u>							
9	-6.1	-3.4	-10.3	-0.3			-16.8	-14.2				
10												
1.1								_				
12		_				<u> </u>						
13									-12.3	-4.3		
14							-4.6	-27.6				
15												
16								<u>-</u>			<u></u>	
17			-8.6	12.3			-21.8	-5.3				
18												

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Page 115

TABLE	в	Continued		

Slide:	Panca 1st	lkes control	Panca 2nd	akes control	Cooki 1st	.es control	Cooki 2nd	es control	Jelly 1st	on toast control	Jelly 2nd	on toast control
Subject	1	2	1	2	1	2	1	2	1	2	1	2
1					0.2	-4.9	0.0	0.8				
2												
4	-											
5												
6	0.0	-13.9			3.1	9.8	9.4	24.1				
7												
8												
9			1.4	-4.7								
10			-4.5	4.8								
1.1												
12												
13			2.3	3.3								
14	<u></u>								-3.3	-7.1	0.6	-15.4
15												
16			-8.4	6.8								
17	7.3	3.5	11.3	-9.7		-						
18												

TABLE B Continued	

.

Slide:	Crea	m Puff	Stick	y Bun	C	Cake	Cake	cut	Stea	k	Frenc	h Fries	Fri	iit
Subject	1	2	1	2	1	2	1	2	1	2	1	2	1	2
1			_								-2.1	1.1		
2														
4 :														
5			9.5	-3.8					4.5	1.1	-0.7	-4.9	3.5	1.3
6			2.9	4.0					-4.0	-5.3	3.5	-8.2	-1.3	1.0
7					0.6	0.9			2.9	-2.9				
8	-													
9			-5.4	0.2	0.4	-2.3							_	
10														
11			-0.7	-0.1					-2.1	-4.8			-3.0	0.8
12														-
13					-3.5	6.5		_ 	16.0	1.8				
14														
15	-1.5	-4.5					_				-10.5	-2.0	-2.4	-0.1
16														
17	3.2	5.2	-4.4	4.9	-3.2	-0.6			·				13.8	2.8
18									_					

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	TABLE	; C			
Cor	rrelations	s of	Change	in	1
Pupi1	Response	witł	ı Varial	oles	s T

Slides:		Peaches <u>1st_cor</u>	Peaches from 1st control		es from ontrol	Carrots from 1st control
<u>Con</u>	dition:	Fed	Not Fed	Fed	Not Fed	Fed
Var	riables					
A)	Eyes Blue(2) Brown (1)	.4315	.1551	.6144	.3611	.0012
B)	Eats all (2) not(1)	.3520	 9485 [*]	.1894	1526	1777
C)	Age	.3385	4416	4683	0582	3097
D)	Experiment Number	.0111	6665	.7210	÷ 6788	.2970
E)	Change in Glucose level	4177	.0521	.0136	.5215	.6714
F)	Change in Glucose slope	.7724 *	.7899	.4519	0520	2340
G)	Days before menses	6349	5760	3978	2450	2632
н)	wt/ht ²	0457	.4972	.5181	.4560	2942
I)	% Fat	3067	.4479	.5448	.4897	.0137
J)	Time of day	2659	.4924	.6839 [*]	.5937	.7135 **
K)	Day of week (Mon.=1)	.0184	.1019	.3804	.4638	.4567
L)	Minutes to 2nd reading	.7273	.1790	.2772	.2772	2073
м) 	Breakfast eate eater(2) not (r .3100 1)	.1790	0580	0580	3307

¹Some data groups were insufficient to provide correlations for the notfed condition. **** p**<**0.01 *** p**<**0.02 **p**<**0.10

	Crackers from 1st control	Crackers from 2nd control	Cheese from 1st control	Cheese 2nd co	from ntrol
<u> </u>	Fed	Fed	Fed	Fed	Not fed
۸)	0540	***	0877	1016	1001
R)	- 3159	7010	1402	1910	4001
C)	- 2026	2072	.1402	2379	4001
C) D)	2020	1822	2310	.1052	900
5) 2)	- 0288	0386	- 0681	1510	.4020
2) 2)	0200	4001	- 0897	1319	9259
2)	- 3344	- 2496	- 0054	.4007	06 50
א (ג ג (ג	2848	2138	0034	2634	00.30
т) т)	.2040	1119	2206	.2034	.1243
т) т)	5702	- 0616	- 1330	.4000	.3240
2) 2)	- 0042	2322	6110	- 0071	.0300
r)	- 0610	2559	- 2200	0071	.7331
с) и)	2640	1361	1746	- 0227	.0499
	Eggs, Sausage 1st control	from Eggs, S 2nd cor	Sausage from	Eggs, Sa from 1st	usage control
	Fed	Fed	Not Fed	Fe	d
1)	. 2260	- 7026	1745	197	. 2
•)	.1716	1389	.1745	339	1
;)	0560	4458	7365	.037	9
))	2057	1013	5799	112	8
;)	1177	1025	1406	.527	3
7)	.2016	.7539	.5547	495	0
;)	.0114	7094	.4690	526	7
H)	0732	2480	3127	.599	4
E)	0831	.1621	4250	.504	.0
J)	1800	.0362	2010	.702	4
()	.3885	.5205	0347	.049	4
.)	.2231	.4280	1707	045	3
4)	.3647				
	**** n< 0.01	** n ∕0.	05		

TABLE C Continued

**** p<0.01 ** p<0.05 *** p<0.02 * p<0.10

	Pancakes from 1st control	Pancake 2nd_con	s from trol	Cookies 1st con	from Co trol 2r	ookies from nd_control
	Fed	Fed	Not Fed	Fed N	ot Fed	Fed
A)	1463	2918	3831	3121	.2466	0381
B)	3717	4535	3831	4740	9626*	1774
C)	4703	1256	.5134	.6549	9957	.5577
D)	.4092	.2134	.3831	.1502	2466	.0449
E)	2178	.4728	5683	5000	*	.1651
F)	2818	1706	9001	.9882		0974
G)	.1468	.1063	.8187	.1954	6760	6104
H)	2551	4096	.9219	.3150	.9654	2708
I)	2629	3273	.9970	.3139 ·		3668
J)	.2462	1459	.9037	.0466	, 9999	.0361
K)	0055	.0779	6084	9597	.7160	.1788
L)	3443	2271	.9489	3630	.7160	.2907
M)	.2718	.5656				
	Jelly from	Jelly from	Cream	S	ticky	Cake
	1st control	2nd control	_Puff]	Bun	
	Fed	Fed	Fed	Fed	Not Fed	Fed
A)	.6577.	.1130	2520	1723	4567	.3677
B)	. 8054 [^]	.1130	2042	1723	4833	.1708
C)	.5876	.2743	3800	.4154	.1416	3243
D)	5514	5555	1784	.0124	.7722	1631
E)	8000,,,,	.9411	.0562	.5219	3827	1852
F)	.8806	.8745	3407	.3579	2282	4801
G)	1743	6243	.0248	.0702	1080	1605
Н)	.4437	.8844	1594	1213	.3800	0405
I)	.3888	.9335	2914	0641	.5087	2441
J)	.0553	.4256	.2594	0400	4318	.2185
K)	5922.	6291	.4295	5237	9101	2598
L)	.8244 🦲	.1146	.0057	4171	4258	0919
М)	9211	9621	2195	.2006	.9101	.0721
	**** ~ ~ (0.1		** ~ < 0 0	5		

TABLE C Continued

**** p<0.01 *** p<0.02 ** p<0.05 * p<0.10

TABLE C Continued

	CakeSteak		eak	French	Fries
<u></u>	Fed	Fed	Not Fed	Fed	Not Fed
A)	1574	2912	2185	.0289	
B)	3250	1407	3428	3253	.0721
C)	1376	0038	3629	2907	.3451
D)	3248	.4647	5559	2633	
E)	1882	6336	.3689	0568	
F)	3209	2153	.5512	0266	
G)	.3048	.2032	4566	.4348	
H)	1113	. .1529	1829	.6452	7561
I)	0330	.0132	2077	.6329 "	4257
J)	.2802	3615	.2784	.4353	
K)	0275	.0989	.5242	.3784	
L)	2908	.3785	1745	.2573	
M)	.1175	.4154	2262	0573	

]	Fruit	
	Fed	Not Fed	
A) B) C) D) E)	.1308 4195 0610 1504 .2955	.1525 .2657 .6038 5960 .9654	
F) G) H)	.0363 .3572 .3569	.9654 .6358 0006	
I) J)	.1602	2331 3128	
K) L) M)	.3498 3057 3611	1146 .7313 .1175	
	**** p.	<0.01 <0.02	** pく0.05 * p<0.10

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Page 122

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TABLE D . Anthropometric Values

Subject	<u>exp. #</u>	ht.(cm.)	wt(kg.)	wt/ht^2 (kg/m ²)	TCa	sip	<u>%Body Fat</u>
01	1	169	67.0	23.6	11	15.5	19.5
01	2		67.0	23.6		24.8	
01	3		67.0	23.6	21.5	29.5	28.0
01	4		67.5	23.8	23.0	19.3	25.0
02	1	162.5	54.0	20.4	12.7	9.8	17.9
02	2		54.0	20.4	12.3	10.3	18.3
02	3		54.5	20.6	13	9	18.0
02	4		53.0	20.0	11.5	7.5	16.9
03	1	162.5	51.0	19.2	13.5	11.5	19.4
04	1	166	58.0	21.6	12.5	17.8	20.8
04	2		58.0	21.8	11	22.7	21.7
04	3		58.5	22	12.3	23.2	22.3
04	4		58.0	21.6	14	22	22.8
05	1	168	53.5	19.0	22	10.5	21.8
05	2		53.5	19.0	16.8	10	19.6
05	3		53.5	19.0	22.7	9	21.6
05	4		53.5	18.9	20.2	10.7	21.0
06	1	151	92.0	40.7	43.0	45	41.8
06	2		91.0	40.0			
06	3		96.0	42.0	40	48.3	41.8
06	4		95.0	41.4	41.3	44	39.8
07	1	184	66.0	19.3	18	8.2	19.6
07	2	,	66.0	19.4	17	9.3	19.5
07	3		67.5	19.9	15.5	10.5	19.4
08	1	161	64.5	24.8	33	21.3	29.3
08	2		65.0	25.0	33.8	21.7	30.2
09	1	164	58.5	21.8	17.3	16.5	22.1
09	2		58.0	21.7	14.3	17.0	21.0
09	3		60.0	22.3	17.5	15.3	21.9
09	4		59.5	22.2	22.8	23.7	26.5
10	1	180	61.5	18.9	12.7	17.7	10.8
10	2		62.0	19.0	13.2	13.0	19.5
10	3		64.0	19.8	13.5	11.5	19.0
10	4		64.5	19.9	14.5	17.7	21.5
11	1	164	65.5	24.4	38.5	16.7	29.9
11	2		65.0	24.2	37.5	13.3	27.7
11	3		63.5	23.8	29.7	14.0	26.0
11	4		62.5	23.4	30.0	11.3	25.1
12	1	169	66.5	23.5	24.3	13.3	23.5
12	2		65.5	23.0	20.5	12.3	24.0
12	3		65.7	23.1	26.7	12.7	24.2
12	4		66.0	23.2	31.U 10.7	14.7	20.7
13	1	100	89.5	34.8 74.8	19.J 71 0	41.5	33.4 77 7
13	2		07.0	34.0 71 6	JI.U 71 7	43.1 13 7	31.3
13	ى م		89.U	. 75	JI.(43.1 11 7	30.9
13	4		90.5	30	44.0	44.0	42.0

TABLE D Continued

Page 123

exp. $\frac{\mu}{\pi}$	<u>ht. (cm.)</u>	wt(kg.)	wt/ht ² <u>(kg/m²)</u>	TC	SI	<u>% Body Fat</u>
1	172.5	65.0	21.9	18.0		
2		64.5	21.7	18.3	19.3	22.7
3		65.0	21.9	21.0	16.2	23.5
4	÷	66.5	22.4	21.2	16.8	23.8
1	153.5	48.0	20.2	22.3	19.0	24.8
2		48.5	20.5	17	16.8	21.9
3		47.5	19.9	17.8	19.7	23.6
4		47.5	19.9	22.3	16.7	23.6
1	164	65.0	24.2	24.8	21.2	26.5
2		64.0	24			
1	186.5	85.0	28.2	31.0	39.7	35.2
2		87.0	28.8	36.7	29.7	33.8
3		87.0	28.8	29.7	34	32.8
4		86.0	28.4	41.3	31	36.0
1	177	66.5	21.2	13.7	17.7	21.0
2		66.5	21.2	13.2	15.0	20.0
3		67	21.3	12.7	17.3	20.5
4		66.5	21.2	13.2	16.7	20.7
	$ \begin{array}{c} exp. \frac{\#}{\pi} \\ 1 \\ 2 \\ 3 \\ 4 \\ 2 \\ 3 \\ 4 \\ 3 \\ 4 \\ 3 \\ 4 \\ 3 \\ 4 \\ 3 \\ 4 \\ 3 \\ 4 \\ 3 \\ 4 \\ 3 \\ 4 \\ 3 \\ 4 \\ 3 \\ 4 \\ 3 \\ 4 \\ 3 \\ 3 \\ 4 \\ 3 \\ 4 \\ 3 \\ 3 \\ 4 \\ 3 \\ 3 \\ 3 \\ $	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$				

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^aTriceps skinfold thickness (mm.) ^bSupra-iliac skinfold thickness (mm.)

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Table	e E . Results of	Glucose Tolerance Test: Fasting	s 60 minutes mg. Glucose/	
Subject Number	Grams CHO	100 ml. plasma	100 ml. plasma	
. 1	66.8	93	83	
1	0	83		
1	66.8	89	101	
1	66.8	96	81	
2	54.5	92	118	
2	0	89		
2	54.5	94	119	
3	51.4	101	113	
4	56.8	85	100	
4	56.8	. 95	82	
4	0	92	100	
4	56.8	97	97	
5	55.4	115	203	
5	0	86	88	
5	55.4	93	135	
5	55.4	73	132	
6	82	83	83	
6	0	91	92	
. 6	82	94	105	
6	82	91	101	
7	63.6	73	47	
7	63.6	89	92	
7	0	88	87	
8	63.6	72	128	
8	63.6	94	132	
9	57.3	101	86	
9	57.3	93	69	
9	0	95		
9	57.3	130	79	
10	61.4	87	146	
10	61.4	82	147	
10	61.4	97	135	
11	61.4	66	78	
11	61.4	85	94	
11	0	79	86	
11	61.4	85.		
12	65.9	93	150	
12	65.9	71	59,	
12	0	105.	90	
12	65.9	99	79	
13	92	105	105	
13	92	90	88	
13	0	91	91	
13	92	83	99,	
14	63.6	87		
14	63.6	99	94	

		Continued	Page 125
	IABLE E	Fasting mg. Glucose/	60 minutes mg. Glucose/
Subject Number	Grams CHO	100 ml. plasma	100 ml. plasma
14	0	93	
14	63.6	85	79,
15	47.3	85	78
15	47.3	85	99
15	0	91	90
15	47.3	69	85
16	63.6	63	87
16	63.6	117	119
17	86.4	95	107
17	86.4	93	98
17	86.4	111	101
17	0	115	106.
18	66	91	73.
18	66	109	129.
18	0	92	88
18	66	87	71,

TABLE F Change in Plasma Glucose Before and After Second Pupil Response Measurement in Fed Condition.

Subject	Experiment Number	Glucose 1 (mg/100 ml)	Glucose 2 (mg/100ml)	\triangle Time (minutes)	Slope (∆mg/100ml/min)
1	1	105	83	15	-1.47
1	3	113	101	21	-0.57
- 1	4	107	81	19	-1.37
2	1	165	118	20	-2.34
2	3	119	67	24	-2.14
4	1	103	100	20	-0 17
4	2	119	82	18	-2.04
4	4	132	97	13	-2.72
5	1	197	203	15	0.40
5	3	161	135	13	-2.05
5	4	161	132	13	-2.25
6	1	91	83	27	-0.27
6	3	129	105	21	-1.14
6	4	136	101	20	-1.77
7	1	76	47	16	-1.83
7	2	129	92	16	-2.33
8	1	137	128	17	-0.55
8	2	165	132	15	-2.22
9	1	113	86	15	-2.75
9	2	71	69	16	-0.16
9	4	73	79	15	0.4
10	2	172	146	13	-2.00
10	3	166	162	20	-0.77
10	4	149	130	13	0.36
11	1	102	78	24	-1.00
11	2	1.06	94	20	-0.07
11	4	123	79	35	-1.24
12	1	181	150	28	-2.70
12	2	95	59	12	-3.05
12	4	111	. 79	16	-2.00
13	1	123	105	16	-1.13
13	2	85	88	16	0.17
13	4	125	99	22	-1.21
14	1	135	108	32	-0.85
14	2	121	94	20	-1.37
14	4	110	79	19	-1.65
15	1	96	78	14	-1.29
15	2	127	99	19	-1.51
15	4	115	85	13	-2.26
10	1	118	87	16	-1.96
10	2	119	119	23	0.05
11	T	121	107	10	-2.75

Page 127

Subject	Experiment Number	Glucose 1 (mg/100 ml)	Glucose 2 (mg/100 ml)	Δ Time (minutes)	Slope <u> Amg/100ml/min</u>)
17	2	123	98	15	-1.64
17	3	147	101	17	-2.67
18	1	116	73	21	-2.06
18	2	157	129	14	-2.04
18	4	90	71	15	-1.28

The following information is necessary before the dates of testing can be scheduled.

NAME:

ADDRESS:

HOME PHONE: WORK PHONE: SOCIAL SECURITY NUMBER: EYE COLOR: BIRTHDATE: SEX: HEIGHT: WE IGHT: Can you see clearly at 2 to 5 feet without correction? Do you have any color blindness? Do you object to having small amounts of blood drawn from your arm? Are you diabetic? Are you using oral contraceptives? If so, what kind? How long have you used oral contraceptives? years mo. Do you regularly take any other medications? If so, what? Are you now pregnant? What mornings are you available between 7 and 11 a.m. for 1½ hours of testing? Would you like to have child care provided during the testing period? Do you anticipate being available for retesting in January or February? Please return this questionnaire to Sandy Blaha in Room 14 Home Economics Building or c/o Foods and Nutrition Department

Figure A . Initial questionnaire

Social Security No.

Date _____

Day of week_____

Time of arising_____

Food	Amount	Time
		· · · · · · · · · · · · · · · · · · ·
······································		
		
	· · · · · · · · · · · · · · · · · · ·	

Unusual physical activity:

time:

Medications used:

time:

Other data:

Retiring time:

Figure B. Food intake record
Page 130

Social Security Number Date

On the graph below please indicate your weight history. Perhaps there are significant milestones that are attached to your memory and theweight that you had at these times stands out. Indicate factors that you think were influential in weight changes such as pregnancy, competitive sports, illness etc.



How often do you weigh?

How much does your weight vary in a year?

In the last year, what was your maximum weight? What month(s) did this occur?

In the last year, what was your minimum weight? What month(s)?

To maintain your present weight, do you:

- 1. Eat all you want?
- 2. Avoid certain high calorie foods?
- 3. Restrict yourself at most meals?
- 4. Restrict between meal eating?
- 5. Skip meals?
- 6. Use maximum will power to restrain your eating?
- 7. Follow an exercise program
- 8. Other?

How long has your weight been at the present, - 5 lbs.?

Figure C. Weight history and control questionnaire