NUTRITION & CENTRAL SYSTEM FUNCTION

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February 2-6, 1992

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Diet Neurotransmitters, Behavior/Food Intake-I

WB 001 APPETITE CONTROL IN CHILDREN, Leann L. Birch, University of Illinois at Urbana-Champaign.

Recent research indicates that children are sensitive to the energy density of foods in controlling their food intake. Evidence will be presented that energy density of foods influences both meal size and food selection. The evidence for the role of energy density will be presented, which has been obtained from three different types of protocols: 1) single meal "preloading" experiments, 2) observations of children's energy intake over 24 hour periods, and 3) experiments investigating associative conditioning of sensory cues to physiological consequences of ingestion. In the preloading experiments, young children are fed fixed amounts of first course preloads that are either high or low in energy density and very similar in sensory characteristics. When they are then given the opportunity of consume what they wish from an array of palatable foods, their energy intake is greater after the low-energy then the high-energy preload. This adjustment in intake is not macronutrient specific. That is, after consuming a low-fat preload, children select meals that are higher in energy but not higher in fat than following a high-fat preload. However, children consume a more restricted variety of foods ad libitum following more energy dense preloads. We also investigated patterns of energy intake by young children in studies in which their 24 hour energy intake was monitored over 6-8 days. Coefficients of variation were calculated for each child for energy intake at meals and snacks and for the 24 hour energy intake. The children's energy intake at individual meals was highly variable, but total daily energy intake was relatively constant for each child. The mean coefficient of variation for children's energy intake at individual meals was 33.6%. In contrast, the mean coefficient of variation for total daily energy intake was 10.4%. In most cases, high energy intake at one meal was followed by low energy intake at the next meal. Although children's energy intake is highly variable from meal to meal, total daily energy intake is relatively constant because children adjust their energy intake at successive meals. There is also evidence that the energy density of food influences children's food selection. Children's preferences for food flavors are shaped in part by the food's energy density. In experiments designed to investigate the association of food flavor cues with consequences, children are given repeated opportunities to consume two different flavors of an initially novel food, such as a yogurt, that also differ in energy density. The same flavor is always paired with high or low energy density. Following experience with eating these two distinctively flavored versions that also differ in energy density, children show a preference for the flavor paired with high energy density. The energy density of foods consumed on one occasion can influence energy intake at subsequent meals, and also the variety of foods consumed. In addition, children acquire preferences for foods based on the food's energy density.

WB 002 APPETITE CONTROL IN ADULTS, George A. Bray, M.D., LSU/Pennington Biomedical Research Center, Baton Rouge, Louisiana.

Control of appetite and food intake can be conceptualized as a feedback problem. A homeostatic approach can be used as the basis for considering the ingestion of individual nutrients. The normal diet consists of about 50% carbohydrate, 35% fat and 15% protein. The amount of carbohydrate eaten each day is similar to what is stored as glycogen, but the daily intake of fat and protein is less than 1-2% of what is in body stores. Experimental studies suggest that the control of body fat content is more stable on a high carbohydrate diet than on a high fat diet. To maintain energy balance requires that the average daily intake of carbohydrate and fat must be the same as the mix of carbohydrate and fat which are used as fuels by the body. Regular physical exercise enhances the oxidation of fat and may thus play a role in maintaining lower body fat stores. Although increasing body fat is observed when most animals and humans eat a high fat diet, this is not always the case. Therefore, there must be one or more mechanisms by which the rate of fat oxidation can be increased in the face of a high fat diet. Information about the intake of nutrients and about body nutrient stores is relayed to the brain by afferent signals. These signals can be the nutrients themselves, hormones released by interactions of nutrients with the gut, or by the effects of food and its nutrients on neural messages to the brain. From this wealth of afferent information the brain must sort out the relevant signals and make decisions about food intake. These processes are integrated in the hypothalamus, among other areas. Several neurotransmitters are involved in this internal signalling, including gamma-amino butyric acid, norepinephrine, serotonin and several peptides. The various peptides used in this process may act to modulate specific types of food intake. Thus, neuropeptide Y stimulates carbohydrate intake, and corticotropin-releasing hormone may be involved in stress related eating. One the brain has made a decision, efferent processes are activated or inhibited. The animal or human can search for food, or stop eating. When food is ingested, the autonomic nervous system and endocrine system are involved in partitioning this intake into body stores. High levels of sympathetic activity are associated with lower levels of body fat. Absence of adrenal glucocorticoid hormones is also associated with lower levels of body fat. On the other hand, high levels of insulin are associated with higher levels of body fat. From this homeostatic model, it is possible to understand the mechanisms involved in the development of obesity and to consider approaches to its treatment.

Diet Neurotransmitters, Behavior/Food Intake-II

WB 003 THE INFLUENCE OF DIETARY PRECURSORS ON CNS NEUROTRANSMITTER PRODUCTION, John D. Fernstrom, Department of Psychiatry, University of Pittsburgh, Pittsburgh PA 15213

The synthesis of two major brain neurotransmitters, serotonin (5HT) and the catecholamines (e.g., dopamine [DA]) are readily influenced by the diet. Each is derived from an amino acid (tryptophan [TRP] and tyrosine [TYR], respectively), the levels of which in brain can be modified by food ingestion. For 5HT, synthesis is readily influenced by brain TRP level, which in turn is sensitive to changes in TRP uptake from blood. Brain TRP uptake, in turn depends on the blood levels of TRP and other large neutral amino acids (LNAA) that compete for uptake. Diet influences 5HT synthesis by changing blood TRP and LNAA levels, and thus brain TRP uptake and levels. By this mechanism, the ability of a very-low-protein meal to raise brain TRP level and 5HT synthesis can be explained, as can that of a moderate-to-high-protein meal to lower brain TRP and 5HT. It now appears that such meal effects can occur with *repeated* food ingestion, if meals are separated by a few hr. This biochemical/metabolic relationship thus appears capable of providing the brain (via 5HT) with a stream of information concerning recent protein ingestion. For DA, synthesis is readily influenced by TYR level. Since TYR (like TRP) is an LNAA, CNS TYR uptake and levels are influenced by diet via the same LNAA transport mechanism described above for TRP. But because the changes in blood TYR (relative to those of the other LNAA) following a meal are different from those for TRP, CNS TYR levels and DA synthesis do not rise much after a very-low-protein meal, and rise markedly after a moderate-to-high-protein meal. Recently, interest has focused on a second DA substrate, phenylalanine (PHE). PHE, formerly thought to inhibit DA synthesis, may actually serve as substrate for up to 1/3 of all DA synthesized in neurons. Currently of great interest is the issue of how dietary modifications of the *relative* levels of TYR and PHE in neurons will influence DA synthesis. Finally, it is presently not known if or how meal-related changes in DA synthesis fit into known CNS mechanisms for monitoring food intake and nutrient selection.

WB 004 FUEL METABOLISM AND APPETITE CONTROL, Mark I. Friedman, Monell Chemical Senses Center, Philadelphia, PA 19104

The nervous system relies on a variety of signals to control different aspects of feeding behavior. Signals associated with the postabsorptive processing of nutrients appear to control the amount of food consumed over the long term, and may provide a link between overall caloric homeostasis and feeding behavior. For many years, food intake was thought to be controlled by separate signals generated in the metabolism of fat and glucose. These "glucostatic" and "lipostatic" signals were believed to operate in a coordinated fashion, and this notion of a coordinated control was used to account for a variety of phenomena. Recent experiments have provided direct evidence for a control of food intake that integrates information from glucose and fat metabolism by showing that combined inhibition of fatty acid and glucose metabolism with substrate analogues produces synergistic increases in food intake in rats. Such an interaction would not be observed if signals from glucose and fat metabolism controlled feeding independently, and suggests that changes in glucose and fat metabolism influence feeding via a common mechanism. How and where such integration takes place has not been specified. Carnitine palmitoyltransferase I (CPT I) regulates the partitioning of free fatty acids between pathways for oxidation and storage. Inhibition of CPT I by methyl palmoxirate (MP) increases food intake in rats fed a high-fat diet, but not in those fed a low-fat diet. Studies of the mechanism by which MP increases food intake show that inhibition of hepatic fatty acid oxidation alone is not sufficient to elicit eating. Rather, the feeding response to inhibition of CPT I is elicited when both oxidation of fatty acids and the supply of glycogen in liver are limited. To further elucidate the interaction between hepatic fatty acid and glucose metabolism in the control of food intake, we examined the effects of combined administration of MP and the fructose analogue, 2,5-anhydro-D-mannitol (2,5-AM). 2,5-AM, which inhibits hepatic glycogenolysis, gluconeogenesis and glycolysis, increases food intake in rats by its action in the liver. In contrast to MP, 2,5-AM increases food intake in rats fed a low-fat, but not high-fat, diet. Combined treatment with MP and 2,5-AM increased food intake in a synergistic manner. The results suggest that an integrated signal for the metabolic control of food intake is generated by changes in oxidative metabolism in the liver.

WB 005 REDUCED FATTY ACID AND GLUCOSE METABOLISM ACTIVATE SEPARATE NEURAL PATHWAYS FOR STIMULATION OF FOOD INTAKE, Sue Ritter, Department of Veterinary and Comparative Anatomy, Pharmacology and Physiology, Washington State University, Pullman, WA 99164-6520.

Decreased glucose utilization ("glucoprivation") and decreased fatty acid oxidation ("lipoprivation") are metabolic signals that stimulate food intake. Glucoprivic and lipoprivic stimuli are additive in their effects on food intake, reflecting an ongoing integration of metabolic signals controlling feeding. Nevertheless, our results show that glucoprivation and lipoprivation stimulate feeding by activation of different receptor cells and bdifferent neural pathways within the brain. Lipoprivic feeding requires capsaicin-sensitive sensory neurons which travel in several subdiaphragmatic vagal branches and terminate centrally in the area postrema/nucleus of the solitary tract (AP/NTS) region. Glucoprivic feeding is not impaired by capsaicin and does not require subdiaphragmatic vagal neurons. Although their precise location is not yet known, a variety of compelling evidence indicates that receptor cells for glucoprivic feeding are located within the brain, possibly in the AP/NTS region. Thus, the AP/NTS region is crucial for both the glucoprivic and lipoprivic control. To further elucidate the central pathways for metabolic control of feeding, we examined the distribution of c-fos-like immunoreactivity (FOSLI) in the rat brain after 2-deoxy-D-glucose (2DG)- and mercaptoacetate (MA)-induced inhibition of glucose and fatty acid metabolism, respectively. C-fos is a proto-oncogene involved in the "immediate early" response of many neurons to stimulation. Accumulation of the protein product of this oncogene can be detected by immunohistochemical techniques and used as a marker of neuronal activation. 2DG (200 mg/kg) and MA (600 and 800 umol/kg) were administered remotely to unrestrained rats through atrial catheters in the absence of food 1-4 hr prior to sacrifice. MA induced FOSLI markedly in the AP/NTS and in two structures innervated by the AP/NTS: the central lateral subnucleus of the lateral parabrachial nucleus (lPBN) and central nucleus of the amygdala (CNA). Induction of FOSLI in brain by MA was abolished by subdiaphragmatic vagotomy. 2DG also increased FOSLI selectively in the AP/NTS and structures innervated by AP/NTS neurons: DMV, lPBN (external lateral subnucleus), locus coeruleus and paraventricular nucleus (PVN) of the hypothalamus. However, induction of FOSLI by 2DG was not significantly altered by subdiaphragmatic vagotomy. Parallel behavioral studies revealed that electrolytic lesions of lPBN and CNA abolish lipoprivic feeding, supporting the hypothesis that this control of feeding is mediated by pathways within the ascending visceral sensory projection. Since these lesions did not abolish glucoprivic feeding, we conclude that glucoprivic and lipoprivic feeding are mediated by different central neural pathways.

Diet Neurotransmitters, Behavior/Food Intake-III

WB 006 SWEETENERS, FOOD INTAKE AND SELECTION. G.H. Anderson and R.M. Black. Department of Nutritional Sciences, University of Toronto, Toronto, Ontario, Canada, M5S 1A8.

A caloric sweetener, such as table sugar, might be expected to have an effect on appetite and feeding behavior that is different from a high intensity (low calorie) sweetener. We and others have been investigating the effects of sweeteners on food intake and food selection, as well as subjective feelings of hunger. The consumption of sugar is widely believed to cause increased caloric intake, and so implying that the energy contained therein is either imperfectly detected or not detected at all by food intake regulator mechanisms. Yet studies of children and of adults indicate that this is not true. For example, in studies with children aged 9 - 10 years, we observed an average 68% caloric compensation at a lunch-time meal 30 min after consumption of a sugar sweetened drink. In addition, there was evidence that increasing the sweetness of the drink (and so increasing the calories) lead to a decrease in the amount of sweet foods chosen at the lunch time meal.

High intensity sweeteners are primarily distinguished from sugar by their absence of calories, and many studies indicate that when these sweeteners are substituted for sugar, food intake is adjusted accordingly. Thus it is logical to predict that the behavioral effects of high intensity sweeteners relate primarily to their absence of calories when they are consumed. In our studies of these sweeteners, we have confirmed the observation that aspartame added to water increases subjective appetite, but not actual food consumption. However, it is important to note that when aspartame is consumed in familiar beverages (e.g. soft drinks), it neither enhances or reduces subjective appetite, nor does it appear to modify energy intake or food selection. Similarly, when aspartame is consumed in pill form, bypassing taste receptors, it does not affect subjective appetite or lunch-time food intake. Finally, while the volume of soft drink consumed has a transitory suppressive effect on appetite, this is unrelated to the aspartame content of the drink. Thus we have concluded that: i) the consumption of caloric sweeteners can alter food selection, possibly as a result of the sweetener's hedonic properties; and ii) any effects of a sweetener on caloric intake, when that sweetener is consumed in a familiar food, are related to the predictable consequences arising from the presence or absence of calories.

Supported by International Life Sciences Institute, and the National Institute of Nutrition (Canada).

WB 007 HUMAN PREFERENCES FOR SUGAR AND FAT, Adam Drewnowski, The University of Michigan School of Public Health, Ann Arbor.

The sense of taste governs food preferences and food choice. Although other behavioral and sociocultural factors also play a role in diet selection, consumers respond primarily to the sensory qualities of food. Preferences for sweet taste, in particular, are widely believed to be a useful predictor of the propensity to consume palatable foods. Human obesity has long been blamed on the so-called "sweet tooth" and the tendency to over consume sweet desserts. Other studies have suggested that a centrally-mediated appetite for carbohydrate-rich foods, many of them sweet, is responsible for obesity and weight gain. Conversely, the pattern of food avoidance in anorexia nervosa has been described as "carbohydrate phobia". Thus, abnormalities in the selection of a single macronutrient, carbohydrate, were thought to be responsible for both weight gain and weight loss. However, recent sensory studies point to the central role of dietary fats in determining sensory quality and the acceptability of different foods (1). Sensory preferences for sugar versus fat have been used to distinguish between clinical populations of obese and anorectic women (2,3). While obese patients selected fat-rich stimuli, anorectic women were chiefly characterized by fat avoidance. Taste preference profiles for sugar/fat mixtures have also been used to characterize potential subtypes of human obesity (4). Higher preferences for cake frostings and ice cream were obtained among obese men and women showing large fluctuations in body weight than among obese subjects whose weights were more stable. In contrast, childhood-onset (age<10) obesity, thought to be an index of familial risk, had no influence on taste preference profiles. Additional studies have shown that preferences for dietary sources of carbohydrate and fat differ between men and women. While obese men listed several protein/fat mixtures (i.e. meat dishes), obese women tended to list foods that contained both fat and carbohydrate, and were moreover, sweet. Preferences for sugar and fat appear to vary as a function of age, gender, degree of overweight and history of caloric restriction and weight cycling.

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2. Drewnowski A, Brunzell JD, Sande K et al. Sweet tooth reconsidered: taste preferences in human obesity. Physiol Behav 1985;35:617-22.
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WB 008 FAT SUBSTITUTES AND REGULATION OF FOOD INTAKE IN RATS, Ruth B.S. Harris, Nutrition Department, Kraft General Foods, Inc., Glenview.

Introduction of fat free processed foods has the potential to reduce fat intake of the general population from approximately 36% to 30% kcal (Lyle et al.,1991). Diet manipulation studies with animal models allow investigation of physiological and metabolic responses to both extreme and moderate changes in fat intake. Initial studies examined responses made by adult and growing animals to removal of non-essential fat from the diet. Growing rats offered diets containing only 2% kcal fat, as essential fatty acids, grew slightly faster than controls receiving diets containing either 17% or 36% kcal fat. The differences in growth were accounted for by increased lean body mass with no differences in body fat content. Adult rats offered diets containing only 2% kcal fat accurately compensated for the reduction in dietary energy concentration so that energy intake, body composition and serum lipid concentrations were identical to those of rats receiving a 21% kcal fat diet. When fat in a very high-fat diet was reduced from 63% to 51% kcal there was a reduction in degree of obesity and prevention of the insulin resistance apparent in the 63% kcal fat rats. Reducing dietary fat content from 40% to 30% kcal fat provides a model that is more appropriate for anticipated changes in fat intake that could be achieved by the use of fat free or fat reduced products by the general population. In adult rats consuming diets of 40% or 30% kcal fat the reduction in fat intake resulted in a decrease in energy intake, body fat content and serum insulin concentrations. Insulin insensitivity induced by a 40% kcal fat diet was also corrected within 3 days of reducing fat intake. The response was the same whether fat was replaced with carbohydrate or with a fat mimetic. Measurements of energy intake and changes in body composition suggested that the reduction in body fat content with a 30% kcal fat diet may partially be accounted for by a reduction in efficiency of energy utilization. In another study in which growing rats were offered either full fat or reduced fat and fat free "cafeteria" foods, the energy intakes of both cafeteria groups were greater than that of the control rats offered a semi-purified 30% kcal fat diet. However, the body fat content of the low fat cafeteria rats was lower than that of both full-fat cafeteria rats and of control animals, possibly because consumption of fat free foods had reduced their fat intake to less than 30% kcal. These results indicate that reducing the fat content of the diet to 30% kcal, or less, has beneficial effects on body composition in both growing and mature animals.

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WB 009 DIETARY FIBER AND ENERGY BALANCE. Allen S. Levine and Charles J. Billington. VA Medical Center and the University of Minnesota, Minneapolis, Minnesota.

The significance of dietary fiber in management of food intake and body weight has been uncertain. Foods with large amounts of dietary fiber may decrease gastric emptying, take longer to consume, alter the absorption of selected nutrients and have low energy density. Studies with fiber isolates, foods supplemented with fiber, and foods naturally high in fiber have been conducted. Although a variety of studies have reported small decreases in body weight associated with the intake of fiber tablets, few have been double blinded and placebo controlled. Furthermore, in some studies, the caloric content of the caloric content of the placebo tablets was greater than that of the fiber tablets. In a double blind, randomized, placebo controlled study Solum et al observed that 60 slightly overweight women taking a 6 g daily fiber supplement, lost 8.5 kg over a 12 week period compared with 6.7 kg in the placebo group. However, in another well controlled study, Rossner et al reported that a 6.5 g dietary fiber supplement failed to alter body weight over a 12 week period in 62 moderately obese females. Several studies have demonstrated that fiber can decrease short term food intake. Porikos and Hagamen found that obese patients consumed fewer calories 30-45 minutes after a sandwich preload containing 6.6 g of fiber compared with one containing only 0.4 g of fiber. We found that patients eating high fiber cereals at breakfast (22.2 g fiber/meal) consumed fewer calories during lunch compared to those who ate a very low fiber cereal at breakfast (<1 g fiber/meal). As expected, ingestion of high fiber cereals increased fermentation by colonic microorganisms, resulting in a larger output of breath hydrogen. However, cereals containing moderate amounts of fiber, which failed to decrease food intake at lunch, also resulted in an increase in gas production. Thus, bloating due to microbial gas production probably does not account for the decrease in food intake. Stevens et al studied energy intake in women ingesting low fiber-wheat crackers, high fiber-psyllium gum crackers.and high fiber-wheat bran crackers. They found that the psyllium gum supplemented fiber crackers decreased intake of digestible energy by 153 kcal/day, whereas there was no effect of the wheat bran cracker. It has also been suggested that an increase in fiber intake may decrease nutrient absorption and lead to a loss in body weight. Rigaud et al found that a dietary fiber supplement (7.3 g/day) increased the number of bowel movements per day and increased fecal energy excretion by 20 kcal/day when compared to the placebo group. High fiber diets have also been shown to increase daily fat excretion by about 2.5 g/day when subjects ingested 100 g fat/day. Thus, dietary fiber may slightly augment weight loss and decrease short term food intake.

WB 010 DIETARY FAT REPLACEMENT AND THE REGULATION OF FOOD INTAKE IN HUMANS, Barbara J. Rolls, The Johns Hopkins University School of Medicine, Baltimore.

Excessive dietary fat intake has been linked to cardiovascular disease, obesity, and some types of cancer. As concern among consumers over the level of fat in their diets has risen, the variety of low-fat foods available has increased. There is only limited understanding of how decreasing the percentage of calories from fat will affect hunger, satiety, food intake and body weight.

A key question is whether fat and carbohydrate (CHO) have similar effects on hunger and satiety since if the proportion of fat in the diet is reduced, the proportion of CHO will increase. We have conducted a number of studies in which we have manipulated the CHO or fat content of foods. In one study, normal-weight non-dieting men and women were fed fixed amounts of yogurts varying in fat and CHO which were formulated to have the same energy content and similar sensory properties, protein content, and volume. It was found that when the preloads were consumed 30, 90, or 180 minutes before a self-selection lunch, there were no differences between the effects of CHO or fat on hunger, fullness, energy intake, or the types of foods or macronutrients consumed.

We also conducted two residential studies lasting for several weeks during which the macronutrient content of the diet was manipulated covertly. In the first study the CHO or fat content of lunch was manipulated by 1674 kJ. Apart from the required consumption of lunch, subjects could eat as much as they wanted from a wide selection of foods. No differences were found between the CHO and fat manipulations. Subjects made up for caloric reductions so that daily energy intake remained constant across conditions. Since the caloric compensation was achieved by adjusting intake of all macronutrients equally, there was no indication that the macronutrient composition of the lunch affected the proportion of macronutrients eaten over the rest of the day. A similar result was obtained with a bigger manipulation of CHO or fat (3000 to 7000 kJ) during three required eating occasions (breakfast, lunch, and afternoon snack). The subjects could eat from a variety of foods over the rest of the day, and again while there was caloric compensation, there was little indication that macronutrients were adjusted in relation to the nutrient content of the required meals.

The studies discussed so far used commercially available foods. Another approach is to replace dietary fat with a non-absorbable fat substitute such as olestra. In studies in which olestra covertly replaced 0, 20, or 36 g of fat at breakfast in non-dieting men, it was found that over the rest of the day subjects compensated for the caloric reduction but not for the fat reduction. This meant that olestra consumption was associated with a decrease in the percentage of calories from fat over the test day.

In all of our studies, subjects have compensated for the reduction in calories associated with low-fat foods. Studies in other labs have sometimes reported caloric compensation, but often compensation is incomplete. This may be because in most of these studies subjects have only been allowed limited access to high-fat foods. Thus, the impact of low-fat foods on energy intake and body weight will depend upon the ability of consumers to adhere to low-fat diets. Eating habits are resistant to change, and it is not clear that the preference for high-fat foods can be readily altered. However, the results of the studies on fat reduction indicate that consumption of low-fat foods will help to lower the percentage of calories from fat in the diet.

WB 011 DIGESTIBLE CARBOHYDRATES AND CARBOHYDRATE APPETITE, Anthony Sclafani, Department of Psychology, Brooklyn College and The Graduate School, City University of New York, Brooklyn, NY 11210.

Carbohydrates in the form of sugar and starch are a major source of food energy for humans and many other animal species. Sugars, although less abundant than starches, have attracted the most research attention because of their palatable sweet taste and presumed obesity promoting effect. Although dietary sugar does not have a "unique role" in the etiology of human obesity, animal research demonstrates that high-sugar diets reliably produce overeating and obesity, but only under certain conditions. Diet hydration is of particular importance; sugar solutions or moist high-sugar diets invariably stimulate hyperphagia in laboratory rodents whereas powdered sugar or dry high-sugar diets are usually associated with normophagia. Although not fully understood, both taste and postingestive factors are implicated in the diet hydration effect. To investigate the role of sweet taste in sugar-induced overeating the feeding responses of rats to sweet (sugars) and nonsweet (hydrolyzed starch) carbohydrate solutions were compared. Initial findings revealed that hydrolyzed starch solutions (Polycose) produced as much or more overeating as did sucrose and glucose solutions. These results appeared to rule out taste as a factor, but it was subsequently discovered that rats can taste hydrolyzed starch and find it very palatable. Unlike humans, rats have separate taste receptors for sugars and hydrolyzed starch. Rats can also detect insoluble (unprocessed) starch using as yet to be identified orosensory receptors. In view of these unexpected findings, new methods are needed to isolate the contribution of taste and postingestive factors in carbohydrate appetite and overeating. One approach is to use intragastric (IG) feeding techniques to bypass orosensory receptors. Rats will readily learn to feed themselves intragastrically when the the intake of flavored water (e.g., grape water) is paired with IG carbohydrate infusions. Furthermore, the animals acquire strong preferences for the flavor paired with the carbohydrate infusions over other flavors or plain water. Preliminary results also indicate that the carbohydrate infusions stimulate overeating but that adding a sweet taste to the flavored water enhances this effect. Taken together, these findings indicate that carbohydrate appetite is mediated by innate attractions to the orosensory qualities of sugar and starch and by flavor preferences conditioned by the postingestive consequences of the carbohydrates. These conditioned preferences can be quite potent and can override unlearned taste preferences and aversions. Although humans lack a starch "taste", their appetite for starches as well as for sugars may be conditioned by postingestive nutritional effects.

WB 012 CEPHALIC PHASE INSULIN RELEASE IN HUMANS: MECHANISM AND FUNCTION, Karen L. Teff, Monell Chemical Senses Center, Philadelphia, Pennsylvania.

Cephalic phase insulin release (CPIR) is the neurally mediated, pre-absorptive insulin released in response to food-related sensory stimuli. Although, many conclusions have been drawn with respect to the mechanisms and function of CPIR, most are extrapolations based on either animal data or on the responses of other cephalic phase reflexes, such as gastric acid and salivary secretion. In actuality, few experiments have attempted to determine either the optimum sensory stimuli or the physiological function of CPIR in humans. This is primarily because of the difficulties associated with the measurement of CPIR. The majority of human work in this area has focused on establishing the existence of the response rather than the specifics of mechanism and function.

Having established a reliable method for the measurement of CPIR in normal weight males, we have initiated a series of studies examining other aspects of the response. For example, it is generally assumed that highly palatable or sweet tasting foods are necessary to stimulate CPIR and although saccharin can elicit the response in rats, the effect of non-nutritive sweeteners on CPIR in humans is controversial. We found that the administration of an aspartame-sweetened, cherry flavored beverage did not increase plasma insulin levels in normal weight men (n=10), suggesting that sweet taste alone may not be an adequate stimulus for eliciting CPIR. To further explore the role of other sensory stimuli in eliciting CPIR, we are presently comparing different sweeteners as well as using a modified sham-feed paradigm.

We have also investigated the relationship between cephalic phase and post-prandial insulin release in normal weight (n=18) and obese (n=15) men. Obese subjects released significantly greater amounts of insulin during both phases of insulin secretion. Significant differences in the characteristics of the cephalic phase insulin response were also found between obese and normal weight subjects. In addition, although a significant correlation between the two phases of insulin release was observed in the normal weight subjects ($r=0.65$, $p<0.01$), this relationship was not observed in the obese subjects ($r=0.04$). These results suggest that the relationship between CPIR and post-prandial insulin release may be impaired in the obese.

Diet Neurotransmitters, Behavior/Food Intake-IV

WB 013 NUTRITIONAL SNACKS AND BEHAVIOR, Robin B. Kanarek[1], Edward Hirsch[2], Erica Norkin[1], Jane Anderson[1], Phillip Holcomb[1], David Swinney[3], and Laurie Lester[2], [1] Tufts University, Medford, MA, and [2] Natick Army Research Laboratories, Natick, MA, [3] City University of New York, New York.

The effects of nutritive snacks on the performance of cognitive tasks in college-aged men and women were examined in a series of experiments. In initial experiments, the effects of snacks fed in the late afternoon were tested in the same subjects after they either consumed or skipped lunch. In the first two studies, the nutritive snack was a confectionery product, while in the third study, the snack was fruit-flavored yogurt. Performance on cognitive tasks following consumption of the calorie-rich snack was compared to performance following consumption of a very low calorie snack (lemon-lime flavored diet soda without caffeine). Four cognitive tasks were used: digit span recall (forward and backward), arithmetic reasoning, reading, and attention (a visual continuous performance task). Both male and female subjects recalled significantly more digits in the backward digit span test and responded significantly faster in the attention task when they had consumed the nutrient-dense snack that when they had consumed the diet soft drink. Additionally, young women correctly solved arithmetic problems significantly more rapidly after consuming the confectionery product than after consuming the diet soft drink. In general, whether subjects had eaten lunch or not had little effect on cognitive performance. The next group of studies investigated whether similar beneficial effects of nutritional snacks would occur if they were fed at other times of day. These studies, using the same tasks as above, examined the effects of a nutritional snack (the confectionery product) on cognitive performance in the latemorning in college-aged men and women who had or had not eaten breakfast. Male subjects remembered more digits in both the forward and backward digit span tasks and displayed faster reaction times and made less errors on the attention task after consuming the confectionery product than after drinking the diet soda. Female subjects also recalled more numbers in the backward digit span task after eating the nutritional snack, but did not display faster reaction times or make less errors on the attention task. To extend our work, the final set of experiments measured not only cognitive performance, but also brain activity using the event-related brain potential (ERP) technique. These experiments employed the attention task used in our previous work and recorded electrical brain activity from 13 locations across the scalp. College-aged men were fed a standard breakfast, skipped lunch and then were tested in the late afternoon after receiving either a fruit-flavored yogurt, a diet soda or no snack. Preliminary data analysis of brain activity suggested that the diet soda produced a larger amplitude positivity between 300 and 600 ms post-target onset than did the yogurt condition, which in turn, produced a larger positivity than the no snack condition. These differences appeared to be greatest over the more anterior electrode sites.

WB 014 FOOD CONSTITUENTS THAT ENHANCE PERFORMANCE, Harris R. Lieberman, Military Performance and Neuroscience Division, U.S. Army Research Institute of Environmental Medicine, Natick, MA. 01760-5007.

Caffeine and tyrosine are two food constituents that, acting via different mechanisms, may enhance human performance. Of these substances, caffeine, which acts on the brain by blocking adenosine receptors, has been the most intensely studied for the longest period of time. Its precise effects on human performance remain controversial and it is often considered to have only marginal effects on human behavior. However, when appropriate methods are employed, caffeine can be shown to reliably increase the ability of individuals to maintain vigilance. Four studies will be discussed that have consistently detected effects of this methylxanthine. Caffeine reliably enhanced both auditory and visual vigilance when administered in doses of 32 to 256 mg, the range found in single and multiple servings of caffeine-containing beverages. Caffeine also affected mood state, increasing self-reported vigor and alertness, consistent with its effects on performance, but did not increase anxiety.

Tyrosine is a large neutral amino acid and a dietary precursor of the catecholamine neurotransmitters. In certain instances, including exposure to a variety of stressors, administration of tyrosine can increase brain catecholamine concentration and turnover. Therefore, tyrosine may have beneficial behavioral effects when individuals are exposed to environmental or other stressors. Several studies have been conducted to test this hypothesis. In one study, tyrosine, administered in a dose of 100 mg/kg, significantly reduced a wide variety of cognitive impairments and adverse symptoms in individuals who exhibited a greater than average response to a combination of stressors - hypobaric hypoxia (4200 m or 4700 m) and cold (15° C degrees). Tyrosine had little effect on behavior when individuals were not exposed to these stressors. In a second study, using similar environmental conditions and many of the same behavioral tests, subjects received 85 and 170 mg/kg of tyrosine. Tyrosine again appeared to reduce a number of adverse consequences of exposure to hypoxia and cold stress among individuals most severely affected by these stressors. In a third study, employing a cardiovascular stressor, lower body negative pressure (LBNP), tyrosine altered an electrophysiologic correlate of information processing, the P300 wave of the auditory evoked potential. This suggests that this neurotransmitter precursor can directly affect brain function during exposure to acute stressors.

Caffeine and tyrosine have very different effects on behavior as would be expected given their different mechanisms of action. Caffeine appears to selectively affect one type of performance - vigilance. Tyrosine alters a wider range of behaviors but its effects have only been observed during stress.

WB 015 EFFECTS OF BREAKFAST ON PERFORMANCE, MOOD AND SATIETY, Bonnie Spring[1], Regina Pingitore[1], Michael J. Bourgeois[2], Margarette Harden[2], Kenneth H. Kessler[1], Elaine Bruckner[1], [1]University of Health Sciences/The Chicago Medical School and Veterans Affairs Medical Center, North Chicago, IL 60064, [2]Texas Tech University Health Sciences Center, Lubbock, Texas

Federal involvement in school-based breakfast feeding programs is based upon the assumption that optimal nutrition leads to optimal cognition. Yet relatively few studies have evaluated whether eating breakfast promotes advantageous effects on performance. The presentation will review findings concerning the acute behavioral effects of skipping breakfast and the chronic effects of consuming breakfast for children, adolescents, and adults. Although much evidence suggests that skipping breakfast has detrimental effects on performance, approximately an equal number of findings suggest that skipping breakfast lacks behavioral consequences. A minority of studies even detect beneficial effects of skipping breakfast. Findings suggest that individuals with pre-existing or current malnourishment and those who usually eat breakfast are most likely to benefit behaviorally from eating breakfast. A series of three studies will be presented comparing the response of healthy adults to unbalanced breakfasts high in carbohydrate and low in protein, balanced breakfasts high in protein and fiber, and no breakfast. In all three studies, skipping breakfast decreased subjective alertness in comparison with eating breakfast. By late morning, when subjects were stressed and worked under relatively continuous time demands, skipping breakfast resulted in irritability and problem solving difficulties that were not evident when subjects were less stressed. A balanced breakfast high in protein and fiber was more satiating than an isocaloric low-protein breakfast, and was somewhat more effective at offsetting fatigue and performance decrements.

WB 016 BREAKFAST AND LUNCH EFFECTS ON WORK PRODUCTIVITY,
David P. Wyon, Quantus R&D, Lillmyravägen 47, 804 27 Gävle, Sweden

Three behavioural experiments were performed to demonstrate the existence of acute effects of breakfast and lunch regimen on work productivity during subsequent hours. In the first experiment, the parents of eighty 10–year–olds were induced to alter their breakfast regimen according to general guidelines common to all families: half of the children, selected at random, were served an "adequate" breakfast in the first week and an "inadequate" breakfast in the second week. The order was reversed for the other children. The class teacher could not know which child had eaten which breakfast on any given day, and the children were unaware of the experiment. Tests of addition, multiplication, logic, reading, number checking and creativity were integrated into normal school work, and each child performed each test only once. There was a significant decrement in the performance of the numerical and logic tests, and of creativity, following an inadequate breakfast. In one class, voluntary physical endurance was tested in warm–up exercises during a physical education class: a significant decrement was found following an inadequate breakfast. The difference in nutritional values between breakfast types, as estimated from parents' logs of actual consumption, was significant: the inadequate breakfasts gave less energy and less protein than the adequate breakfasts. In the second experiment, 22 factory workers were served four different breakfasts, two of which were inadequate, over a period of two weeks in a balanced design. The subjects evaluated each breakfast on a questionnaire and believed they were taking part in a market survey. They did not know that their detailed individual work records for the period, and for reference weeks before and after the period, were available to the researchers. The provision of free breakfasts caused a significant increase in productivity, as would be expected if the effect was caused only by "goodwill", but there was also a significant difference in productivity in the predicted direction between breakfast types, which appeared only in the second 2–hour period, as would be expected if the effect was due to differences in nutritional value. In the third experiment, 110 students, 75% of whom were female, volunteered to perform mental work for 3 hours following a free lunch. Half of them, selected at random, were served only coffee and a chocolate bar, the others ate a canteen lunch. Significant differences in test performance were found for female subjects in all six 30–minute test periods: performance of addition, multiplication, logic and creativity tests decreased by 8–18% in the group eating only a snack instead of lunch.

Regulatory Applications and Implications

WB 017 SAFETY EVALUATION: TESTING FOR THE EFFECTS OF DIET ON THE NERVOUS SYSTEM, Thomas J. Sobotka, Food and Drug Administration, Washington, D.C. 20204.

Developments in the field of neurotoxicology have led to an increasing appreciation of the vulnerability of the nervous system to perturbation by toxic substances. Concerns about the potential mental health consequences of chemically induced neurotoxicity have led to increasing demands for some assurance that appropriate and effective measures are being taken to minimize the risk of human exposure to neurotoxic substances. In response to these concerns, increased attention has been focussed on the need to develop more specific information about the adverse effects of chemicals on the structural and functional integrity of the nervous system as an integral part of the toxicological profile routinely developed in the process of assessing chemical safety. To aid in the development of the appropriate type and level of information needed for a reasonable assessment of neurotoxic hazard, regulatory agencies have initiated efforts to provide guidelines for the formulation of test strategies and for the design and conduct of scientifically sound protocols. The guidelines being proposed by the Food and Drug Administration for assessing the potential neurotoxic hazards of food related chemicals suggest a strategy of tiered testing. This is consistent with the approach used by other regulatory groups. Accordingly, chemicals would be initially screened for signs of adverse effects to nervous system. Screening would be integrated into the toxicological protocols used routinely for testing of proposed food chemicals. Those chemical identified as potentially neurotoxic would then become candidates for subsequent specialized neurotoxicity testing, as warranted, to define the extent of nervous system involvement and to determine the dose-response kinetics, including the no adverse effect levels. Typically, at each level of tiered testing, a combination of increasingly specialized and appropriate neuropathological and behavioral/physiological endpoints would be used to provide a comprehensive assessment of treatment related neurotoxicity. As with any type of toxicological information, the significance of the neurotoxicity data for regulatory application is dependent upon a number of considerations including the validity of the methodology, the reliability and rigor of the data in defining dose response relationships, and the adequacy of the data for assessing the hazardous nature of the effects.

Free Amino Acids and CNS Function

WB 018 FREE AMINO ACIDS - FOOD OR DRUG, John T. Brosnan, Department of Biochemistry, Memorial University of Newfoundland, St. John's, NF, Canada, A1B 3X9.

The availability of free amino acids at relatively low cost has resulted in many individuals in North America, and elsewhere, ingesting various amino acid products in substantial quantities over relatively long periods. Amino acids have been recommended by assorted experts for assorted users - from depression, sleep disorders and pre-menstrual syndrome to alcoholism, hyperlipidemia and "turning fat into muscle". In addition to scientific studies published in the conventional medical literature, these products have been heavily promoted in popular magazines dealing with life-style, body building, slimming, etc. Several issues are raised by this phenomenon - in particular those of efficacy and safety. It may be stated outright that ingestion of free amino acids as nutritional supplements is an expensive substitute for eating a well-balanced diet. Scientific justification for the efficacy of most of the popular claims for benefits of free amino acid ingestion is lacking. The issue of safety involves two aspects: firstly, there is comparatively little information available concerning the effects of ingestion of gram quantities of highly purified amino acids over long periods of time; secondly, since free amino acids purchased in outlets such as health-food stores do not necessarily meet drug standards, questions of purity and contamination arise. The eosinophilia-myalgia syndrome is a case in point. This syndrome which resulted in more than 150 deaths in the USA alone, together with significant morbidity in a much larger number of individuals, has been shown to be due to ingestion of a minor contaminant in certain tryptophan preparations. These, and other related issues will be discussed.

WB 019 EXCITOTOXINS OF DIETARY ORIGIN, Brian S. Meldrum, Department of Neurology, Institute of Psychiatry, De Crespigny Park, London SE5 8AF, U.K.

Acute excitotoxic cell death has been extensively studied *in vitro* and *in vivo* and a detailed account can be given of its morphology and its ionic dependence, and a slightly less adequate account of its associated biochemical features. In contrast chronic excitotoxicity remains ill-defined in terms of morphology or pathophysiology. Dietary excitotoxins can be described under 4 or more headings:

1. Toxins of marine plant origin (domoic acid, kainic acid) that induce limbic seizures and limbic system pathology in animals and man (domoic acid occurring in toxic doses in blue mussels). This syndrome presumably depends on activation of kainate receptors in the hippocampus; much of the pathology may however be indirect and dependent on seizure activity and endogenous glutamate.
2. Glutamate and analogues that induce acute pathology in periventricular structures when given in high doses to neonatal mice, rats and monkeys. This syndrome has never been described in man.
3. β-N-oxalylamino-L-alanine, BOAA, the toxin of the chick pea, *Lathyrus sativus*, is thought to be responsible for neurolathyrism a disorder of subacute or chronic onset with loss of upper and lower motorneurons. BOAA is a potent excitotoxin acting on AMPA receptors. This could be relevant to its neuropathological effects but other mechanisms may account for the selective pathology.
4. Two compounds that are not excitotoxins, β-N-methyl-amino-L-alanine (BMAA) and L-cysteine, become excitotoxic in the presence of bicarbonate, 20 mM, *in vitro*. High doses in rodents can produce selective pathology - BMAA in the cerebellum, L-cysteine in cortex, striatum, hippocampus and thalamus. There is no clear evidence that either compound acts as a dietary toxin to cause neurological disorders.

Various metabolic poisons (e.g. aminooxyacetic acid) cause neurons to become vulnerable to the excitotoxic action of endogenous compounds (most probably glutamate). This mechanism may lead to false conclusions being drawn from experiments showing protection against degeneration provided by excitatory amino acid antagonists.

WB 020 NEUROTOXICITY OF ACIDIC AMINO ACIDS, John W. Olney, Washington University Medical School, St. Louis, MO

In recent years, glutamate (Glu) and aspartate have become recognized as the Jekyll/Hyde molecules of the CNS. These common acidic amino acids, which are naturally present in high concentrations in the CNS, serve vitally important metabolic, neurotrophic and neurotransmitter roles, but also harbor treacherous neurotoxic potential. Significant progress has been made in understanding the neurotoxic (excitotoxic) properties of Glu and related excitatory amino acids (EAA). Three EAA receptor subtypes that mediate excitotoxicity have been identified, drugs with anti-excitotoxic actions have been discovered, and evidence for the complicity of both exogenous and endogenous excitotoxins in neurodegenerative disorders has begun to unfold.

The neurotoxicity of Glu also warrants attention in a separate context -- a food safety context. Glu is used extensively in processed foods as a flavoring agent; typically, the amounts added to foods are large because the flavoring properties of Glu are weak. I consider this a reckless and imprudent practice in that it exposes immature humans to oral doses of Glu (mg/kg body wt) comparable to those that destroy neurons in the hypothalamus of immature animals, and ingestion of a given dose of Glu causes much higher blood Glu levels in humans than in animals. Unfortunately, the Glu and food industries have adopted a position, based on flawed data and biased reasoning, that Glu is non-toxic to primates, and FDA uncritically has accepted this view, the result being that Glu continues to be classified as GRAS (generally regarded as safe), and millions of immature humans continue to be exposed routinely to potentially dangerous amounts of Glu.

At doses lower than those required to produce brain damage, Glu poses another type of risk to the immature consumer. When administered systemically in subtoxic doses to monkeys or rodents, Glu enters the endocrine hypothalalmus and triggers release of hypophysiotrophic hormones, resulting in a sharp rise in blood levels of growth and luteinizing hormones. There is no sound basis for assuming that the immature human does not experience similar erratic neuroendocrine perturbations as a result of ingesting foods to which gram quantities of Glu have been added. Nor is it safe to assume that such perturbations would not have an adverse influence on somatosexual development. The truth is that under current food additive practices, immature consumers are being exposed to Glu (along with other excitotoxins) at levels that provide essentially no margin of safety. In my opinion, it is time for the Glu and food industries and FDA officials to quit denying this truth, and quit playing Russian roulette with Glu bullets aimed at hypothalamic neurons in the brains of millions of immature consumers.

Dietary Fat and The Central Nervous System

WB 021 CHANGES IN DIETARY FAT COMPOSITION: IMPACT ON BEHAVIOR, Carol E. Greenwood, Department of Nutritional Sciences, Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada. M5S 1A8.

There is considerable evidence demonstrating that the developing brain is sensitive to dietary supply of essential fatty acids (EFAs). Developmental EFA deficiency is associated with alterations in membrane fatty acid composition and functional deficits. In contrast to these studies, our interest in the role of dietary fat in maintaining CNS function has focused on the mature animal (i.e. post rapid neuronal membrane fatty acid accretion). Diet manipulation (20% (w/w) lard (supplemented with 5% sunflower and soybean oils) or soybean oil (SBO) diets) is commenced in rapidly growing animals (80-100 g BW) and continued for a 2 to 4 month period. Results from our initial studies demonstrated that pain sensitivity, degree of d-amphetamine induced hypothermia in a cold environment, and feeding behavior (protein and carbohydrate selection) are all influenced by the source of dietary fat fed. To pursue our observation that dietary fat composition influences behaviour, we examined higher brain functions by using the Morris water maze to test spatial memory in rats. The results indicated superior performance by the SBO-fed rats. A more systematic investigation followed in which several tasks designed to assess different aspects of learning and memory were administered. Rats were tested on an Olton radial arm maze (RAM), Hebb-Williams maze (HWM) and a variable-interval delayed alternation (VIDA) task. In general, rats consuming the SBO-based diets showed superior performance to those consuming the lard-based diets. For example, on Olton's RAM, the lard-fed rats displayed a slight but significant deficit in spatial memory. In contrast, their temporal memory over short and long intervals was severely impaired on the VIDA test and, on the HWM, they were deficient in learning various maze configurations. Taken together, these results suggest that dietary fat has a modest impact on brain function and that this impact is most likely to be observed in those behaviours that depend on the integrity of multiple neuronal systems. To determine whether the alterations in behavior could be attributed to specific dietary fat characteristics, blends of fats were produced which allowed us to alter either the amount and ratio of the EFAs or the proportion of saturated (SFA), monounsaturated (MUFA) and polyunsaturated (PUFA) fatty acids. In studies of protein and carbohydrate selection, the results demonstrated that alterations in the amount or ratio of EFAs had no effect on diet selection. In contrast, protein and carbohydrate selection were highly and linearly correlated with the amount of SFA fed. Increasing the proportion of SFA resulted in a reduced protein and increased carbohydrate selection, with alterations in SFA content of the diet accounting for up to 40% of the variance ($r^2 = 0.42$) in diet selection observed. Whether changes in the SFA content of the diet can account for the other behavioral changes observed is presently unknown. In an attempt to determine the physiologic mechanism underlying the behavioral changes, membrane phospholipid fatty acid profile was examined. While dietary fat resulted in alterations in membrane fatty acid profile, the fatty acid changes did not correlate with the alterations in diet selection observed suggesting that alterations in bulk membrane composition were not sufficient to explain the altered feeding behaviour. Furthermore, feeding the experimental diets for up to 2 months had no effect on the number or affinity of striatal D_2-dopamine and cortical S_2-serotonin receptors. Thus, at present the mechanism underlying the behavioral change is unknown. (Research supported by grants from NSERC, ILSI-NF, and MRC.)

WB 022 IMPACT OF ω-3 FATTY ACID DEFICIENCY ON THE DEVELOPMENT OF VISUAL FUNCTION IN VERY LOW BIRTH WEIGHT INFANTS

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The LBW infant is at risk for EFA deficit despite the fact that most formulas provide ample linoleic acid (18:2 ω-6). Brain lipids and other membrane phospholipids have a preferential accretion of ω-3 PUFAs especially (22:6 ω-3). The dietary intake of ω-3 and -6 LCPUFAs provided by human milk may be of vital importance to the developing brain and eye in the LBW infant.

We have recently completed a 4 year study of 83 infants with birth weights between 1000-1500 g; 28 - 33 wks gestation fed either human milk (HM) or formulas containing different amounts of ω-6 and ω-3 EFA. Infants whose mothers chose not to provide human milk were randomly assigned to three artificial formulas. Formula A, based on MCT/coconut/corn oil provided solely linoleic acid, 18:2 ω-6 as EFA and corresponds to commercial powdered premature formula. Formula B, based on MCT/coconut/soy oil, supplied 18:2 ω-6 and 18:3 ω-3 and corresponded to liquid ready-to-feed premature formula. Formula C an experimental product specially prepared for the study was similar to B but was supplemented with marine oils to provide LCPUFA's (EPA (0.6%) and DHA (0.4%)) similar to that found in HM. The fatty acid compositions of plasma and RBC lipids were similar on entry (day 10 of life) but marked diet-induced differences were evident on discharge from the nursery (day 30-45 of life) at 36-37 wks conceptional age. Group C (receiving EPA + DHA) was similar to the HM-fed infants but group A (ω-3 deficient) had markedly lower total ω-3 LCPUFA and DHA in plasma and tissues on discharge. Group B receiving ω-3 and ω-6 EFA but no LCPUFAs had intermediate LCPUFA values in their both blood lipid fractions. After discharge, the infants received an additional 5 months term infant formula with an EFA composition that was similar to the preterm formula diets. The changes in blood lipid profiles at the 57 week conceptional age follow up were accentuated relative to the 36 weeks results. The retinal function tests demonstrated significantly higher threshold, lower amplitude and lower semisaturation constant values in rod photoreceptors from the ω-3 deficient group (group A) at the time of discharge relative to groups receiving ω-3 fatty acids. Cone function was not significantly affected by diet although the trends were similar to the results from rods.

Function of the visual cortex measured by pattern reversal visual evoked potentials (VEP) and forced preferential looking (FPL) acuity response also showed improved visual function in the HM and group C at the 36 weeks and 57 month follow-up relative to infants fed formulas devoid of DHA. The group receiving soy as a source of ω-3 fatty acids was different in VEP and FPL acuity relative to the HM and marine oil fed groups. A group of 30 healthy full term breast fed infants matched by conceptional age were used as controls; their visual acuity at 4 months was virtually identical to the HM and marine oil fed premie groups. These results suggest that ω-3 LCPUFAs are needed for optimal development of visual function in the human. (Supported by grant NICHD 22380 UCP R375-87 and in part by NIH EY 05235 and EY 05236).

WB 023 REQUIREMENT FOR CHOLINE: DO BREAST MILK AND OR INFANT FORMULAS PROVIDE OPTIMAL AMOUNTS,

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We observed that serum choline concentration in the fetal and newborn rat was extremely high (65 μM {± 4 SEM} at birth and declined as the rat matured until adult values were attained (10 μM {± 0.8 SEM}). Neonatal humans had much higher serum choline concentrations than did adult humans (39.8 μM {± 5.6 SEM} in neonates versus 12.2 μM {± 0.03 SEM} in adults). In the human, serum choline concentration gradually declined during the first weeks of life. High circulating levels of choline in the neonate presumably ensure enhanced availability of choline to tissues. We observed that increased serum choline in the neonatal rat was associated with an increase in brain choline concentration. The fetus derives choline from maternal blood across the placenta. The choline concentration in maternal plasma is not especially high (12 μM). Metabolism of choline by mother and placenta diminish availability to the fetus. We found that dietary intake of choline contributed to the maintenance of high serum choline concentrations in the neonate. During the first days after delivery of the infant, human milk choline concentration was high (650 μM), and decreased thereafter to 150 μM in mature milk. Commercially available infant formulas and bovine milk also contained choline and choline-containing compounds. Formulas made from soy protein contained more free choline (as much as 648 nmoles/ml) and more PtdCho (240 nmoles/ml), and they contained much less sphingomyelin than bovine or mature human milk.Rat milk contained 100-300 μM unesterified choline. We found that rat and human mammary epithelial cells are capable of concentrative uptake of choline from maternal blood. We characterized choline uptake by mammary epithelial cells (the site of milk production) of the lactating rat. We observed two uptake processes, one saturable and obeying Michaelis-Menten kinetics, and the other non-saturable and linear. We also have shown that mammary epithelial cells are capable of *de novo* synthesis of choline. We identified phosphatidylethanolamine N-methyltransferase activity in rat mammary. Humans require choline in their diets, and we showed that adults humans, when deprived of choline develop liver dysfunction. We will discuss recent observations that indicate that supplemental choline, administered during critical periods of development, permanently alters brain function.

Supported by grants #HD26553 and AG09525 from the NIH.

Aging and Central Nervous System Function

WB 024 NUTRITIONAL STATUS AND COGNITIVE FUNCTION IN THE ELDERLY,

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Among the most commonly emphasized changes associated with aging is decline in function of the central nervous system. This may take the form of mild memory loss or cognitive change in the elderly or a more devastating and debilitating dementia as that which occurs in Alzheimer's disease or in association with advanced cerebrovascular disease. While a great deal more needs to be understood about the process of aging of the central nervous system, it can now be stated clearly that there is a nutritional basis for changes in cognitive and neurologic function that are associated with aging. Neuroendocrine factors, membrane receptor function, and neurotransmitter function can all be influenced by diet and nutritional factors.Both clinical and epidemiologic studies are addressing measures of nutritional status as indicators of neurologic and cognitive function and dysfunction. Increasingly, this permits examination of specific nutrient interactions with central nervous system function and the identification of subtle or subclinical deficiencies which are associated with cognitive impairment. The vitamins B12 and folic acid are "problem" vitamins in the elderly in view of their uncertain absorption especially in individuals with atrophic gastritis and loss of stomach acid. Subclinical deficiency may be identified by measures of metabolic intermediates in the blood such as homocysteine, and methyl malonic acid. Hyperhomocysteinemia is, in turn, associated with an increased risk of cerebrovascular disease, a major cause of dementia in the elderly. Vitamin B6 is another nutrient of importance in respect to brain function and neurotransmitter metabolism and is also a determinant of post-prandial homocysteine blood levels. Critical processes of methylation which are necessary for the maintenance of nerve cell membrane phospholipid content, receptor function,and neurotransmitter levels, depend ultimately on systems which are folate and vitamin B12 dependent. Dietary and endogenous sources of choline and betaine may also be influential in these processes.

WB 025 TASTE AND SMELL: THE EFFECT OF AGING, DISEASE STATES, AND MEDICATIONS. SUSAN S. SCHIFFMAN, DEPARTMENTS OF PSYCHIATRY AND PSYCHOLOGY, DUKE UNIVERSITY, DURHAM, NC 27706

Alterations in taste and smell sensitivity result from normal aging, disease states, and medications. Increased taste thresholds have been reported in both healthy and sick elderly persons for sweet, sour, salty, and bitter tastes as well as amino acids and weak galvanic current. The losses are not uniform across tastants but tend to vary with the molecular structure of the compound. Common offenders in taste loss are herpes viruses, antirheumatic and antiproliferative drugs, and pharmaceutical agents that have sulfhydryl groups in their molecular structure such as captopril and penicillamine. The relative losses in smell perception with age are greater than for taste. Elevated thresholds have been reported for coal-gas, food odors, steroids, and a wide range of common chemicals. Odor thresholds are 11 times higher on average in the elderly. Losses in odor perception frequently result from viral infections, normal aging, injuries to the head that sever the neurons coursing through the cribriform plate, local obstructions, and industrial chemicals. Amplification of foods and beverages with flavors can compensate for olfactory losses. Recent studies suggest that pharmacologic methods can be used to alter transduction mechanisms in taste bud membranes to ameliorate unpleasant taste sensations from medications.

Diet, Food Intake and Behavior

WB 100 ASPARTAME AND WATER: SHORT TERM ENHANCEMENT AND SUPPRESSION OF SUBJECTIVE APPETITE BUT NOT FOOD INTAKE. R.M. Black, L.A. Leiter & G.H. Anderson. Dept. of Nutritional Sciences and Dept. of Medicine, University of Toronto, Toronto, Canada, M5S 1A8.

Although it has been 5 years since the first report that the non-nutritive sweetener aspartame (APM) increases appetite when consumed in water, other research groups have been unable to duplicate the phenomenon. However, previous attempts to replicate these findings used sweetened flavoured drinks, not water, a possible confound. For Example, we previously reported that consuming 280 ml of an APM sweetened diet soft drink (170 mg APM) did not increase subjective appetite or alter food intake or food selection at a lunch-time meal, while consuming 560 ml of the same drink (340 mg APM) suppressed appetite over the next 30 to 45 min. Therefore, the purpose of the present study was two-fold. First, to examine the cause of this appetite reduction, i.e. volume of the drink, or the postingestive action of APM; second, to replicate the initial conditions under which were reported the appetite enhancing effects of APM ingestion. Eighteen male subjects (age 19-25 yrs, BMI 21-25) received 5 treatments in a random order, one per week: 280 ml mineral water (MW); 560 ml MW; 280 ml MW and 340 mg APM in 2 capsules; 280 ml MW sweetened with 340 mg APM; 560 ml APM sweetened soft drink. The drink was consumed over a 10 min period, starting 60 min prior to a lunch time meal. Consuming APM capsules with MW did not reduce subjective appetite compared to MW alone. But, both 560 ml of MW and 560 ml of diet soft drink reduced subjective appetite for the next 20 to 30 min. Conversely, consuming APM sweetened MW produced a short term increase in subjective appetite. No treatment affected total lunch time intake. The data indicate that APM as a sweetener in water increases appetite, and that volume of a drink, not the postingestive action of APM, suppresses hunger in this subject population. Research supported by International Life Sciences Institute - Nutrition Foundation, and the National Institute of Nutrition (Canada).

WB 101 DO PLASMA AMINO ACIDS OR FOOD PREFERENCES PREDICT THE EFFECT OF SEROTONERGIC DRUGS IN OBESE PATIENTS DURING LONG-TERM TREATMENT?. Leif Breum, S.E. Møller, T. Andersen, A. Astrup, P. Damsbo & F. Quaade. Dept. of Endocrinology, Hvidovre Hospital, Dept. of Medicine C, Glostrup County Hospital, Hvidøre Hospital, Clinical Research Lab. and Human Research Institute, University of Copenhagen, Denmark.

Dexfenfluramine (dF) and fluoxetine (F) have been shown to affect body weight by stimulating brain serotonergic function. As found in depressive disorders there might in obesity exist an association between drug efficacy and pre-treatment plasma ratios of tryptophan (Trp) and tyrosine (Tyr) to other large neutral amino acids (LNAA). In order to test this hypothesis and to elucidate the importance of the pre-treatment carbohydrate/protein intake (CHO/PROT), data from 3 uniform studies were pooled. 100 obese diabetic (type-2) or non-diabetic patients were studied before and after 6 months of double-blind treatment with either: (A) dF 60 mg/day (non-diabetics), (B) F 30 mg/day (impaired glucose tolerance or diabetics) and (C) dF 60 mg/day (diabetics). Macronutrient selection were measured by food records. Fasting plasma amino acids were measured in study A and B. The effect of treatment was studied by dichotomizing patients into groups with Trp, Trp/LNAA or Tyr/LNAA below or above the median value. Weight loss was independent of group and treatment. In patients treated with active drugs, weight loss was unassociated with pre-treatment levels of CHO-intake and CHO/PROT. The drugs did not affect body weight, CHO-intake and CHO/PROT ratio significantly compared to placebo. In conclusion, basal plasma amino acid profiles and food preferences are not predictors of weight loss during long-term serotonergic treatment.

WB 102 MALADAPTIVE COPING PATTERNS IN THE RAT INDUCED BY HIGH DIETARY PROTEIN:CARBOHYDRATE RATIO, J.W. Brock, K. Ross and C. Prasad, Neuroscience Lab, Pennington Biomedical Research Center, Baton Rouge; Dept. of Medicine, LSUMC, New Orleans, LA 70112.

Rats that consume a high protein:carbohydrate (P:C) ratio diet are hyperresponsive to nociceptive stimuli and have increased basal arousal levels. It is unknown whether these behaviors are related to a more generalized inability in the animals on a high P:C diet to cope with stress. Male, Sprague-Dawley rats (4 months old) were fed diets of 50% casein/35% carbohydrate (high P:C ratio group) and 20% casein/65% carbohydrate (normal P:C ratio group), ad lib. Both diets also consisted of 5% corn oil. After consuming their respective diets for 32 weeks, the animals were tested for 5 days (1 trial/day) in the swimming cylinder, which tests emotional adaptation to stress. At the time of testing, the animals weighed 471 $\pm$ 14 grams (normal P:C) and 474 $\pm$ 8 grams (high P:C). The total number of seconds that each animal remained in an immobile stance in 35-37°C water was recorded (immobility time, T) during a 5-minute trial. On Day 1, T for the normal and high P:C groups were similar (171 $\pm$ 5 vs. 184 $\pm$ 13 sec., respectively; $p>0.05$). T for both groups increased with each successive day of testing. In the normal P:C group, T increased at a greater rate than in the high P:C group and was significantly greater by Day 5 (262 $\pm$ 6 vs. 211 $\pm$ 24 sec, respectively; $p<0.05$). These data suggest that the behavioral responses to acute stress were not sensitive to changes in dietary P:C ratio. However, animals on the high P:C diet were less able to develop an effective strategy for coping with repeated stress. Alternatively, the high P:C diet may have had a mood-elevating effect in the rats, which inhibited the development of learned helplessness. (Supported by the Dept. of the Army)

WB 103 EFFECT OF DIET TYPE AND DRUG GROUP ON TRYPTOPHAN\LNAA RATIOS AND MOOD IN PMS, **Candace S. Brown, Eddie M. Lancaster, Frank W. Ling, Kris L. Arheart, Kristi A. Boehm, Richard A. Helms, Departments of Clinical Pharmacy, Obstetrics and Gynecology, and Biostatistics, University of Tennessee, Memphis, TN 38163**

Premenstrual Syndrome (PMS) is a cyclic disorder which is characterized by emotional and physical symptoms which occur during the luteal phase and remit with the onset of menses. Serotonin has been implicated as an etiological factor in PMS based on clinical presentation and concordance with major depression. Carbohydrate craving is commonly associated with PMS and is believed to improve mood by increasing the proportion of tryptophan in the blood relative to the other large neutral amino acids (e.g., Tryptophan/LNAA ratio), thus facilitating tryptophan brain entry and conversion to serotonin. Serotonergic agonists improve mood by promoting postsynaptic neurotransmission of serotonin. As part of a 6-month, double-blind, placebo-controlled trial of the serotonin agonist buspirone, tryptophan/LNAA ratios and mood were measured in 7 women meeting Diagnostic and Statistical Manual (DSM-III-R) criteria for PMS at 0, 120, and 240 minutes after consuming a randomly-assigned carbohydrate-rich or protein-rich meal. A significantly greater tryptophan/LNAA ratio was observed with the buspirone-carbohydrate combination (0.18 $\pm$ 0.03) than with buspirone-placebo (0.12 $\pm$ 0.03), placebo-carbohydrate (0.07 $\pm$ 0.03), or placebo-placebo combinations (0.07 $\pm$ 0.03) ($t=2.36$, $p<0.05$). In addition, the buspirone-carbohydrate combination produced a greater reduction in depression ($t = 2.58$, $p< 0.05$) and anger ($t = 2.96$, $p< 0.01$) than any other diet-drug combination. Our data suggest that ingesting complex carbohydrates along with serotonergic agents may maximize improvement in mood. More research is needed to explore the value of nutrients and medication as combination therapy.

WB 104 CHILDREN'S SENSITIVITY TO ENERGY DENSITY IS RELATED TO PARENT'S EATING AND DISCIPLINARY STYLES, S.L. Johnson and L.L. Birch, Division of Nutritional Sciences, Child Development Lab, University of Illinois, Urbana, IL 61801

In the home, children are subject to general parenting strategies and beliefs regarding proper nutrition and food choices. The transmission of this information can involve considerable adult control and coercion. Thirty-three parents and their preschool children (2-4 years of age, 15 girls and 17 boys) participated in an investigation of the relationships between parents' dieting behaviors/ general parenting style and children's energy intake patterns. Mothers and fathers completed the Three Factor Eating Questionnaire which measures 3 aspects of dieting behavior: dietary restraint, disinhibition, and perceived hunger. General attitudes toward child rearing and family life were assessed by The Parent Attitude Research Instrument (PARI Q4) which rates parenting style for degree of authoritarian control. Children participated in 2 pairs of preload/consumption trials during which they drank a high or low density preload followed by a lunch consumed ad libitum. Food intake was measured by pre- and post-weighing all foods and subsequently energy intake was calculated from manufacturer's nutrient data. From these data, an individual percent compensation was computed to serve as an index (COMPX) for each child. This COMPX is an indicator of the child's sensitivity to caloric density differences of the drink preloads. Parents' questionnaire scores were strongly correlated with children's COMPX's. In the case of dieting behavior, parents' disinhibition was significantly related to children's COMPX ($r=-0.44$, $p<0.01$; $n=33$) suggesting that parents reporting more disinhibition have children who are less likely to attend to internal cues of hunger and satiety. In addition, parents with more authoritarian parenting styles are also more likely to have children who less accurately compensate ($r=-0.39$, $p<0.05$; $n=26$). A combined parental score for disinhibition and authoritarianism produced the most powerful correlations with children's COMPX ($r=-0.60$, $p<0.001$; $n=26$). These preliminary results suggest that parents attitudes toward child rearing as well as their dieting behaviors may have an impact upon children's energy intake patterns.

WB 105 FAT DISTRIBUTION AND EATING BEHAVIOR

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Fat distribution measured as waist:hip girth ratio (WHR) is a significant risk factor for most metabolic complications of obesity. Gender and sex hormones are determinants of fat distribution via unknown mechanisms. We tested the hypothesis that sex differences in eating behavior might be related to fat distribution by covertly measuring eating rates on an eating monitor in 17 severely obese women and 11 severely obese men in whom we measured WHR. The correlation between WHR and eating rate was 0.29 ($p<0.01$) and was also significant for women and men separately. Body mass index was inversely related to eating rate ($r=-0.30$;$p<0.01$). We conclude that gender-specific eating patterns are related to fat distribution.

WB 106 ENERGY STRATEGIES : A MODEL FOR NUTRITIONAL BEHAVIOR, Dina Ralt, Department of Membrane Research and Biophysics, The Weizmann Institute of Science, 76100 Rehovot, Israel

One of the main issues in understanding obesity is the near impossibility of continually controlling food intake. A model is proposed which deals with this particular question, as well as providing a unifying concept to explain a variety of weight disorders. The model suggests a functional compartment (A-compartment) and an integrative controller (regulator). The A-compartment consists of the total available energy (available for immediate use e.g., membrane potential etc.). The role of the regulator is to scan the A-compartment, ensuring its full capacity at all times via regulation of food intake and energy expenditure. Obesity, according to this model, is the result of lowered capacity of the A-compartment i.e., the regulator senses deficiency of energy and constantly instructs the body to increase food intake and reduce physical activity. The size of the A-compartment is probably determined genetically. It could, however, be manipulated to fit specific physiological states (e.g., diets cause a decrease and physical activity causes an increase in the capacity of the A-compartment). This model predicts that below a minimal threshold size of the A-compartment it will no longer be possible to keep a set point weight and thus continuous increase in body weight is anticipated (morbid obesity). It explains why dieting, in the long run, fails (i.e., eating is ultimately regulated by A-compartment size) and suggests that an increase in A-compartment (via, for example, passive or active physical activity) is the limiting step and a prerequisite for weight control.

WB 107 FEEDING METHOD AND ACTIVITY LEVEL IN THREE-MONTH-OLD INFANTS,

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The purpose of this study was to examine whether method of infant feeding (i.e., breastmilk vs. formula) is associated with temperament in general, and motoric activity in particular. To assess temperament, 46 mothers of 3-month-old infants completed the Infant Behavior Questionnaire (Rothbart, 1978). This instrument provides estimates of activity level, smiling/laughter, fear, distress to limitations, duration of orienting, and soothability. To measure motoric activity, limb movements over eight minutes were recorded by means of a specially-designed, computer-driven actometer (McDonnell, Corkum & Wilson, 1989). The device allows for separate and synchronous measurement of the infant's arm and leg movements. Relative to the 13 formula-fed infants, the 33 infants who were breastfed were more motorically active, both in terms of total activity and separate limb movement. For the breastfed group only, arm movements exceeded leg movements, and activity in response to an animated mobile was inhibited. Breastfeeding mothers reported greater distress to limitations in their infants, though not a significantly higher activity level. As infant research incresingly bridges the disciplines of psychology and nutrition, it is recommended that feeding method be considered an important variable in studies of early human behavior.

WB 108 THE EFFECT OF ADRENALECTOMY ON THE RESPONSE OF FOOD INTAKE TO ENTEROSTATIN IN OBESE RATS. David A. York, Shuichi Okada and George A. Bray, Pennington Biomedical Research Center, Louisiana state University, Baton Rouge, LA 70808.

Enterostatin is the aminoterminal pentapeptide of procolipase which is released by tryptic hydrolysis in the small intestine. We have previously shown that this peptide, administered either peripherally or centrally, specifically inhibits fat intake in rats fed a macronutrient choice diet. We have investigated the effects of enterostatin on food intake of lean and obese Zucker fa/fa rats fed a high fat diet. After an overnight fast, enterostatin (122nMoles ip) had no effect on food intake of lean rats (5.6±0.5 and 5.5±0.7grams in 1 hour by vehicle and enterostatin groups) but inhibited intake of obese rats (vehicle 6.0±0.6; enterostatin 3.9±0.7grams). Adrenalectomy reduced food intake of obese rats and abolished the response to enterostatin but had no effect in lean rats.

RNA was extracted from pancreas of all rats and used for Northern blot analysis of mRNA for procolipase, the parent molecule of enterostatin and 18S ribosomal RNA as a control. These data showed that procolipase mRNA was reduced in obese rats compared to lean rats but increased to the levels observed in pancreas of lean rats after adrenalectomy. Adrenalectomy had no effect on mRNA for procolipase in lean rats. Previous results have shown that the differing responses to enterostatin in Osborne-Mendel and S5B/Pl rats was also related to endogenous colipase activities. Since procolipase synthesis is equivalent to enterostatin production, these results suggest that the response to exogenous enterostatin may depend upon the endogenous synthesis of this peptide and that the hyperphagia and fat preference of obese fa/fa rats may relate to the reduction in enterostatin synthesis.

Diet and The Nervous System

WB 200 DIETARY POLYUNSATURATED FATTY ACIDS (PUFA) AND NEURONAL MEMBRANE ALTERATIONS DURING CHRONIC ALCOHOL INTOXICATION IN RATS. Françoise J. Beaugé, Gilles Aufrère and Bernard Le Bourhis, Centre de Recherche Pernod-Ricard, 94015 Créteil, France.

Dietary PUFA supply can influence the fatty acid pattern of brain and disturb membrane associated events. The present study adresses the possible interacting effects of dietary n6 and n3 PUFA and chronic ethanol intoxication on synaptic membrane lipid composition and "fluidity" in connection with tolerance to and dependence on the drug. Wistar rats were fed with different diets either rich in PUFA (soya oil:SO) or deficient in 18:3n3(sunflower oil SFO) eventually rich in long chain n3 PUFA (SFO + cod liver oil:CLO). Adult males from the 2nd generation were alcoholized by intubation or inhalation during 3-4 weeks.Synaptic membrane lipid composition, "fluidity" and sensitivity to ethanol (fluorescence polarization of DPH probes) were determined as well as functional tolerance and behavioural dependence. Clear-cut differences were noted in the responses to ethanol intoxication according to the various diets. Rats fed SFO or ClO diets were unable to develop tolerance at the membrane level as well as functionnally, contrarily to the rats fed SO diet or an usual lab chow. These animals were also more prone to develop behavioural dependence.The n6/n3 PUFA balance needs to be maintained within very narrow limits to enable the membrane adaptation to ethanol. The total n6 + n3 FA content seems to regulate the changes in "fluidity" of the polar regions of the membrane, emphasizing some specific structural roles for the essential PUFA. Dietary lipid modulations can alter the brain membrane adaptation to ethanol and interfere with tolerance and dependence development.

WB 201 LIPOPROTEIN LIPASE IN THE SPINAL CORD RESPONDS TO FEEDING, IS INCREASED IN OBESE RATS AND FUNCTIONS IN THE UPTAKE OF DIETARY FAT, Daniel H. Bessesen, Connie L. Richards, Robert H. Eckel, University of Colorado Health Sciences Center, Denver, CO 80262

Lipoprotein lipase is an enzyme synthesized by adipose tissue and muscle where it plays an important role in the metabolism of triglyceride rich lipoproteins. It has also been found in the hippocampus, and to a lesser extent, other brain regions. We have found LPL in the rat spinal cord (SC) at levels 3-4x higher than those found in other parts of the neuroaxis; levels comparable to muscle or adipose tissue. Levels of enzyme activity are highest in the cauda equina, increase in response to feeding, and decrease as the rats age. SCLPL activity is higher in genetically obese Zucker rats, when compared to lean rats. Weight reduction of obese rats results in a decrease in SCLPL activity. 14C labeled fatty acids were fed to rats and uptake within the CNS determined. These studies show that uptake of dietary fat within the CNS parallels the activity of LPL, with the highest uptake being seen in obese rats. In obese rats almost 70% of the dietary fat is oxidized within 6 hours, whereas in lean rats, only 30% is oxidized over 6 hours. These studies suggest that within the CNS, the spinal cord plays an important role in the removal and oxidation of dietary fat, a process which may be important in the transmission of metabolic information about dietary fat to the CNS.

WB 202 EFFECTS OF DIETARY CALCIUM ON LEAD ACCUMULATION IN THE BRAIN AND KIDNEY, John D. Bogden, Sheldon B. Gertner, Sylvia Christakos, Francis W. Kemp, Zhengang Yang, Suzanne R. Katz, and Ching Chu, UMDNJ-New Jersey Medical School, Newark, NJ 07103

Lead is a ubiquitous environmental contaminant present in air, water, and numerous other sources. Its occurrence at elevated levels in agricultural soils has produced widespread contamination of foods. Other dietary components, particularly calcium, can influence the absorption of lead from the gastrointestinal tract and its subsequent metabolism. Since the brain and kidneys are major target organs for lead toxicity, we studied the effects of chronic administration of lead and modified calcium diets on kidney and brain concentrations of lead, magnesium, iron, copper, and zinc, and on renal levels of the 28,000 dalton calcium-binding protein calbindin-D28K. Seventy-two weanling male Sprague-Dawley rats were randomly assigned to one of nine treatment groups. Rats were fed diets containing 0.1%, 0.5%, or 2.5% Ca for 52 weeks and were simultaneously given either 0, 50, or 100 micrograms lead/ml in their drinking water. Rats fed the 0.1% diet had brain and kidney concentrations that were about 5 and 20-fold greater, respectively, than the corresponding animals fed 0.5% Ca. Rats fed diets with 2.5% Ca had the lowest brain and kidney lead concentrations. Other tissues analyzed (femur, whole blood, liver, testes, heart) also had the highest lead concentrations in rats fed 0.1% Ca and the lowest in rats fed 2.5% Ca. Despite substantial effects of diet Ca on organ lead concentrations, Ca did not significantly influence brain or kidney concentrations of the other divalent metals studied. For rats not given lead, renal calbindin levels were highest in rats fed 0.1% calcium, and lowest in rats fed 2.5% Ca. Lead inhibited the expected increase in renal calbindin in the rats fed 0.1% Ca, but paradoxically increased renal calbindin levels in animals fed 2.5% Ca. Calbindin-D28K can bind 4 lead atoms per molecule and is present in rat brain; this protein may be involved in lead detoxification in the kidney and central nervous system. Age related changes in its expression may help explain the effects of age on susceptibility to lead toxicity.

WB 203 REGION SPECIFIC MODULATION OF RAT BRAIN DOPAMINE LEVELS BY LONG TERM CHANGES IN THE DIETARY PROTEIN.

Shakeel M. Farooqui, Jeffery W. Brock, Joseph W. Lafleur and Chandan Prasad. Laboratory of Neurosciences, Pennington Biomedical Research Center, Baton Rouge, LA. and Dept. of Medicine, LSU MC, New Orleans, LA.

Changes in the composition of macronutrient in diet are known to affect brain function. For example, rats on 50% protein diet exhibit increased spontaneous locomotor activity and stereotypy; the mechanism of which remains unknown. It has been suggested, however, that a high-protein diet may increase the availability of tyrosine, a precursor for the synthesis of dopamine and other catecholamines. Therefore, we have examined the effect of dietary protein on the regional distribution of dopamine and its metabolites in rat brain. Male Sprague-Dawley rats were fed equicaloric high protein (50%), low protein (8%) and medium protein (20%) diets (H-, L- and M- diets respectively) for 36 weeks. Thirty six nuclei of the brain were dissected and analyzed for dopamine (DA), homovanillic acid (HVA) and 3,4-dihydroxyphenylacetic acid (DOPAC). The results show an elevated level of DA in the caudate putamen of rats fed H-diet compared to those fed M-diet (H-diet; 238±32, M-diet; 140±18; ng/mg protein; mean+SEM; n=6; p=0.03). In contrast the levels of two DA metabolites, HVA and DOPAC, did not differ significantly in the three dietary groups. Furthermore, the levels of DA and its metabolites in mesocortical areas represented by frontal and entorhinal cortices and ventral tegmental area, did not change significantly ($p<0.05$) following dietary protein manipulation. In conclusion, these data demonstrate the level of DA and its metabolites change following dietary protein manipulation in a region specific manner. Differential modulation of dopaminergic activity in the mesolimbic and mesocortical systems may be a mechanism by which dietary protein influences the expression of locomotor behavior in rats. (Supported by Dept. of the Army)

WB 204 RECOGNITION OF ESSENTIAL AMINO ACID DEFICIENCY: ROLE OF NOREPINEPHRINE IN THE PREPYRIFORM CORTEX, Dorothy W. Gietzen, Department of Physiological Sciences, School of Veterinary Medicine, and Food Intake Laboratory, University of California, Davis, Davis CA 95616

Organisms from bacteria to primates recognize the lack of an essential amino acid (eAA) in their milieu. Prokaryotes produce an alarm hormone (alarmone) when an eAA is removed from their medium. The response in most higher animals is a reduction in food intake. We use the AA imbalanced diet (IMB) model to induce a specific AA depletion. Replacement of the eAA into the prepyriform cortex (PPC) restored feeding of IMB, but only if protein synthesis was unimpaired. The concentration of norepinephrine (NE) was reduced in homogenates of the PPC prior to and just after the anorectic response to IMB. Decreased tissue NE could be due to increased release and metabolism or decreased synthesis. Injection of the autoreceptor (α_2) agonist clonidine into the PPC, to block NE release, increased intake of IMB. We have also observed a decrease in cAMP in the PPC 2.5 hr after introducing IMB, suggesting that increased NE activity at the α_2 receptor may decrease cAMP (and protein synthesis). In the present study, we addressed the question of increased NE release more directly. Rats were implanted with guide cannulae directed at the PPC (stereotaxic coordinates: AP +11.4, L 4.0, D 6.5). Push pull perfusates were assayed for NE and metabolites by HPLC with electrochemical detection. At 2 and 4 hr after introduction of an IMB diet, NE in the perfusate was significantly increased over baseline. Values were (mean ± SE): 136.7 ± 7.9 pg/20 μl at 2 hr, $p<0.005$ and 120.3 ± 13.5 at 4 hr $p<0.05$ vs 76.9 ± 7.9 before diet presentation. There were no such increases after 2 or 4 hr of eating the basal control diet. Therefore, ingestion of IMB apparently increased NE release in the PPC. NE activity in the PPC could serve as the vertebrate alarmone, signaling the lack of an eAA. Supported by # 87-CRCR-1-2418 and 90-37200-5440 from CRGO/USDA, DK42274 and DK35747 to the UCD Clinical Nutrition Research Unit.

WB 205 MACRONUTRIENTS MODIFICATION ALTERS D2 DOPAMINE RECEPTOR PROPERTIES IN RAT BRAIN, Anwar Hamdi*, Emmanuel S. Onaivi* and Chandan Prasad**, *Laboratory of Neuroscience, Pennington Biomedical Research Center, Baton Rouge, LA 70808 and *Section of Endocrinology, Department of Medicine, Louisiana State University, Medical Center, New Orleans, LA 70112

The properties of D2 dopamine (DA) receptors in rat striatum and mesolimbic area, two regions richly innervated with DAergic neurons, were evaluated after long-term dietary manipulation. Groups of rats were pair-fed with equicaloric diet containing low protein (8%)-high carbohydrate, high protein (52%)-low carbohydrate and normal protein (20%) for 36 weeks. Results showed that the low protein-high carbohydrate fed rats exhibited a significant decrease in the density of the D2 DA receptors, in the striatum (28%) and the mesolimbic regions (36%). However, the affinity (Kd) of the receptors for the specific antagonist [^{3}H]YM-09151-2 remained unaltered. The properties of D2 DA receptors in the high protein-low carbohydrate fed rats were not different from the control. These findings suggest that consumption of a long-term, low protein-high carbohydrate diet leads to modulation in the D2 DA receptor density and may be an important determinant regulating the central DAergic function.

WB 206 THE EFFECT OF MALNUTRITION ON CEREBRAL PROTEIN METABOLISM, Abel Lajtha, Miriam Banay-Schwartz, and Agnes Kenessey, Center for Neurochemistry, N.S. Kline Institute for Psychiatric Research, Orangeburg, NY 10962

Food or protein deficiency during development will affect cerebral protein content, but such deficiency in adults does not lead to loss of protein in the brain, even though it does so throughout the rest of the organism. These findings indicate that in brain the controls of protein metabolism, and the response of this metabolism to nutritional influences, differs from those of other tissues.

We recently investigated the effects of brief food withdrawal or longer term low protein diets on the levels of proteases in the brain and other organs in 3-, 12-, and 24-month-old Fischer rats. The response was different in the various tissues, and it was dependent on the age of the animal. The changes were also different for the different proteases. For example, brief starvation caused no change in cathepsin D activity in brain, but caused an increase in liver and a decrease in spleen. Calcium-dependent neutral protease (calpain) activity increased with age in the brain and decreased in other organs. Brief starvation caused an increase of calpain levels in the brain in young, but a decrease in the brain of aged animals.

Measurement of in vivo turnover rates showed that malnutrition affects synthesis and breakdown and these effects are different from those in other organs. These results show that factors controlling cerebral protease activity are different from those in other organs, and that they undergo changes with age and affect the activity of the enzymes in a complex pattern.

WB 207 CORRECTION OF DEFICIENT LIVER PHOSPHOLIPID ARACHIDONATE IN OBESE ZUCKER RATS, WITH REDUCED FOOD INTAKE AND WEIGHT GAIN, Stephen Phinney, Anna B. Tang, Debbie C. Thurmond, Manabu Nakamura, and Judith S. Stern, Depts of Medicine and Nutrition, Univ of CA, Davis, 95616.

We have recently reported low levels of arachidonic acid (AA) in the serum phospholipids (PL) of obese humans, which persist following weight loss. Obese Zucker rats have also been reported to have low levels of AA in liver, presumably due to impaired desaturase activity. We studied lean (FaFa) and obese (fafa) weanling Zucker rats fed a semi-purified ad libitum diet for 60 days. Eight lean and 8 obese animals were gavaged daily with 0.1 ml soy oil, and identical groups were gavaged with black currant oil (BCO) methyl ester concentrate (70% γ-linolenic acid). Food intake ($p < 0.06$), weight gain ($p < 0.0001$), and % fat ($p < 0.05$) were reduced in the obese animals given BCO compared to soy; but these parameters were unaffected by BCO gavage in lean animals. Final mean weights (g) for the groups were: soy obese 435±12, BCO obese 402±17, soy lean 328±13, BCO lean 323±15. Liver and brain tissue from subgroups of 2-8 animals were extracted for total lipid and the constituent fractions and fatty acids separated by thin layer and capillary gas chromatography. Liver PL AA was low in soy obese compared to soy lean (n=8, $p < 0.002$), and was normalized with BCO. Normal or elevated levels of other desaturase products in soy obese, however, indicates this enzyme system was unimpaired. Liver PL fractions showed phosphatidyl inositol (PI) to have 30% less AA in soy obese than soy lean (n=4 each group, $p < 0.01$). Analysis of brain PL (n=2 each group) showed no obvious difference between obese and leans fed soy. We conclude that there is a paucity of AA in the liver PL of obese Zucker rats, and that its correction by feeding low dose BCO (an AA intermediate) is associated with reduced hyperphagia and adiposity in the obese genotype. Initial studies suggest that the disturbance of AA metabolism is more marked in liver PL, especially in the PI fraction, than in the brain. These observations of altered AA distribution in animals and humans suggest parallels in a metabolic correlate of obesity across species, and clearly warrents further study.

WB 208 ASPARTAME AND AMINERGIC NEUROTRANSMISSION IN ADULT AND WEANLING RAT BRAIN, Margaret A. Reilly and Abel Lajtha, Center for Neurochemistry, N.S. Kline Institute for Psychiatric Research, Orangeburg, NY 10962

Aspartame (APM, L-aspartyl-L-phenylalanine methyl ester) has become a widely used food additive in the United States since its introduction in 1981. We have been interested in the possible effect of APM consumption on the nervous system under normal conditions. APM is rapidly metabolized in the gastrointestinal tract to methanol, aspartate, and phenylalanine (Phe), which are then absorbed into the circulatory system. Phe is the precursor of the neurotransmitters dopamine (DA) and norepinephrine (NE), and as a large neutral amino acid can affect the brain entry of other amino acids including tryptophan, the precursor of the neurotransmitter serotonin (5-hydroxytryptamine, 5-HT). Thus, ingestion of large amounts of APM might have an effect on neurotransmission in DA, NE, and 5-HT systems, which appear to modulate many aspects of physiological and behavioral activity. Our studies have focused on the effects of chronic ingestion of APM on these neurotransmitter systems in adult rat brain, and also in the weanling rat brain following maternal ingestion of APM throughout pregnancy and lactation. Adult male rats were given APM 50 or 500 mg/kg per day for 30 days in their drinking water, to simulate the ingestion of APM by humans: gradually over a period of time rather than in a large single dose. No evidence was found in these animals for any effect of APM on DA, NE, or 5-HT neurotransmission: kinetics for two receptors in each system were unaltered, as were levels of the amines in brain, and of their related amino acids in plasma and brain.

Similar studies were done in weanling rats, to determine whether the increased sensitivity of the developing brain to neurotoxins might predispose younger animals to APM-induced changes in these systems. Rats were given APM 500 mg/kg per day throughout pregnancy and lactation; weanling brain was taken for assay at 20-22 days of age. As in adults, no evidence was found for alteration in receptor kinetics or in levels of DA, NE, and 5-HT or in their related amino acids. It is concluded that exposure of either young or adult rats to APM does not affect aminergic neurotransmission in brain.