PHYSIOLOGICAL PSYCHOLOGY

B.Sc. Counselling Psychology

COMPLEMENTARY COURSE

IV Semester

UNIVERSITY OF CALICUT

SCHOOL OF DISTANCE EDUCATION
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Study Material
IV Semester

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THE ELEMENTS OF PHYSIOLOGICAL PSYCHOLOGY

MODULE 1
PHYSIOLOGICAL BASIS OF MOTIVATION

EATING

Eating is ingesting food to provide for all humans and animals nutritional needs, particularly for energy and growth. All creatures must eat in order to survive: carnivores eat other animals, herbivores eat plants, and omnivores consume a mixture of both. Eating is an activity of daily living.

Eating practices

Many homes have a kitchen room or outside (in the tropics) kitchen area devoted to preparation of meals and food, and may have a dining room, dining hall, or another designated area for eating. Some trains have a dining car. Dishware, silverware, drinkware, and cookware come in a wide array of forms and sizes. Most societies also have restaurants, food courts, and/or food vendors, so that people may eat when away from home, when lacking time to prepare food, or as a social occasion (dining club). At their highest level of sophistication, these places become "theatrical spectacles of global cosmopolitanism and myth." Occasionally, such as at picnics, potlucks, and food festivals, eating is in fact the primary purpose of the social gathering. However, this is not always true, such as in religious gatherings.

People commonly have two or three meals a day at regular times. Snacks of smaller amounts may be consumed between meals. Some propose not snacking, yet advocate three meals a day (of 600 kcal per meal) with four to six hours between. Having three well-balanced meals (thus 1/2 of the plate with vegetables, 1/4 protein food as meat, ... and 1/4 carbohydrates as pasta, rice, ...) will then account to some 1800–2000 kcal; which is the average requirement for a regular person.

The issue of healthy eating has long been an important concern to individuals and cultures. Among other practices, fasting, dieting, and vegetarianism are all techniques employed by individuals and encouraged by societies to increase longevity and health. Some religions promote vegetarianism, considering it wrong to consume animals. Leading nutritionists believe that instead of indulging oneself in three large meals each day, it is much healthier and easier on the metabolism to eat five smaller meals each day (e.g. better digestion, easier on the lower intestine to deposit wastes; whereas larger meals are tougher on the digestive tract and may call for the use of laxatives). However, psychiatrists with Yale Medical School have found that people who suffer from Binge Eating Disorder (BED) and consume three meals per day weigh less than those who have more frequent meals. Eating can also be a way of making money.
Emotional eating

Emotional eating is “the tendency to eat in response to negative emotions”. Empirical studies have indicated that anxiety leads to decreased food consumption in people with normal weight and increased food consumption in the obese.

Many laboratory studies showed that overweight individuals are more emotionally reactive and are more likely to overeat when distressed than people of normal weight. Furthermore, it was consistently found that obese individuals experience negative emotions more frequently and more intensively than do normal weight persons.

The naturalistic study of Lowe and Fisher compared the emotional reactivity and emotional eating of normal and overweight female college students. The study confirmed the tendency of obese individuals to overeat, but these findings applied only to snacks, not to meals. That means that obese individuals did not tend to eat more while having meals – rather, the amount of snacks they ate between meals was greater. One possible explanation that Lowe and Fisher suggest is that obese individuals often eat their meals with others and do not eat more than average due to the reduction of distress because of the presence of other people. Another possible explanation would be that obese individuals do not eat more than the others while having meals due to social desirability. Conversely, snacks are usually eaten alone.

Satiety and human metabolism

The control of food intake is a physiologically complex, motivated behavioral system. Hormones such as cholecystokinin, bombesin, neurotensin, anorectin, calcitonin, enterostatin, leptin and corticotropin-releasing hormone have all been shown to suppress food intake.

Disorders

Physiologically, eating is generally triggered by hunger, but there are numerous physical and psychological conditions that can affect appetite and disrupt normal eating patterns. These include depression, food allergies, ingestion of certain chemicals, bulimia, anorexia nervosa, pituitary gland misfunction and other endocrine problems, and numerous other illnesses and eating disorders.

A chronic lack of nutritious food can cause various illnesses, and will eventually lead to starvation. When this happens in a locality on a massive scale it is considered a famine.

If eating and drinking is not possible, as is often the case when recovering from surgery, alternatives are enteral nutrition and parenteral nutrition.
FEEDING CENTERS IN THE BRAIN

Feeding center is a group of cells in the lateral hypothalamus that when stimulated cause a sensation of hunger.

The lateral hypothalamus or lateral hypothalamic area is a part of the hypothalamus. It is concerned with hunger. Damage to this area can cause reduced food intake. Stimulating the lateral hypothalamus causes a desire to eat, while stimulating the ventromedial hypothalamus causes a desire to stop eating.

**Function**

The glucostatic explanation is based on the homeostatic theory which indicates that the body has balanced states of equilibrium for each system. When out of balance, the body will be pushed to restore balance. Therefore, when the blood sugar level drops, the glucostatic receptors in the blood take a message to the lateral hypothalamus, which is the feeding center of the brain. This causes certain neurons in the brain to fire in unison, creating the sensation of hunger. Now the person wants to eat.

When the glucose level increases because the person is eating or has eaten, the glucostatic receptors in the blood then send a message to the Ventro-medial Hypothalamus (the satiety or satisfaction center) and the sensation of fullness occurs.

Damage to the lateral hypothalamus may lead to a condition known as Fröhlich's syndrome.

**EATING SIGNALS - METABOLIC SIGNALS**

Eating requires at least two basic decisions: what to eat, which is a decision about food choice, and how much to eat, which is a decision about food intake. This distinction is important because food choice and intake involve different behaviors, different controlling signals and different physiological mechanisms.

Feeding behavior is controlled by a variety of signals. ‘Cephalic’ signals, such as the taste, smell, sound and sight of food, control food choice and can influence the amount of food consumed in the short-term. Gastrointestinal signals resulting from changes in distention or the release of gut peptides may play a role in the control of short-term intake within a meal or across several meals. Metabolic signals generated by the supply and utilization of metabolic fuels not only influence food choice, but also how much food is consumed in the short-term. Metabolic signals also determine food intake in the long-term and are important in maintaining energy balance over a nutritionally significant interval.

Traditionally, research emphasized separate signals associated with glucose and fat metabolism. ‘Glucostatic’ hypotheses about these signals have focused on either
changes in the circulating level of glucose or on intracellular glucose utilization, whereas ‘lipostatic’ hypotheses have targeted the amount of body fat or, more recently, the adipose hormone, leptin. A less well known line of research has looked to metabolic processes common to the metabolism of both glucose and fat for metabolic signals controlling food intake. This perspective was initially proposed by Ugolev and Kassil (1961), who investigated the tricarboxylic acid cycle as a source of a common, ‘oxidative’ metabolic signal. More recently, research in this area has focused on aspects of ATP production.

**Receptor site**

Russek (1963) first proposed the liver as a site where changes in metabolism are detected to control feeding behavior. Although his hypothesis was initially ignored for many years, it is now generally accepted that information about hepatic metabolism is communicated to the brain and contributes to the control of food intake.

Work in our laboratory on the role of the liver in feeding behavior has taken a number of different directions, although perhaps the most compelling evidence stems from comparing the effects on food intake of hepatic portal and jugular vein infusion of nutrients and metabolic inhibitors. In one series of experiments, taking a cue from Russek’s studies, we compared the effects of hepatic portal and jugular (i.e. systemic) infusions of glucose on satiety in rats. These studies showed that, under relatively normal feeding conditions, glucose infusions within the physiological range suppressed food intake more effectively when delivered into the hepatic portal vein than when given by a jugular route (see Friedman et al., 1996). In other experiments, we studied the role of the liver in hunger by comparing hepatic portal and jugular infusions of the fructose analogue, 2,5-anhydro-D-mannitol (2,5-AM), which we had shown triggered feeding in rats when given by gastric gavage or an intraperitoneal route. The results showed clearly that portal infusion of 2,5-AM elicited food intake more rapidly and at lower doses than did infusions into the jugular vein (see Tordoff et al., 1991).

**Nature of the stimulus**

Since studies in our laboratory first demonstrated an inverse relationship between hepatocyte ATP concentration and food intake, we have been focused on testing the role of changes in hepatic energy status as a stimulus for hunger and satiety. Under a variety of conditions, eating behavior triggered by injection of 2,5-AM was associated with the analogue’s effect of reducing liver ATP (e.g. Friedman et al., 2002). The decrease in ATP was due largely to trapping of phosphate in phosphorylated forms of 2,5-AM (Rawson et al., 1994). Most telling therefore was the observation that preventing the decrease in ATP by administration of exogenous phosphate also prevented the eating response (Rawson and Friedman, 1994). Subsequently, we found that eating behavior stimulated by administration of other metabolic inhibitors, including fatty acid oxidation inhibitors, was also associated with lowered hepatic ATP levels (e.g. Ji et al., 2000).
Additional experiments investigated the relationship between liver energy status and food intake under other conditions. Confirming earlier studies, we found that fasting reduced hepatic energy status and that the time course of compensatory hyperphagia during refeeding paralleled that in the restoration in liver energy status (Ji and Friedman, 1999). The dramatic increase in food intake in rats with experimental diabetes and its prevention with fat feeding were also found to be associated with, respectively, lower and normalized liver energy status (unpublished data). Most recently, we have examined the role of hepatic energy status in dietary, genetic and neurological rat models of overeating and obesity (unpublished data). In all three models, obese rats showed lowered hepatic energy status than controls, in some cases despite marked hyperphagia.

Transduction mechanism

Little is known about how changes in hepatocyte energy metabolism are transduced into a signal the nervous system can interpret. We have begun to investigate this question along two tracks. In one set of studies (Rawson et al., 2003), we studied the effects of 2,5-AM on intracellular Ca2+ concentration in hepatocytes as such changes are well known to be involved in cellular signaling in a variety of tissues. The results showed that 2,5-AM produced an increase in intracellular Ca2+ in ~50% of hepatocytes and that the rise was due to release of intracellular calcium stores. In another set of experiments (Friedman et al., 2003), we tested a hypothesis that changes in hepatocyte ATP levels generate a signal by lowering activity of the sodium pump, causing cellular depolarization (Langhans and Scharrer, 1987). Using nuclear magnetic spectroscopy, we showed that 2,5-AM increased intracellular sodium with a latency consistent with that of the eating response, a finding supporting Langhans and Scharrer’s conjecture. These intriguing results require considerable follow-up before the effects of 2,5-AM seen in vitro can be understood and directly related to the behavioral response seen in vivo.

Transmission of the signal

Theoretically, changes in hepatic energy status could be transmitted to the brain via a neural or humoral route; at present, however, there is evidence only for a neural connection, specifically via vagal afferent neurons. Evidence that vagal sensory fibers carry the metabolic signals from liver that control food intake stem from a variety of studies (see Langhans, 1998; Horn et al., 2001) showing that interruption of vagal afferent transmission can alter ad libitum food intake and prevent the eating response to metabolic inhibitors that act in liver. Other studies using the immunocytohistochemical expression of Fos as a marker for neural activity have demonstrated that metabolic inhibitors that stimulate feeding behavior activate areas in the brain known to receive and process vagal afferent input.

Electrophysiological experiments provide the most direct demonstration that metabolic perturbations trigger hepatic vagal sensory neurons. Niijima (this volume) was the first to show that infusion of glucose can decrease activity in the hepatic branch of the vagus. Subsequently, Niijima and his colleagues reported that these
fibers respond to a range of nutrients, hormones and other agents. Using techniques that allow for measurement of single unit activity in the hepatic branch of the vagus, we recently found (Horn and Friedman, 2004) afferent responses to infusion of serotonin (5-HT) and choleystokinin (CCK). By comparing the effects of hepatic portal and jugular infusions of these agents it was possible to identify ‘portal’ and ‘jugular’ responsive units. In keeping with the anatomical observation that fibers in the hepatic branch also innervate the stomach and intestine, we found that cutting the gastroduodenal sub-branch (GDB) of the hepatic vagus eliminated ~75% of the spontaneous activity in the hepatic branch as well as most of the response to 5-HT and CCK. These and other findings indicate that only a small proportion of afferents in the hepatic branch innervate the liver and that afferents of hepatic origin have a different pharmacology than those from the gastrointestinal tract.

HYPOTHALAMIC REGULATIONS

Hypothalamic Regions Important in Appetite Regulation

Arcuate Nucleus

The ARC is a key hypothalamic nucleus in the regulation of appetite. In mice, lesions of the ARC using monosodium glutamate produce obesity and hyperphagia.[12] Anatomically related to the median eminence, the ARC is not fully insulated from the circulation by the blood-brain barrier and, hence, is strategically positioned to integrate a number of peripheral signals controlling food intake. Two major neuronal populations in the ARC are prominently implicated in the regulation of feeding. One population, localized more medially in the ARC, increases food intake and coexpresses neuropeptide Y (NPY) and Agouti-related protein (AgRP). The second population of neurons, coexpressing cocaine- and amphetamine-related transcript (CART) and pro-opiomelanocortin (POMC), inhibits food intake and tends to cluster more laterally in the ARC. Neuronal projections from these two populations then communicate with other hypothalamic areas involved in appetite regulation, such as the PVN, DMN and LHA. This network of neuronal circuitry can be modulated by peripheral signals, such as leptin and insulin.

Paraventricular Nucleus

The PVN lies to either side of the roof of the third ventricle and it is thought to play a major role in the control of both appetite and endocrine function. The PVN is particularly important in the detection and integration of NPY, AgRP and melanocortin signals. Microinjection of almost all known orexigenic peptides into the PVN, including NPY and AgRP, stimulate feeding. NPY/AgRP and POMC neurons from the ARC communicate with PVN neurons containing corticotrophin-releasing hormone (CRH) and thyrotropin-releasing hormone (TRH). Both CRH and TRH have been implicated in the control of energy balance, by contributions to both food intake and energy expenditure. Therefore, in energy balance, a key role for the PVN is to convey information from the ARC to other brain areas involved in appetite regulation.
Lateral Hypothalamic Area

The LHA is another key downstream target of neuronal projections from the ARC and contains the orexigenic neuropeptides melanin-concentrating hormone (MCH) and orexins. NPY, AgRP and α-MSH immunoreactive terminals are extensive in the LHA and are in contact with MCH and orexin-expressing cells. MCH immunoreactive fibers project to the cortex and spinal cord, consistent with a potential role in appetite control and energy expenditure. Interestingly, work by another group found that a subpopulation of MCH neurons express CART and mainly project to the brainstem. By contrast, MCH fibers lacking CART have been found to project to the forebrain, suggesting MCH may modulate food intake and energy expenditure through two separate neuronal projections depending on the presence of CART. Lesioning of the LHA reduces bodyweight. The severity of the LHA syndrome and near-normal recovery of food intake and bodyweight depends on the location and size of the lesion. These observations led to the conception that the LHA was a 'feeding center' under restraint by signals from the VMN.

Dorsomedial Nucleus

Destruction of the DMN results in hyperphagia and obesity, though less dramatically than VMN lesioning. The DMN contains a high level of NPY terminals and α-MSH terminals originating in the ARC. α-MSH fibers also project from the DMN to the PVN, terminating on TRH-containing neurons. In the DMN, α-MSH fibers are in close apposition to NPY neurons. α-MSH may suppress NPY gene expression in the DMN indirectly via separate inhibitory interneurons, possibly through GABAergic pathways. It is proposed that decreased POMC input from the ARC to the DMN causes a reduction in MC4-R signaling, leading to decreased GABAergic inhibition of DMN NPY neurons and, hence, increased NPY mRNA expression. In diet-induced obesity, obese Agouti mice and MC4-R-knockout mice, NPY mRNA expression is increased in the DMN, whereas it is reduced in the ARC. This difference in NPY response is again highlighted by the finding that NPY levels in the DMN, in contrast to the ARC and PVN, are not elevated during fasting. It is thought that lack of leptin signaling on NPY neurons in the DMN may partly account for this since leptin-deficient ob/ob mice show increased NPY mRNA in the ARC but not in the DMN.

Ventromedial Nucleus

Lesions of the VMN result in rapid-onset hyperphagia and obesity, leading to the hypothesis that the VMN is a satiety center, acting as a restraint on feeding. Consistent with this, neuroimaging studies in humans have shown increased signaling in the area of the VMN following an oral glucose load. The VMN has a large population of glucoreponsive neurons that respond to blood glucose levels and numerous histamine, dopamine, serotonin and GABA neurons that respond to feeding-related stimuli. The VMN receives NPY, AgRP and POMC neuronal projections from the ARC. Brain-derived neurotrophic factor (BDNF) is highly expressed in the VMN and is important during development for neuronal survival.
It is a member of the neurotrophin family, which binds to the TrkB receptor, a human mutation of which has been described, resulting in severe obesity. Lateral ventricle administration of BDNF reduces food intake and bodyweight. Recent work implicates the role of ARC POMC neurons in activating VMN BDNF neurons to decrease food intake. The VMN has also recently been described as the site of a novel hypothalamic appetite-regulatory circuit involving triiodothyronine (T3).

**OBESITY**

**Obesity** is a *medical condition* in which excess *body fat* has accumulated to the extent that it may have an adverse effect on health, leading to reduced *life expectancy* and/or increased health problems. *Body mass index* (BMI), a measurement which compares *weight* and height, defines people as *overweight* (*pre-obese*) when their BMI is between 25 kg/m² and 30 kg/m², and obese when it is greater than 30 kg/m².

Obesity increases the likelihood of *various diseases*, particularly *heart disease*, *type 2 diabetes*, *breathing difficulties during sleep*, certain types of *cancer*, and *osteoarthritis*. Obesity is most commonly caused by a combination of excessive *dietary calories*, lack of physical activity, and *genetic susceptibility*, although a few cases are caused primarily by *genes*, *endocrine disorders*, *medications* or *psychiatric illness*. Evidence to support the view that some obese people eat little yet gain weight due to a slow metabolism is limited; on average obese people have a greater energy expenditure than their thin counterparts due to the energy required to maintain an increased body mass.

The primary treatment for obesity is *dieting* and *physical exercise*. To supplement this, or in case of failure, *anti-obesity drugs* may be taken to reduce appetite or inhibit fat absorption. In severe cases, *surgery* is performed or an intragastric balloon is placed to reduce stomach volume and/or bowel length, leading to earlier satiation and reduced ability to absorb nutrients from food.

Obesity is a leading *preventable cause of death* worldwide, with increasing *prevalence* in adults and *children*, and authorities view it as one of the most serious *public health* problems of the 21st century. Obesity is *stigmatized* in the modern *Western world*, though it has been perceived as a symbol of wealth and fertility at other times in history, and still is in many parts of Africa.

**Classification**

Obesity is a *medical condition* in which excess *body fat* has accumulated to the extent that it may have an adverse effect on health. It is defined by *body mass index* (BMI) and further evaluated in terms of fat distribution via the *waist-hip ratio* and total cardiovascular risk factors. BMI is closely related to both *percentage body fat* and total body fat.
Some modifications to the WHO definitions have been made by particular bodies. The surgical literature breaks down "class III" obesity into further categories whose exact values are still disputed.

- Any BMI ≥ 35 or 40 is severe obesity
- A BMI of ≥ 35 or 40–44.9 or 49.9 is morbid obesity
- A BMI of ≥ 45 or 50 is super obese

As Asian populations develop negative health consequences at a lower BMI than Caucasians, some nations have redefined obesity; the Japanese have defined obesity as any BMI greater than 25 while China uses a BMI of greater than 28.

Effects on health

Excessive body weight is associated with various diseases, particularly cardiovascular diseases, diabetes mellitus type 2, obstructive sleep apnea, certain types of cancer, and osteoarthritis. As a result, obesity has been found to reduce life expectancy.

Mortality

Obesity is one of the leading preventable causes of death worldwide. Large-scale American and European studies have found that mortality risk is lowest at a BMI of 22.5–25 kg/m² in non-smokers and at 24–27 kg/m² in current smokers, with risk increasing along with changes in either direction. A BMI above 32 has been associated with a doubled mortality rate among women over a 16-year period. In the United States obesity is estimated to cause an excess 111,909 to 365,000 death per year, while 1 million (7.7%) of deaths in the European Union are attributed to excess weight. On average, obesity reduces life expectancy by six to seven years: a BMI of 30–35 reduces life expectancy by two to four years, while severe obesity (BMI > 40) reduces life expectancy by 10 years.

Morbidity

Obesity increases the risk of many physical and mental conditions. These comorbidities are most commonly shown in metabolic syndrome, a combination of medical disorders which includes: diabetes mellitus type 2, high blood pressure, high blood cholesterol, and high triglyceride levels.

Complications are either directly caused by obesity or indirectly related through mechanisms sharing a common cause such as a poor diet or a sedentary lifestyle. The strength of the link between obesity and specific conditions varies. One of the strongest is the link with type 2 diabetes. Excess body fat underlies 64% of cases of diabetes in men and 77% of cases in women.

Health consequences fall into two broad categories: those attributable to the effects of increased fat mass (such as osteoarthritis, obstructive sleep apnea, social
stigmatization) and those due to the increased number of fat cells (diabetes, cancer, cardiovascular disease, non-alcoholic fatty liver disease). Increases in body fat alter the body's response to insulin, potentially leading to insulin resistance. Increased fat also creates a proinflammatory state, and a prothrombotic state.

**Obesity survival paradox**

Although the negative health consequences of obesity in the general population are well supported by the available evidence, health outcomes in certain subgroups seem to be improved at an increased BMI, a phenomenon known as the obesity survival paradox. The paradox was first described in 1999 in overweight and obese people undergoing hemodialysis, and has subsequently been found in those with heart failure and peripheral artery disease (PAD).

In people with heart failure, those with a BMI between 30.0–34.9 had lower mortality than those with a normal weight. This has been attributed to the fact that people often lose weight as they become progressively more ill. Similar findings have been made in other types of heart disease. People with class I obesity and heart disease do not have greater rates of further heart problems than people of normal weight who also have heart disease. In people with greater degrees of obesity, however, risk of further events is increased. Even after cardiac bypass surgery, no increase in mortality is seen in the overweight and obese. One study found that the improved survival could be explained by the more aggressive treatment obese people receive after a cardiac event. Another found that if one takes into account chronic obstructive pulmonary disease (COPD) in those with PAD the benefit of obesity no longer exists.

**Causes**

At an individual level, a combination of excessive caloric intake and a lack of physical activity is thought to explain most cases of obesity. A limited number of cases are due primarily to genetics, medical reasons, or psychiatric illness. In contrast, increasing rates of obesity at a societal level are felt to be due to an easily accessible and palatable diet, increased reliance on cars, and mechanized manufacturing.

A 2006 review identified ten other possible contributors to the recent increase of obesity: (1) insufficient sleep, (2) endocrine disruptors (environmental pollutants that interfere with lipid metabolism), (3) decreased variability in ambient temperature, (4) decreased rates of smoking, because smoking suppresses appetite, (5) increased use of medications that can cause weight gain (e.g., atypical antipsychotics), (6) proportional increases in ethnic and age groups that tend to be heavier, (7) pregnancy at a later age (which may cause susceptibility to obesity in children), (8) epigenetic risk factors passed on generationally, (9) natural selection for higher BMI, and (10) assortative mating leading to increased concentration of obesity risk factors (this would not necessarily increase the number of obese people, but would increase the average population weight). While there is substantial evidence supporting the
influence of these mechanisms on the increased prevalence of obesity, the evidence is still inconclusive, and the authors state that these are probably less influential than the ones discussed in the previous paragraph.

Diet

The per capita dietary energy supply varies markedly between different regions and countries. It has also changed significantly over time. From the early 1970s to the late 1990s the average calories available per person per day (the amount of food bought) has increased in all parts of the world except Eastern Europe. The United States had the highest availability with 3,654 calories per person in 1996. This increased further in 2003 to 3,754. During the late 1990s Europeans had 3,394 calories per person, in the developing areas of Asia there were 2,648 calories per person, and in sub-Saharan Africa people had 2,176 calories per person. Total calorie consumption has been found to be related to obesity.

The widespread availability of nutritional guidelines has done little to address the problems of overeating and poor dietary choice. From 1971 to 2000, obesity rates in the United States increased from 14.5% to 30.9%. During the same period, an increase occurred in the average amount of calories consumed. For women, the average increase was 335 calories per day (1,542 calories in 1971 and 1,877 calories in 2004), while for men the average increase was 168 calories per day (2,450 calories in 1971 and 2,618 calories in 2004). Most of these extra calories came from an increase in carbohydrate consumption rather than fat consumption. The primary source of these extra carbohydrates are sweetened beverages, which now account for almost 25 percent of daily calories in young adults in America. Consumption of sweetened drinks is believed to be contributing to the rising rates of obesity.

As societies become increasingly reliant on energy-dense, big-portion, fast-food meals, the association between fast-food consumption and obesity becomes more concerning. In the United States consumption of fast-food meals tripled and calorie intake from these meals quadrupled between 1977 and 1995.

Agricultural policy and techniques in the United States and Europe have led to lower food prices. In the United States, subsidization of corn, soy, wheat, and rice through the U.S. farm bill has made the main sources of processed food cheap compared to fruits and vegetables.

Obese people consistently under-report their food consumption as compared to people of normal weight. This is supported both by test of people carried out in a calorimeter rooms and by direct observation.

Sedentary lifestyle

A sedentary lifestyle plays a significant role in obesity. Worldwide there has been a large shift towards less physically demanding work, and currently at least 60% of the world’s population gets insufficient exercise. This is primarily due to increasing use
of mechanized transportation and a greater prevalence of labor-saving technology in the home. In children there appears to be declines in levels of physical activity due to less walking and physical education. World trends in active leisure time physical activity are less clear. The World Health Organization indicates that people worldwide are taking up less active recreational pursuits, while a study from Finland found an increase and a study from the United States found leisure-time physical activity has not changed significantly.

In both children and adults there is an association between television viewing time and the risk of obesity. A 2008 meta-analysis found that 63 of 73 studies (86%) showed an increased rate of childhood obesity with increased media exposure, with rates increasing proportionally to time spent watching television.

Genetics

Like many other medical conditions, obesity is the result of an interplay between genetic and environmental factors. Polymorphisms in various genes controlling appetite and metabolism predispose to obesity when sufficient calories are present. As of 2006 more than 41 of these sites have been linked to the development of obesity when a favorable environment is present. The percentage of obesity that can be attributed to genetics varies, depending on the population examined, from 6% to 85%.

Obesity is a major feature in several syndromes, such as Prader-Willi syndrome, Bardet-Biedl syndrome, Cohen syndrome, and MOMO syndrome. (The term "non-syndromic obesity" is sometimes used to exclude these conditions.) In people with early-onset severe obesity (defined by an onset before 10 years of age and body mass index over three standard deviations above normal), 7% harbor a single point DNA mutation.

Studies that have focused upon inheritance patterns rather than upon specific genes have found that 80% of the offspring of two obese parents were obese, in contrast to less than 10% of the offspring of two parents who were of normal weight.

The thrifty gene hypothesis postulates that certain ethnic groups may be more prone to obesity in an equivalent environment. Their ability to take advantage of rare periods of abundance by storing energy as fat would be advantageous during times of varying food availability, and individuals with greater adipose reserves would be more likely to survive famine. This tendency to store fat, however, would be maladaptive in societies with stable food supplies. This is the presumed reason that Pima Indians, who evolved in a desert ecosystem, developed some of the highest rates of obesity when exposed to a Western lifestyle.

Medical and psychiatric illness

Certain physical and mental illnesses and the pharmaceutical substances used to treat them can increase risk of obesity. Medical illnesses that increase obesity risk
include several rare genetic syndromes (listed above) as well as some congenital or acquired conditions: hypothyroidism, Cushing's syndrome, growth hormone deficiency, and the eating disorders: binge eating disorder and night eating syndrome. However, obesity is not regarded as a psychiatric disorder, and therefore is not listed in the DSM-IVR as a psychiatric illness. The risk of overweight and obesity is higher in patients with psychiatric disorders than in persons without psychiatric disorders.

Certain medications may cause weight gain or changes in body composition; these include insulin, sulfonylureas, thiazolidinediones, atypical antipsychotics, antidepressants, steroids, certain anticonvulsants (phenytoin and valproate), pizotifen, and some forms of hormonal contraception.

Social determinants

While genetic influences are important to understanding obesity, they cannot explain the current dramatic increase seen within specific countries or globally. Though it is accepted that calorie consumption in excess of calorie expenditure leads to obesity on an individual basis, the cause of the shifts in these two factors on the societal scale is much debated. There are a number of theories as to the cause but most believe it is a combination of various factors.

The correlation between social class and BMI varies globally. A review in 1989 found that in developed countries women of a high social class were less likely to be obese. No significant differences were seen among men of different social classes. In the developing world, women, men, and children from high social classes had greater rates of obesity. An update of this review carried out in 2007 found the same relationships, but they were weaker. The decrease in strength of correlation was felt to be due to the effects of globalization. Among developed countries, levels of adult obesity, and percentage of teenage children who are overweight, are correlated with income inequality. A similar relationship is seen between US states: more adults, even in higher social classes, are obese in more unequal states.

Many explanations have been put forth for associations between BMI and social class. It is thought that in developed countries, the wealthy are able to afford more nutritious food, they are under greater social pressure to remain slim, and have more opportunities along with greater expectations for physical fitness. In undeveloped countries the ability to afford food, high energy expenditure with physical labor, and cultural values favoring a larger body size are believed to contribute to the observed patterns. Attitudes toward body mass held by people in one's life may also play a role in obesity. A correlation in BMI changes over time has been found between friends, siblings, and spouses. Stress and perceived low social status appear to increase risk of obesity.

Smoking has a significant effect on an individual's weight. Those who quit smoking gain an average of 4.4 kilograms (9.7 lb) for men and 5.0 kilograms (11.0 lb) for
women over ten years. However, changing rates of smoking have had little effect on the overall rates of obesity.

In the United States the number of children a person has is related to their risk of obesity. A woman's risk increases by 7% per child, while a man's risk increases by 4% per child. This could be partly explained by the fact that having dependent children decreases physical activity in Western parents.

In the developing world urbanization is playing a role in increasing rate of obesity. In China overall rates of obesity are below 5%; however, in some cities rates of obesity are greater than 20%.

Malnutrition in early life is believed to play a role in the rising rates of obesity in the developing world. Endocrine changes that occur during periods of malnutrition may promote the storage of fat once more calories become available.

Infectious agents

The study of the effect of infectious agents on metabolism is still in its early stages. Gut flora has been shown to differ between lean and obese humans. There is an indication that gut flora in obese and lean individuals can affect the metabolic potential. This apparent alteration of the metabolic potential is believed to confer a greater capacity to harvest energy contributing to obesity. Whether these differences are the direct cause or the result of obesity has yet to be determined unequivocally.

An association between viruses and obesity has been found in humans and several different animal species. The amount that these associations may have contributed to the rising rate of obesity is yet to be determined.

Pathophysiology

Flier summarizes the many possible pathophysiological mechanisms involved in the development and maintenance of obesity. This field of research had been almost unapproached until leptin was discovered in 1994. Since this discovery, many other hormonal mechanisms have been elucidated that participate in the regulation of appetite and food intake, storage patterns of adipose tissue, and development of insulin resistance. Since leptin's discovery, ghrelin, insulin, orexin, PYY 3-36, cholecystokinin, adiponectin, as well as many other mediators have been studied. The adipokines are mediators produced by adipose tissue; their action is thought to modify many obesity-related diseases.

Leptin and ghrelin are considered to be complementary in their influence on appetite, with ghrelin produced by the stomach modulating short-term appetitive control (i.e. to eat when the stomach is empty and to stop when the stomach is stretched). Leptin is produced by adipose tissue to signal fat storage reserves in the body, and mediates long-term appetitive controls (i.e. to eat more when fat storages are low and less when fat storages are high). Although administration of leptin may
be effective in a small subset of obese individuals who are leptin deficient, most obese individuals are thought to be leptin resistant and have been found to have high levels of leptin. This resistance is thought to explain in part why administration of leptin has not been shown to be effective in suppressing appetite in most obese people.

While leptin and ghrelin are produced peripherally, they control appetite through their actions on the central nervous system. In particular, they and other appetite-related hormones act on the hypothalamus, a region of the brain central to the regulation of food intake and energy expenditure. There are several circuits within the hypothalamus that contribute to its role in integrating appetite, the melanocortin pathway being the most well understood. The circuit begins with an area of the hypothalamus, the arcuate nucleus, that has outputs to the lateral hypothalamus (LH) and ventromedial hypothalamus (VMH), the brain's feeding and satiety centers, respectively.

The arcuate nucleus contains two distinct groups of neurons. The first group coexpresses neuropeptide Y (NPY) and agouti-related peptide (AgRP) and has stimulatory inputs to the LH and inhibitory inputs to the VMH. The second group coexpresses pro-opiomelanocortin (POMC) and cocaine- and amphetamine-regulated transcript (CART) and has stimulatory inputs to the VMH and inhibitory inputs to the LH. Consequently, NPY/AgRP neurons stimulate feeding and inhibit satiety, while POMC/CART neurons stimulate satiety and inhibit feeding. Both groups of arcuate nucleus neurons are regulated in part by leptin. Leptin inhibits the NPY/AgRP group while stimulating the POMC/CART group. Thus a deficiency in leptin signaling, either via leptin deficiency or leptin resistance, leads to overfeeding and may account for some genetic and acquired forms of obesity.

Management

The main treatment for obesity consists of dieting and physical exercise. Diet programs may produce weight loss over the short term, but keeping this weight off can be a problem and often requires making exercise and a lower calorie diet a permanent part of a person's lifestyle. Success rates of long-term weight loss maintenance are low and range from 2–20%. In a more structured setting, however, 67% of people who lost greater than 10% of their body mass maintained or continued to lose weight one year later. An average maintained weight loss of more than 3 kg (6.6 lb) or 3% of total body mass could be sustained for five years. Some studies have found significant benefits in mortality in certain populations with weight loss. In a prospective study of obese women with weight related diseases, intentional weight loss of any amount was associated with a 20% reduction in mortality. In obese women without obesity related illnesses a weight loss of greater than 9 kg (20 lb) was associated with a 25% reduction in mortality. A recent review concluded that certain subgroups such as those with type 2 diabetes and women show long term benefits in all cause mortality, while outcomes for men do not seem to be improved with weight loss. A subsequent study has found benefits in mortality from intentional weight loss in those who have severe obesity.
The most effective treatment for obesity is bariatric surgery; however, due to its cost and the risk of complications, researchers are searching for other effective yet less invasive treatments.

**Dieting**

Diets to promote weight loss are generally divided into four categories: low-fat, low-carbohydrate, low-calorie, and very low calorie. A meta-analysis of six randomized controlled trials found no difference between three of the main diet types (low calorie, low carbohydrate, and low fat), with a 2–4 kilogram (4.4–8.8 lb) weight loss in all studies. At two years these three methods resulted in similar weight loss irrespective of the macronutrients emphasized.

Very low calorie diets provide 200–800 kcal/day, maintaining protein intake but limiting calories from both fat and carbohydrates. They subject the body to starvation and produce an average weekly weight loss of 1.5–2.5 kilograms (3.3–5.5 lb). These diets are not recommended for general use as they are associated with adverse side effects such as loss of lean muscle mass, increased risks of gout, and electrolyte imbalances. People attempting these diets must be monitored closely by a physician to prevent complications.

**Exercise**

With use, muscles consume energy derived from both fat and glycogen. Due to the large size of leg muscles, walking, running, and cycling are the most effective means of exercise to reduce body fat. Exercise affects macronutrient balance. During moderate exercise, equivalent to a brisk walk, there is a shift to greater use of fat as a fuel. To maintain health the American Heart Association recommends a minimum of 30 minutes of moderate exercise at least 5 days a week.

A meta-analysis of 43 randomized controlled trials by the Cochrane Collaboration found that exercising alone led to limited weight loss. In combination with diet, however, it resulted in a 1 kilogram weight loss over dieting alone. A 1.5 kilogram (3.3 lb) loss was observed with a greater degree of exercise. Even though exercise as carried out in the general population has only modest effects, a dose response curve is found, and very intense exercise can lead to substantial weight loss. During 20 weeks of basic military training with no dietary restriction, obese military recruits lost 12.5 kg (27.6 lb). High levels of physical activity seem to be necessary to maintain weight loss. A pedometer appears useful for motivation. Over an average of 18-weeks of use physical activity increased by 27% resulting in a 0.38 decreased in BMI.

Signs that encourage the use of stairs as well as community campaigns have been shown to be effective in increasing exercise in a population. The city of Bogota, Colombia for example blocks off 113 kilometers (70 miles) of roads every Sunday and on holidays to make it easier for its citizens to get exercise. These pedestrian zones are part of an effort to combat chronic diseases, including obesity.
**Weight loss programs**

Weight loss programs often promote lifestyle changes and diet modification. This may involve eating smaller meals, cutting down on certain types of food, and making a conscious effort to exercise more. These programs also enable people to connect with a group of others who are attempting to lose weight, in the hopes that participants will form mutually motivating and encouraging relationships.

A number of popular programs exist, including Weight Watchers, Overeaters Anonymous, and Jenny Craig. These appear to provide modest weight loss (2.9 kg, 6.4 lb) over dieting on one's own (0.2 kg, 0.4 lb) over a two year period. Internet-based programs appear to be ineffective. The Chinese government has introduced a number of "fat farms" where obese children go for reinforced exercise, and has passed a law which requires students to exercise or play sports for an hour a day at school.

**Medication**

The two most commonly used medications to treat obesity: orlistat (Xenical) and sibutramine (Meridia)

Only two anti-obesity medications are currently approved by the FDA for long term use. One is orlistat (Xenical), which reduces intestinal fat absorption by inhibiting pancreatic lipase; the other is sibutramine (Meridia), which acts in the brain to inhibit deactivation of the neurotransmitters norepinephrine, serotonin, and dopamine (very similar to some anti-depressants), therefore decreasing appetite. Rimonabant (Acomplia), a third drug, works via a specific blockade of the endocannabinoid system. It has been developed from the knowledge that cannabis smokers often experience hunger, which is often referred to as "the munchies". It had been approved in Europe for the treatment of obesity but has not received approval in the United States or Canada due to safety concerns. European Medicines Agency in October 2008 recommended the suspension of the sale of rimonabant as the risk seem to be greater than the benefits.

Weight loss with these drugs is modest. Over the longer term, average weight loss on orlistat is 2.9 kg (6.4 lb), sibutramine is 4.2 kg (9.3 lb) and rimonabant is 4.7 kg (10.4 lb). Orlistat and rimonabant lead to a reduced incidence of diabetes, and all three drugs have some effect on cholesterol. However, there is little information on how these drugs affect the longer-term complications or outcomes of obesity. In 2010 the FDA noted concerns that sibutramine increases the risk of heart attacks and strokes in patients with a history of cardiovascular disease.

There are a number of less commonly used medications. Some are only approved for short term use, others are used off-label, and still others are used illegally. Most are appetite suppressants that act on one or more neurotransmitters. Phendimetrazine (Bontril), diethylpropion (Tenuate), and phentermine (Adipex-P) are approved by
the FDA for short term use, while bupropion (Wellbutrin), topiramate (Topamax), and zonisamide (Zonegran) are sometimes used off-label.

The usefulness of certain drugs depends upon the comorbidities present. Metformin (Glucophage) is preferred in overweight diabetics, as it may lead to mild weight loss in comparison to sulfonylureas or insulin. The thiazolidinediones, on the other hand, may cause weight gain, but decrease central obesity. Diabetics also achieve modest weight loss with fluoxetine (Prozac), orlistat and sibutramine over 12-57 weeks. Preliminary evidence has however found higher number of cardiovascular events in people taking sibutramine verses control (11.4% vs. 10.0%). The long-term health benefits of these treatments remain unclear.

Fenfluramine and dexfenfluramine were withdrawn from the market in 1997, while ephedrine (found in the traditional Chinese herbal medicine má huáng made from the Ephedra sinica) was removed from the market in 2004. Dexamphetamines are not approved by the FDA for the treatment of obesity due to concerns regarding addiction. The use of these drugs is not recommended due to potential side effects. However, people do occasionally use these drugs illegally.

**Surgery**

Bariatric surgery ("weight loss surgery") is the use of surgical intervention in the treatment of obesity. As every operation may have complications, surgery is only recommended for severely obese people (BMI > 40) who have failed to lose weight following dietary modification and pharmacological treatment. Weight loss surgery relies on various principles: the two most common approaches are reducing the volume of the stomach (e.g. by adjustable gastric banding and vertical banded gastroplasty), which produces an earlier sense of satiation, and reducing the length of bowel that comes into contact with food (gastric bypass surgery), which directly reduces absorption. Band surgery is reversible, while bowel shortening operations are not. Some procedures can be performed laparoscopically. Complications from weight loss surgery are frequent.

Surgery for severe obesity is associated with long-term weight loss and decreased overall mortality. One study found a weight loss of between 14% and 25% (depending on the type of procedure performed) at 10 years, and a 29% reduction in all cause mortality when compared to standard weight loss measures. A marked decrease in the risk of diabetes mellitus, cardiovascular disease and cancer has also been found after bariatric surgery. Marked weight loss occurs during the first few months after surgery, and the loss is sustained in the long term. In one study there was an unexplained increase in deaths from accidents and suicide, but this did not outweigh the benefit in terms of disease prevention. When the two main techniques are compared, gastric bypass procedures are found to lead to 30% more weight loss than banding procedures one year after surgery.

The effects of liposuction on obesity are less well determined. Some small studies show benefits while others show none. A treatment involving the placement of an
intragastric balloon via gastroscopy has shown promise. One type of balloon lead to a weight loss of 5.7 BMI units over 6 months or 14.7 kg (32.4 lb). Regaining lost weight is common after removal, however, and 4.2% of people were intolerant of the device.

BASES OF SPECIFIC HUNGER

A type of hunger that is satisfied by specific dietary requirements, such as vitamins and minerals. Many animals vary their food intake according to the nutritive value of the products of digestion. A variety of mechanisms are involved in this type of regulation. The simplest mechanism is the direct detection of the substance in the food, as is the case with sodium. Animals can detect sodium in the diet in two main ways. First, sodium salt (NaCl) is a primary aspect of taste in most vertebrates. Secondly, sodium has profound effects upon the body fluids, and its presence there can be directly detected. Sodium appetite appears to be innate, but many animals are adept at learning and remembering the location of sources of sodium.

There are many vitamins and minerals that animals are not able to detect, either by taste or by their levels in the blood. Nevertheless, deficient animals develop strong preferences for foods containing the missing substances. Rats (Rattus norvegicus) deficient in thiamine show an immediate marked preference for a novel food, even when that food is thiamine deficient. The preference is short lived. If consumption of a novel food is followed by recovery from the dietary deficiency, however, then the rat rapidly learns to prefer the novel food. Such rapid learning on the basis of the physiological consequences of ingestion enables the rat to exploit new sources of food, and to find out which contains the required ingredients.

The effects of a vitamin-deficient diet have much in common with poison avoidance. Vitamin-deficient rats are reluctant to eat familiar food, and show a more than normal interest in novel foods. The aversion to previously familiar food persists even after the animals have recovered from the deficiency. Rats that become sick after eating poisoned food also show an aversion to familiar food and an interest in novel foods.

THIRST

Thirst is the craving for fluids, resulting in the basic instinct of animals to drink. It is an essential mechanism involved in fluid balance. It arises from a lack of fluids and/or an increase in the concentration of certain osmolites, such as salt. If the water volume of the body falls below a certain threshold or the osmolite concentration becomes too high, the brain signals thirst.

Continuous dehydration can cause many problems, but is most often associated with neurological problems such as seizures and renal problems.

Excessive thirst, known as polydipsia, along with excessive urination, known as polyuria, may be an indication of diabetes.
There are receptors and other systems in the body that detect a decreased volume or an increased osmolite concentration. They signal to the central nervous system, where central processing succeeds. Some sources therefore distinguish "extracellular thirst" from "intracellular thirst", where extracellular thirst is thirst generated by decreased volume and intracellular thirst is thirst generated by increased osmolite concentration. Nevertheless, the craving itself is something generated from central processing in the brain, no matter how it is detected.

Detection

There are many different receptors for sensing decreased volume or an increased osmolite concentration.

Decreased volume

- **Renin-angiotensin system**

Hypovolemia leads to activation of the renin angiotensin system (RAS) and a decrease in atrial natriuretic peptide. These mechanisms, along their other functions, contribute to elicit thirst, by affecting the subfornical organ. For instance, angiotensin II, activated in RAS, is a powerful dipsogen (ie it stimulates thirst) which acts via the subfornical organ.

- **Other**
  
  - Arterial baroreceptors sense a decreased arterial pressure, and signals to the central nervous system in the area postrema and nucleus tractus solitarius.
  
  - Cardiopulmonary receptors sense a decreased blood volume, and signal to area postrema\(^2\) and nucleus tractus solitarius\(^2\) as well.

Increased osmolite concentration

An increase in osmotic pressure, e.g. after eating a salty meal activates osmoreceptors. There are osmoreceptors already in the central nervous system, more specifically in the hypothalamus, notably in two circumventricular organs that lack an effective blood-brain barrier, the organum vasculosum of the lamina terminalis\(\text{organum vasculosum of the lamina terminalis (OVLT)}\) and the subfornical organ (SFO). However, although located in the same parts of the brain, these osmoreceptors that evoke thirst are distinct from the neighbouring osmoreceptors in the OVLT and SFO that evoke arginine vasopressin release to decrease fluid output.

In addition, there are visceral osmoreceptors. These project to the area postrema and
Salt craving

Because sodium is also lost from the plasma in hypovolemia, the body’s need for salt proportionately increases in addition to thirst in such cases. This is also a result of the renin-angiotensin system activation.

Elderly

For adults over age 50, the body’s thirst sensation diminishes and continues diminishing with age, causing many to suffer symptoms of dehydration.

Central processing

The area postrema and nucleus tractus solitarius signal, by 5-HT, to lateral parabrachial nucleus, which in turn signal to median preoptic nucleus. In addition, the area postrema and nucleus tractus solitarius also signal directly to subfornical organ.

Thus, the median preoptic nucleus and subfornical organ receive signals of both decreased volume and increased osmolite concentration. They signal to higher integrative centers, where ultimately the conscious craving arises. However, the true neuroscience of this conscious craving is not fully clear.

OSMOTIC AND HYPOVOLEMIC THIRST

There are mainly 2 kinds of thirsts reported, Osmotic thirst and Hypovolemic thirst

Osmotic thirst

It’s the thirst resulting from eating salty foods. Eating salty food causes sodium ions to spread through the blood and extracellular fluid of the cell. The higher concentration of solutes outside the cell results in osmotic pressure, drawing water from the cell to the extracellular fluid. Certain neurons detect the loss of water and trigger osmotic thirst to help restore the body to the normal state.

The brain detects osmotic pressure from:

- Receptors around the third ventricle.
- The OVLT (organum vasculosum laminae terminalis) and the subfornical organ (detect osmotic pressure and salt content).
- Receptors in the periphery, including the stomach, which detect high levels of sodium.
- Receptors in the OVLT, subfornical organ, stomach and elsewhere relay information to areas of the hypothalamus including:
the supraoptic nucleus and paraventricular nucleus.

Both control the rate at which the posterior pituitary releases vasopressin. Receptors also relay information to the lateral preoptic area which controls drinking.

When osmotic thirst is triggered, water that you drink has to be absorbed through the digestive system. To inhibit thirst, the body monitors swallowing and detects the water contents of the stomach and intestines.

**Hypovolemic thirst**

It’s the thirst resulting from loss of fluids due to bleeding or sweating. Thirst is thirst associated with low volume of body fluids. Triggered by the release of the hormones vasopressin and angiotensin II, which constrict blood vessels to compensate for a drop in blood pressure. Angiotensin II stimulates neurons in areas adjoining the third ventricle. Neurons in the third ventricle send axons to the hypothalamus where angiotensin II is also released as a neurotransmitter.

Animals with osmotic thirst have a preference for pure water. Animals with hypovolemic thirst have a preference for slightly salty water as pure water dilutes body fluids and changes osmotic pressure.

**REGULATING DRINKING BEHAVIOUR**

Thirst is a conscious sensation that results in a desire to drink. Although all normal humans experience thirst, science can offer no precise definition of this phenomenon because it involves numerous physiological responses to a change in internal fluid status, complex patterns of central nervous system function, and psychological motivation. Three factors are typically recognized as components of thirst: a body water deficit, brain integration of central and peripheral nerve messages relating to the need for water, and an urge to drink. In laboratory experiments, thirst is measured empirically with subjective perceptual scales (for example, ranging from "not thirsty at all" to "very, very thirsty") and drinking behavior is quantified by observing the timing and volume of fluid consumed.

Psychologists classify thirst as a drive, a basic compelling urge that motivates action. Other human drives involve a lack of nutrients (for example, glucose, sodium), oxygen, or sleep; these are satiated by eating, breathing, and sleeping. Clark Hull published a major, relevant theory describing the nature of human drives in 1943. He observed that learned habits, in addition to the thirst drive, influence drinking strongly. If a behavior reduces thirst, that behavior is reinforced and learned as a habit. Irrelevant behaviors (for example, sneezing, grooming) provide no reinforcement, have no effect on drinking, and do not become habits. Further, Hull realized that external incentives, such as the qualities or quantity of a fluid, also influence fluid consumption. On a hot summer day, for example, a cold beverage is more attractive than a cup of hot tea. Yet when chilled to a very low temperature, a cold beverage becomes an aversive stimulus to drinking behavior. Physiologists
have popularized the term alliesthesia (from Greek root words referring to altered sensation) to describe the fact that the sensation of thirst may have either pleasant or unpleasant qualities, depending on the intensity of the stimulus and the state of the person.

Numerous investigations have verified that thirst and drinking behavior are complex entities. For example, drinking behavior (that is, the timing and the amount of fluid consumed) is not linearly related to the intensity of perceived thirst. Nor should we infer that individuals experience thirst simply because they drink. These facts indicate that thirst and drinking behavior are distinct entities that influence each other and are influenced by numerous internal and external factors.

**Physiological Components of Thirst**

Thirst is often viewed by physiologists and physicians as a central nervous system mechanism that regulates the body’s water and minerals. The significance of the thirst drive is emphasized by three facts: 50 to 70 percent of adult body weight is water, the average adult ingests and loses 2.5 liters of water each day, and body weight is regulated within 0.2 percent from one day to the next. Clearly, water is essential to life and the body responds in a manner that ensures survival.

In 1954, Edward Adolph and colleagues proposed a multiple-factor theory of thirst that has not been refuted to date. This theory states that no single mechanism can account for all drinking behavior and that multiple mechanisms, sometimes with identical functions, act concurrently. Because water is essential to life, the existence of redundant mechanisms has great survival value. Among these, thirst appears to be regulated primarily by evaluation of changes in the concentration of extracellular fluid, measured as the osmolality of blood plasma. (Osmolality is a measurement that describes the concentration of all dissolved solids in a solution, that is, dissolved substances per unit of solvent. In research and clinical laboratories, the unit for osmolality of blood is mOsm/kg or milliosmoles per kilogram of water.)

Below a certain threshold level of plasma osmolality, thirst is absent. Above this threshold, a strong desire to drink appears in response to an increase of 2 to 3 percent in the level of dissolved substances in blood. The brain's thirst center lies deep within the brain, in an area known as the hypothalamus. This anatomical site contains cells that respond to changes in the concentration of body fluids. When the thirst center is stimulated by an increased concentration of blood (that is, dehydration), thirst and fluid consumption increase.

As the brain senses the concentration of blood, it allows a minor loss of body water before stimulating the drive to drink. This phenomenon has been named voluntary dehydration. Specifically, several research studies since the 1930s have observed that adults and children replace only 34 to 87 percent of the water lost as sweat, by drinking during exercise or labor in hot environments. The resulting dehydration is due to the fact that thirst is not perceived until a 1 to 2 percent body weight loss occurs. Interindividual differences, resulting in great voluntary dehydration in some individuals, have caused them to be named reluctant drinkers.
Reduced extracellular fluid volume, including blood volume, also increases thirst. Experiments (for example, reducing blood volume without altering blood concentration) have demonstrated that volume-sensitive receptors in the heart and blood vessels likely regulate drinking behavior by increasing the secretion of hormones. This effect is relatively minor, however. Animal research suggests that a change in extracellular fluid concentration accounts for most (for example, 70 percent) of the increased fluid consumption that follows moderate whole-body dehydration, whereas a decrease of fluid volume per se plays a secondary role.

Thus, thirst is extinguished when body fluid concentration decreases and fluid volume increases. Osmolality-sensitive nerves in the mouth, throat, and stomach also play a role in abating thirst. As fluid passes through the mouth and upper gastrointestinal tract, the sense of dryness decreases. When this fluid fills the stomach, stretch receptors sense an increase in gastric fullness and the thirst drive diminishes.

As dehydration causes the body's extracellular fluid to become more concentrated, the fluid inside cells moves outward, resulting in intracellular dehydration and cell shrinkage, and the hormone arginine vasopressin (AVP, also known as the antidiuretic hormone) is released from the brain. AVP serves two purposes: to reduce urine output at the kidneys and to enhance thirst; both serve to restore normal fluid balance. Other hormones influence fluid-mineral balance directly and thirst indirectly. Renin, angiotensin II, and aldosterone are noteworthy examples. As dehydration reduces circulating blood volume, blood pressure decreases and renin is secreted from blood vessels inside the kidneys. Renin activates the hormone angiotensin II, which subsequently stimulates the release of aldosterone from the adrenal glands. Both angiotensin II and aldosterone increase blood pressure and enhance the retention of sodium and water; these effects indirectly reduce the intensity of thirst. Angiotensin II also affects thirst directly. When injected into sensitive areas of the brain, it causes a rapid increase in water consumption that is followed by a slower increase in sodium chloride consumption and water retention by the kidneys.

**Host Factors**

Repeated training sessions in cool or hot environments alter fluid consumption in four ways. First, physical training increases the secretion of the hormone AVP, which stimulates drinking and body water retention. Second, exercise-heat acclimation (that is, adaptations due to exercise in a hot environment over eight days) increases the volume of fluid consumed and the number of times that adults drink during exercise. Third, frequent rest periods, in the midst of labor or exercise, will increase fluid replacement time and enhance fluid consumption. Humans tend to drink less when they are preoccupied or are performing physical or mental tasks. Fourth, learned behaviors can enhance fluid consumption when thirst is absent. This phenomenon is widely appreciated among military personnel and athletes who are trained to consume water at regular intervals, whether they are thirsty or not.
Several research groups have reported that chronological age influences thirst and drinking behavior. Elderly men experience a blunted thirst drive and reduced fluid intake, perhaps due to their brains' reduced ability to sense changes in plasma osmolality or blood volume. Further, elderly individuals experience a decrease in the ability of their kidneys to conserve water. This suggests that the elderly are predisposed to dehydration when illness increases water loss (that is, vomiting, diarrhea) or when physical incapacity prevents access to water.

**Fluid and Environmental Characteristics**

Many fluid characteristics stimulate or enhance drinking, during or after exposure to a hot environment. Fluid temperature (consumption is greatest at 14 to 16°C, reduced above 37°C), turbidity, sweetness, fruit flavorings (for example, cherry, grape, orange, lemon), addition of citric acid which imparts a citrus flavor, and addition of sodium chloride or other minerals are examples. These components enhance palatability and increase fluid consumption. The addition of a small amount of salt (sodium chloride), besides enhancing palatability, may result in thirst and increased drinking, due to the specific action of sodium on fluid movements. An increased sodium concentration outside of cells causes water to leave cells via osmosis. The resulting cellular dehydration is an important stimulus for drinking. Increased beverage carbonation tends to reduce the palatability of a fluid as well as the volume of fluid consumed, without an increase in thirst. In addition, intakes of food and water are closely related. During 24-hour observations of fluid intake, most studies report that the majority of fluid (69 to 78 percent) is consumed during meals. The foregoing characteristics, therefore, tend to reduce the magnitude of voluntary dehydration.

Conversely, fluid characteristics may influence drinking behavior negatively, regardless of the intensity of thirst. Experiments conducted during mild prolonged exercise have shown that the following qualities are perceived as undesirable: nausea, bloating, an objectionable feeling in the mouth, excessive viscosity, and excessive sweetness (see Passe, 1996). Exercise and high ambient temperature may independently alter an individual's perception of fluid palatability. For example, drinking behavior increases when air temperature exceeds 25°C. Fluid consumption can also be enhanced by changing the shape of a fluid container, proximity of fluid containers to the drinker, volume of fluid that is available, and time allowed for drinking.

Societal customs may influence fluid consumption, as evidenced by cross-cultural differences in beverage preferences. Even rituals, such as accepting the friendly offer of a beverage in a social setting, may enhance fluid intake beyond that driven by physiological cues. These factors usually involve learned habits. Similarly, when people repeatedly drink fluids with initially unfamiliar flavors, the palatability of the fluids is enhanced.

Although a comprehensive theory of thirst and fluid balance eludes description, it is likely that the thirst drive increases and diminishes because multiple factors (for
example, oral dryness, gastric distension, osmolality, volume, fluid qualities) are integrated concurrently by the brain's thirst center.

Factors That Alter Thirst

Increase Thirst

increased concentration of blood

decreased blood volume

decreased blood pressure

mouth and throat dryness

increased angiotensin II

Decrease Thirst

decreased concentration of blood

increased blood volume

increased blood pressure

increased stomach fullness

decreased angiotensin II

SLEEP

Sleep is a naturally recurring state of relatively suspended sensory and motor activity, characterized by total or partial unconsciousness and the inactivity of nearly all voluntary muscles. It is distinguished from quiet wakefulness by a decreased ability to react to stimuli, and it is more easily reversible than hibernation or coma. Sleep is a heightened anabolic state, accentuating the growth and rejuvenation of the immune, nervous, skeletal and muscular systems. It is observed in all mammals, all birds, and many reptiles, amphibians, and fish.

STAGES OF SLEEP

In mammals and birds, sleeping is divided into two broad types: rapid eye movement (REM) and non-rapid eye movement (NREM or non-REM) sleep. Each type has a distinct set of associated physiological, neurological, and psychological features. The American Academy of Sleep Medicine (AASM) further divides NREM into three stages: N1, N2, and N3, the last of which is also called delta sleep or slow-wave sleep (SWS).

Sleep proceeds in cycles of REM and NREM, the order normally being N1 → N2 → N3 → N2 → REM. There is a greater amount of deep sleep (stage N3) early in the night, while the proportion of REM sleep increases later in the night and just before natural awakening.
The stages of sleep were first described in 1937 by Alfred Lee Loomis and his coworkers, who separated the different electroencephalography (EEG) features of sleep into five levels (A to E), which represented the spectrum from wakefulness to deep sleep. In 1953, REM sleep was discovered as distinct, and thus William Dement and Nathaniel Kleitman reclassified sleep into four NREM stages and REM. The staging criteria were standardized in 1968 by Allan Rechtschaffen and Anthony Kales in the "R&K sleep scoring manual." In the R&K standard, NREM sleep was divided into four stages, with slow-wave sleep comprising stages 3 and 4. In stage 3, delta waves made up less than 50% of the total wave patterns, while they made up more than 50% in stage 4. Furthermore, REM sleep was sometimes referred to as stage 5.

In 2004, the AASM commissioned the AASM Visual Scoring Task Force to review the R&K scoring system. The review resulted in several changes, the most significant being the combination of stages 3 and 4 into Stage N3. The revised scoring was published in 2007 as The AASM Manual for the Scoring of Sleep and Associated Events. Arousals and respiratory, cardiac, and movement events were also added.

Sleep stages and other characteristics of sleep are commonly assessed by polysomnography in a specialized sleep laboratory. Measurements taken include EEG of brain waves, electrooculography (EOG) of eye movements, and electromyography (EMG) of skeletal muscle activity. In humans, each sleep cycle lasts from 90 to 110 minutes on average, and each stage may have a distinct physiological function. This can result in sleep that exhibits loss of consciousness but does not fulfill its physiological functions (i.e., one may still feel tired after apparently sufficient sleep).

NREM sleep

According to the 2007 AASM standards, NREM consists of three stages. There is relatively little dreaming in NREM.

Stage N1 refers to the transition of the brain from alpha waves having a frequency of 8 to 13 Hz (common in the awake state) to theta waves having a frequency of 4 to 7 Hz. This stage is sometimes referred to as somnolence or drowsy sleep. Sudden twitches and hypnic jerks, also known as positive myoclonus, may be associated with the onset of sleep during N1. Some people may also experience hypnagogic hallucinations during this stage, which can be troublesome to them. During N1, the subject loses some muscle tone and most conscious awareness of the external environment.

Stage N2 is characterized by sleep spindles ranging from 11 to 16 Hz (most commonly 12–14 Hz) and K-complexes. During this stage, muscular activity as measured by EMG decreases, and conscious awareness of the external environment disappears. This stage occupies 45% to 55% of total sleep in adults.

Stage N3 (deep or slow-wave sleep) is characterized by the presence of a minimum of 20% delta waves ranging from 0.5 to 2 Hz and having a peak-to-peak amplitude >75 μV. (EEG standards define delta waves to be from 0 – 4 Hz, but sleep standards
in both the original R&K, as well as the new 2007 AASM guidelines have a range of 0.5 – 2 Hz.) This is the stage in which parasomnias such as night terrors, nocturnal enuresis, sleepwalking, and somniloquy occur. Many illustrations and descriptions still show a stage N3 with 20%-50% delta waves and a stage N4 with greater than 50% delta waves; these have been combined as stage N3.

**REM sleep**

Rapid eye movement sleep, or REM sleep, accounts for 20%–25% of total sleep time in most human adults. The criteria for REM sleep include rapid eye movements as well as a rapid low-voltage EEG. Most memorable dreaming occurs in this stage. At least in mammals, a descending muscular atonia is seen. Such paralysis may be necessary to protect organisms from self-damage through physically acting out scenes from the often-vivid dreams that occur during this stage.

**Timing**

**The human biological clock**

Sleep timing is controlled by the circadian clock, sleep-wake homeostasis, and in humans, within certain bounds, willed behavior. The circadian clock—an inner timekeeping, temperature-fluctuating, enzyme-controlling device—works in tandem with adenosine, a neurotransmitter that inhibits many of the bodily processes associated with wakefulness. Adenosine is created over the course of the day; high levels of adenosine lead to sleepiness. In diurnal animals, sleepiness occurs as the circadian element causes the release of the hormone melatonin and a gradual decrease in core body temperature. The timing is affected by one's chronotype. It is the circadian rhythm that determines the ideal timing of a correctly structured and restorative sleep episode.

Homeostatic sleep propensity (the need for sleep as a function of the amount of time elapsed since the last adequate sleep episode) must be balanced against the circadian element for satisfactory sleep. Along with corresponding messages from the circadian clock, this tells the body it needs to sleep. Sleep offset (awakening) is primarily determined by circadian rhythm. A person who regularly awakens at an early hour will generally not be able to sleep much later than his or her normal waking time, even if moderately sleep-deprived.

**Functions**

The multiple theories proposed to explain the function of sleep reflect the as-yet incomplete understanding of the subject. It is likely that sleep evolved to fulfill some primeval function and took on multiple functions over time. (As an analogy, the larynx in all mammals controls the passage of food and air, but may have descended in humans to take on speech capabilities in addition.)

It has been pointed out that, if sleep were not essential, one would expect to find 1) animal species that do not sleep at all, 2) animals that do not need recovery sleep when they stay awake longer than usual, and 3) animals that suffer no serious
consequences as a result of lack of sleep. No animals have been found to date that satisfy any of these criteria.

NEURAL MECHANISM OF SLEEP

Sleep process would start with the activation of sleep-promoting neurons located in the preoptic area of the anterior hypothalamus. This activation leads to the inhibition of wake-promoting neurons located in the posterior hypothalamus, basal forebrain and mesopontine tegmentum, which, in turn, removes inhibition from the sleep-promoting structures, thereby enhancing the sleep process. Sleep-promoting neurons are supposed to contain γ-aminobutyric acid and inhibit cholinergic, noradrenergic, serotonergic or histaminergic wake-promoting neurons at sleep onset and during sleep.

PARADOXICAL SLEEP

This is one of the two basic states of sleep and is notable for a presence of rapid eye movement (REM). It is a deep stage of sleep with intense brain activity in the forebrain and midbrain. It is characterized by dreaming and the absence of motor function with the exception of the eye muscles and the diaphragm. It occurs cyclically several times during sleep, but it comprises the smallest portion of the sleep cycle.

SLEEP DISORDER

A sleep disorder (somnipathy) is a medical disorder of the sleep patterns of a person or animal. Some sleep disorders are serious enough to interfere with normal physical, mental and emotional functioning. A test commonly ordered for some sleep disorders is the polysomnography.

Common disorders

The most common sleep disorders include:

- Primary insomnia: Chronic difficulty in falling asleep and/or maintaining sleep when no other cause is found for these symptoms.
- Bruxism: Involuntarily grinding or clenching of the teeth while sleeping.
- Delayed sleep phase syndrome (DSPS): inability to awaken and fall asleep at socially acceptable times but no problem with sleep maintenance, a disorder of circadian rhythms. Other such disorders are advanced sleep phase syndrome (ASPS) and Non-24-hour sleep-wake syndrome (Non-24), both much less common than DSPS.
- Hypopnea syndrome: Abnormally shallow breathing or slow respiratory rate while sleeping.
- Narcolepsy: Excessive daytime sleepiness (EDS) often culminating in falling asleep spontaneously but unwillingly at inappropriate times.
• Cataplexy: a sudden weakness in the motor muscles that can result in collapse to the floor.
• Night terror: Pavor nocturnus, sleep terror disorder: abrupt awakening from sleep with behavior consistent with terror.
• Parasomnias: Disruptive sleep-related events involving inappropriate actions during sleep stages - sleep walking and night-terrors are examples.
• Periodic limb movement disorder (PLMD): Sudden involuntary movement of arms and/or legs during sleep, for example kicking the legs. Also known as nocturnal myoclonus. See also Hyptic jerk, which is not a disorder.
• Rapid eye movement behavior disorder (RBD): Acting out violent or dramatic dreams while in REM sleep.
• Restless legs syndrome (RLS): An irresistible urge to move legs. RLS sufferers often also have PLMD.
• Situational circadian rhythm sleep disorders: shift work sleep disorder (SWSD) and jet lag.
• Obstructive sleep apnea: Obstruction of the airway during sleep, causing lack of sufficient deep sleep; often accompanied by snoring. Other forms of sleep apnea are less common.
• Sleep paralysis: is characterized by temporary paralysis of the body shortly before or after sleep. Sleep paralysis may be accompanied by visual, auditory or tactile hallucinations. Not a disorder unless severe. Often seen as part of Narcolepsy.
• Sleepwalking or somnambulism: Engaging in activities that are normally associated with wakefulness (such as eating or dressing), which may include walking, without the conscious knowledge of the subject.
• Nocturia: A frequent need to get up and go to the bathroom to urinate at night. It differs from Enuresis, or bed-wetting, in which the person does not arouse from sleep, but the bladder nevertheless empties.
• Somniphobia: a dread of sleep.

Classifications

• Dyssomnias - A broad category of sleep disorders characterized by either hypersomnolence or insomnia. The three major subcategories include intrinsic (i.e., arising from within the body), extrinsic (secondary to environmental conditions or various pathologic conditions), and disturbances of circadian rhythm. MeSH
  o Insomnia
  o Narcolepsy
  o Obstructive sleep apnea
  o Restless leg syndrome
  o Periodic limb movement disorder
  o Hypersomnia
Recurrent hypersomnia - including Kleine-Levin syndrome
- Posttraumatic hypersomnia
- "Healthy" hypersomnia

- Circadian rhythm sleep disorders
  - Delayed sleep phase syndrome
  - Advanced sleep phase syndrome
  - Non-24-hour sleep-wake syndrome

- Parasomnias - A category of sleep disorders that involve abnormal and unnatural movements, behaviors, emotions, perceptions, and dreams in connection with sleep.
  - REM sleep behaviour disorder
  - Sleep terror
  - Sleepwalking (or somnambulism)
  - Bruxism (Tooth-grinding)
  - Bedwetting or sleep enuresis.
  - Sleep talking (or somniloquy)
  - Sleep sex (or sexsomnia)
  - Exploding head syndrome - Waking up in the night hearing loud noises.

- Medical or Psychiatric Conditions that may produce sleep disorders
  - Psychoses (such as Schizophrenia)
  - Mood disorders
    - Depression
    - Anxiety
  - Panic
  - Alcoholism

- Sleeping sickness - a parasitic disease which can be transmitted by the Tsetse fly.
- Snoring - Not a disorder in and of itself, but it can be a symptom of deeper problems.

**General principles of treatment**

Treatments for sleep disorders generally can be grouped into four categories:

- behavioral/ psychotherapeutic treatments
- rehabilitation/management
- medications
- other somatic treatments

None of these general approaches is sufficient for all patients with sleep disorders. Rather, the choice of a specific treatment depends on the patient's diagnosis, medical and psychiatric history, and preferences, as well as the expertise of the treating
clinician. Often, behavioral/psychotherapeutic and pharmacological approaches are not incompatible and can effectively be combined to maximize therapeutic benefits. Management of sleep disturbances that are secondary to mental, medical, or substance abuse disorders should focus on the underlying conditions.

Medications and somatic treatments may provide the most rapid symptomatic relief from some sleep disturbances. Some disorders, such as narcolepsy, are best treated pharmacologically. Others, such as chronic and primary insomnia, may be more amenable to behavioral interventions, with more durable results.

Chronic sleep disorders in childhood, which affect some 70% of children with developmental or psychological disorders, are under-reported and under-treated. Sleep-phase disruption is also common among adolescents, whose school schedules are often incompatible with their natural circadian rhythm. Effective treatment begins with careful diagnosis using sleep diaries and perhaps sleep studies. Modifications in sleep hygiene may resolve the problem, but medical treatment is often warranted.

Special equipment may be required for treatment of several disorders such as obstructive apnea, the circadian rhythm disorders and bruxism. In these cases, when severe, an acceptance of living with the disorder, however well managed, is often necessary.

Sleep medicine

Due to rapidly increasing knowledge about sleep in the 20th century, including the discovery of REM sleep and sleep apnea, the medical importance of sleep was recognized. The medical community began paying more attention than previously to primary sleep disorders, such as sleep apnea, as well as the role and quality of sleep in other conditions. By the 1970s in the USA, clinics and laboratories devoted to the study of sleep and sleep disorders had been founded, and a need for standards arose.

Sleep Medicine is now a recognized subspecialty within internal medicine, family medicine, pediatrics, otolaryngology, psychiatry and neurology in the United States. Certification in Sleep Medicine shows that the specialist:

"has demonstrated expertise in the diagnosis and management of clinical conditions that occur during sleep, that disturb sleep, or that are affected by disturbances in the wake-sleep cycle. This specialist is skilled in the analysis and interpretation of comprehensive polysomnography, and well-versed in emerging research and management of a sleep laboratory."

Competence in sleep medicine requires an understanding of a myriad of very diverse disorders, many of which present with similar symptoms such as excessive daytime sleepiness, which, in the absence of volitional sleep deprivation, "is almost inevitably caused by an identifiable and treatable sleep disorder", such as sleep
apnea, narcolepsy, idiopathic central nervous system (CNS) hypersomnia, Kleine-Levin syndrome, menstrual-related hypersomnia, idiopathic recurrent stupor, or circadian rhythm disturbances. Another common complaint is insomnia, a set of symptoms which can have a great many different causes, physical and mental. Management in the varying situations differs greatly and cannot be undertaken without a correct diagnosis.

Sleep dentistry (bruxism, snoring and sleep apnea), while not recognized as one of the nine dental specialties, qualifies for board-certification by the American Board of Dental Sleep Medicine (ABDSM). The resulting Diplomate status is recognized by the American Academy of Sleep Medicine (AASM), and these dentists are organized in the Academy of Dental Sleep Medicine (USA). The qualified dentists collaborate with sleep physicians at accredited sleep centers and can provide oral appliance therapy and upper airway surgery to treat or manage sleep-related breathing disorders.

In the UK, knowledge of sleep medicine and possibilities for diagnosis and treatment seem to lag. Guardian.co.uk quotes the director of the Imperial College Healthcare Sleep Centre: "One problem is that there has been relatively little training in sleep medicine in this country - certainly there is no structured training for sleep physicians." The Imperial College Healthcare site shows attention to obstructive sleep apnea syndrome (OSA) and very few other sleep disorders.

**Insomnia**

**Insomnia** is a symptom which can accompany several sleep, medical and psychiatric disorders, characterized by persistent difficulty falling asleep and/or difficulty staying asleep. Insomnia is typically followed by functional impairment while awake.

Both organic and non-organic insomnia without other cause constitute a sleep disorder, primary insomnia. One definition of insomnia is "difficulties initiating and/or maintaining sleep, or nonrestorative sleep, associated with impairments of daytime functioning or marked distress for more than 1 month."

According to the United States Department of Health and Human Services in the year 2007, approximately 64 million Americans regularly suffer from insomnia each year. Insomnia is 41% more common in women than in men.

**Classification**

**Types of insomnia**

Although there are several different degrees of insomnia, three types of insomnia have been clearly identified: transient, acute, and chronic.
1. **Transient insomnia** lasts for less than a week. It can be caused by another disorder, by changes in the sleep environment, by the timing of sleep, severe depression, or by stress. Its consequences - sleepiness and impaired psychomotor performance - are similar to those of sleep deprivation.

2. **Acute insomnia** is the inability to consistently sleep well for a period of less than a month.

3. **Chronic insomnia** lasts for approximately a month. It can be caused by another disorder, or it can be a primary disorder. Its effects can vary according to its causes. They might include being unable to sleep, muscular fatigue, hallucinations, and/or mental fatigue; but people with chronic insomnia often show increased alertness. Some people that live with this disorder see things as if they are happening in slow motion, wherein moving objects seem to blend together. Can cause double vision.

### Patterns of insomnia

1. **Onset insomnia** - difficulty falling asleep at the beginning of the night, often associated with anxiety disorders.

2. **Middle-of-the-Night Insomnia** - Insomnia characterized by difficulty returning to sleep after awakening in the middle of the night or waking too early in the morning. Also referred to as nocturnal awakenings. Encompasses middle and terminal insomnia.

3. **Middle insomnia** - waking during the middle of the night, difficulty maintaining sleep. Often associated with pain disorders or medical illness.

4. **Terminal (or late) insomnia** - early morning waking. Often a characteristic of clinical depression.

### Insomnia versus poor sleep quality

Poor sleep quality can occur as a result of sleep apnea or major depression. Poor sleep quality is caused by the individual not reaching stage 4 or delta sleep which has restorative properties. There are, however, people who are unable to achieve stage 4 sleep due to brain damage who lead perfectly normal lives.

Sleep apnea is a condition that occurs when a sleeping person's breathing is interrupted, thus interrupting the normal sleep cycle. With the obstructive form of the condition, some part of the sleeper’s respiratory tract loses muscle tone and partially collapses. People with obstructive sleep apnea often do not remember awakening or having difficulty breathing, but they complain of excessive sleepiness during the day. Central sleep apnea interrupts the normal breathing stimulus of the central nervous system, and the individual must actually wake up to resume breathing. This form of apnea is often related to a cerebral vascular condition, congestive heart failure, and premature aging.
Major depression leads to alterations in the function of the hypothalamic-pituitary-adrenal axis, causing excessive release of cortisol which can lead to poor sleep quality.

Nocturnal polyuria, excessive nighttime urination, can be very disturbing to sleep.

Some sleep disorders such as insomnia have been found to compromise glucose metabolism.

**Signs and symptoms**

A survey of 1.1 million residents in the United States conducted by the American Cancer Society found that those who reported sleeping about 7 hours per night had the lowest rates of mortality, whereas those who slept for fewer than 6 hours or more than 8 hours had higher mortality rates. Getting 8.5 or more hours of sleep per night increased the mortality rate by 15%. Severe insomnia - sleeping less than 3.5 hours in women and 4.5 hours in men - also led to a 15% increase in mortality. However, most of the increase in mortality from severe insomnia was discounted after controlling for comorbid disorders. After controlling for sleep duration and insomnia, use of sleeping pills was also found to be associated with an increased mortality rate.

The lowest mortality was seen in individuals who slept between six and a half and seven and a half hours per night. Even sleeping only 4.5 hours per night is associated with very little increase in mortality. Thus mild to moderate insomnia for most people is associated with increased longevity and severe insomnia is only associated with a very small effect on mortality.

As long as a patient refrains from using sleeping pills there is little to no increase in mortality associated with insomnia but there does appear to be an increase in longevity. This is reassuring for patients with insomnia in that despite the sometimes unpleasantness of insomnia, insomnia itself appears to be associated with increased longevity.

It is unclear why sleeping longer than 7.5 hours is associated with excess mortality.

**Causes**

Insomnia can be caused by:

- Psychoactive drugs or stimulants, including certain medications, herbs, caffeine, nicotine, cocaine, amphetamines, methylphenidate, MDMA and modafinil
- Fluoroquinolone antibiotic drugs, see Fluoroquinolone toxicity, associated with more severe and chronic types of insomnia
• Restless Legs Syndrome can cause insomnia due to the discomforting sensations felt and need to move the legs or other body parts to relieve these sensations. It is difficult if not impossible to fall asleep while moving.

• Pain[12] Any injury or condition that causes pain. Pain can preclude an individual from finding a comfortable position in which to fall asleep, and in addition can cause awakening if, during sleep, the person rolls over and puts pressure on the injured or painful area of the body.

• Hormone shifts such as those that precede menstruation and those during menopause

• Life problems like fear, stress, anxiety, emotional or mental tension, work problems, financial stress.

• Mental disorders such as bipolar disorder, clinical depression, generalized anxiety disorder, post traumatic stress disorder, schizophrenia, or obsessive compulsive disorder.

• Disturbances of the circadian rhythm, such as shift work and jet lag, can cause an inability to sleep at some times of the day and excessive sleepiness at other times of the day. Jet lag is seen in people who travel through multiple time zones, as the time relative to the rising and setting of the sun no longer coincides with the body's internal concept of it. The insomnia experienced by shift workers is also a circadian rhythm sleep disorder.

• Certain neurological disorders, brain lesions, or a history of traumatic brain injury

• Medical conditions such as hyperthyroidism and rheumatoid arthritis[13]

• Abuse of over-the counter or prescription sleep aids can produce rebound insomnia

• Poor sleep hygiene, e.g., noise

• Parasomnia, which includes a number of disruptive sleep events including nightmares, sleepwalking, violent behavior while sleeping, and REM behavior disorder, in which a person moves his/her physical body in response to events within his/her dreams

• A rare genetic condition can cause a prion-based, permanent and eventually fatal form of insomnia called fatal familial insomnia.

• Physical exercise. Exercise-induced insomnia is common in athletes, causing prolonged sleep onset latency.

Sleep studies using polysomnography have suggested that people who have insomnia with sleep disruption have elevated nighttime levels of circulating cortisol and adrenocorticotropic hormone They also have an elevated metabolic rate, which does not occur in people who do not have insomnia but whose sleep is intentionally disrupted during a sleep study. Studies of brain metabolism using positron emission tomography (PET) scans indicate that people with insomnia have higher metabolic
rates by night and by day. The question remains whether these changes are the causes or consequences of long-term insomnia.

Insomnia can be common after the loss of a loved one, even years or decades after the death, if they have not gone through the grieving process. Overall, symptoms and the degree of their severity affect each individual differently depending on their mental health, physical condition, and attitude or personality.

A common misperception is that the amount of sleep required decreases as a person ages. The ability to sleep for long periods, rather than the need for sleep, appears to be lost as people get older. Some elderly insomniacs toss and turn in bed and occasionally fall off the bed at night, diminishing the amount of sleep they receive.

**Diagnosis**

Specialists in sleep medicine are qualified to diagnose the many different sleep disorders. Patients with various disorders including delayed sleep phase syndrome are often mis-diagnosed with insomnia.

If a patient has trouble getting to sleep, but has normal sleep pattern once asleep, a circadian rhythm disorder is a likely cause.

**Treatment for insomnia**

In many cases, insomnia is caused by another disease, side effects from medications, or a psychological problem. It is important to identify or rule out medical and psychological causes before deciding on the treatment for the insomnia. Attention to sleep hygiene is an important first line treatment strategy and should be tried before any pharmacological approach is considered.

**Non-pharmacological**

Non-pharmacological strategies are superior to hypnotic medication for insomnia because tolerance develops to the hypnotic effects. In addition, dependence can develop with rebound withdrawal effects developing upon discontinuation. Hypnotic medication is therefore only recommended for short term use, especially in acute or chronic insomnia. Non pharmacological strategies however, have long lasting improvements to insomnia and are recommended as a first line and long term strategy of managing insomnia. The strategies include attention to sleep hygiene, stimulus control, behavioral interventions, sleep-restriction therapy, paradoxical intention, patient education and relaxation therapy.

EEG biofeedback has demonstrated effectiveness in the treatment of insomnia with improvements in duration as well as quality of sleep.

Stimulus control therapy is a treatment for patients who have conditioned themselves to associate the bed, or sleep in general, with a negative response. As
stimulus control therapy involves taking steps to control the sleep environment, it is sometimes referred interchangeably with the concept of sleep hygiene. Examples of such environmental modifications include using the bed for sleep or sex only, not for activities such as reading or watching television; waking up at the same time every morning, including on weekends; going to bed only when sleepy and when there is a high likelihood that sleep will occur; leaving the bed and beginning an activity in another location if sleep does not result in a reasonably brief period of time after getting into bed (commonly ~20 min); reducing the subjective effort and energy expended trying to fall asleep; avoiding exposure to bright light during nighttime hours, and eliminating daytime naps.

A component of stimulus control therapy is sleep restriction, a technique that aims to match the time spent in bed with actual time spent asleep. This technique involves maintaining a strict sleep-wake schedule, only sleeping at certain times of the day and for specific amounts of time to induce mild sleep deprivation. Complete treatment usually lasts up to 3 weeks and involves making oneself sleep for only a minimum amount of time that they are actually capable of on average, and then, if capable (i.e. when sleep efficiency improves), slowly increasing this amount (~15 min) by going to bed earlier as the body attempts to reset its internal sleep clock. Bright light therapy, which is often used to help early morning wakers reset their natural sleep cycle, can also be used with sleep restriction therapy to reinforce a new wake schedule. Although applying this technique with consistency is difficult, it can have a positive effect on insomnia in motivated patients.

Paradoxical intention is a cognitive reframing technique where the insomniac, instead of attempting to fall asleep at night, makes every effort to stay awake (i.e. essentially stops trying to fall asleep). One theory that may explain the effectiveness of this method is that by not voluntarily making oneself go to sleep, it relieves the performance anxiety that arises from the need or requirement to fall asleep, which is meant to be a passive act. This technique has been shown to reduce sleep effort and performance anxiety and also lower subjective assessment of sleep-onset latency and overestimation of the sleep deficit (a quality found in many insomniacs).

Cognitive behavior therapy

A recent study found that cognitive behavior therapy is more effective than hypnotic medications in controlling insomnia. In this therapy, patients are taught improved sleep habits and relieved of counter-productive assumptions about sleep. Common misconceptions and expectations that can be modified include: (1) unrealistic sleep expectations (e.g., I need to have 8 hours of sleep each night), (2) misconceptions about insomnia causes (e.g., I have a chemical imbalance causing my insomnia), (3) amplifying the consequences of insomnia (e.g., I cannot do anything after a bad night’s sleep), and (4) performance anxiety after trying for so long to have a good night’s sleep by controlling the sleep process. Numerous studies have reported positive outcomes of combining cognitive behavioral therapy treatment with treatments such as stimulus control and the relaxation therapies. Hypnotic medications are equally effective in the short term treatment of insomnia but their
effects wear off over time due to tolerance. The effects of cognitive behavior therapy have sustained and lasting effects on treating insomnia long after therapy has been discontinued. The addition of hypnotic medications with CBT adds no benefit in insomnia. The long lasting benefits of a course of CBT shows superiority over pharmacological hypnotic drugs. Even in the short term when compared to short term hypnotic medication such as zolpidem (Ambien), CBT still shows significant superiority. Thus CBT is recommended as a first line treatment for insomnia.

**Medications**

Many insomniacs rely on sleeping tablets and other sedatives to get rest, with research showing that medications are prescribed to over 95% of insomniac cases. Certain classes of sedatives such as benzodiazepines and newer nonbenzodiazepine drugs can also cause physical dependence which manifests in withdrawal symptoms if the drug is not carefully tapered down. The benzodiazepine and nonbenzodiazepine hypnotic medications also have a number of side effects such as day time fatigue, motor vehicle crashes, cognitive impairments and falls and fractures. Elderly people are more sensitive to these side effects. The non-benzodiazepines zolpidem and zaleplon have not adequately demonstrated effectiveness in sleep maintenance. Some benzodiazepines have demonstrated effectiveness in sleep maintenance in the short-term but in the longer term is associated with tolerance and dependence. Drugs are in development which may prove more effective and safer than existing drugs for insomnia.

In comparing the options, a systematic review found that benzodiazepines and nonbenzodiazepines have similar efficacy which was not significantly more than for antidepressants. Benzodiazepines did not have a significant tendency for more adverse drug reactions. Chronic users of hypnotic medications for insomnia do not have better sleep than chronic insomniacs who do not take medications. In fact, chronic users of hypnotic medications actually have more regular nighttime awakenings than insomniacs who do not take hypnotic medications. A further review of the literature regarding benzodiazepine hypnotic as well as the nonbenzodiazepines concluded that these drugs caused an unjustifiable risk to the individual and to public health and lack evidence of long term effectiveness. The risks include dependence, accidents and other adverse effects. Gradual discontinuation of hypnotics in long term users leads to improved health without worsening of sleep. Preferably hypnotics should be prescribed for only a few days at the lowest effective dose and avoided altogether wherever possible in the elderly.

**Benzodiazepines**

The most commonly used class of hypnotics prescribed for insomnia are the benzodiazepines. Benzodiazepines bind unselectively to the GABA<sub>A</sub> receptor. These include drugs such as temazepam, flunitrazepam, triazolam, flurazepam, midazolam, nitrazepam and quazepam. These drugs can lead to tolerance, physical dependence and the benzodiazepine withdrawal syndrome upon discontinuation,
especially after consistent usage over long periods of time. Benzodiazepines while inducing unconsciousness, actually worsen sleep as they promote light sleep whilst decreasing time spent in deep sleep such as REM sleep. A further problem is with regular use of short acting sleep aids for insomnia, day time rebound anxiety can emerge. Benzodiazepines can help to initiate sleep and increase sleep time but they also decrease deep sleep and increase light sleep. Although there is little evidence for benefit of benzodiazepines in insomnia and evidence of major harm prescriptions have continued to increase. There is a general awareness that long-term use of benzodiazepines for insomnia in most people is inappropriate and that a gradual withdrawal is usually beneficial due to the adverse effects associated with the long-term use of benzodiazepines and is recommended whenever possible.

Non-benzodiazepines

Nonbenzodiazepine sedative-hypnotic drugs, such as zolpidem, zaleplon, zopiclone and eszopiclone, are a newer classification of hypnotic medications. They work on the benzodiazepine site on the GABA<sub>A</sub> receptor complex similarly to the benzodiazepine class of drugs. Some but not all of the nonbenzodiazepines are selective for the α<sub>1</sub> subunit on GABA<sub>A</sub> receptors which is responsible for inducing sleep and may therefore have a cleaner side effect profile than the older benzodiazepines. Zopiclone and eszopiclone like benzodiazepine drugs bind unselectively to α<sub>1</sub>, α<sub>2</sub>, α<sub>3</sub> and α<sub>5</sub> GABA<sub>A</sub> benzodiazepine receptors. Zolpidem is more selective and zaleplon is highly selective for the α<sub>1</sub> subunit, thus giving them an advantage over benzodiazepines in terms of sleep architecture and a reduction in side effects. However, there are controversies over whether these non-benzodiazepine drugs are superior to benzodiazepines. These drugs appear to cause both psychological dependence and physical dependence though less than traditional benzodiazepines and can also cause the same memory and cognitive disturbances along with morning sedation.

Alcohol

Alcohol is often used as a form of self-treatment of insomnia to induce sleep. However, alcohol use to induce sleep can be a cause of insomnia. Long-term use of alcohol is associated with a decrease in NREM stage 3 and 4 sleep as well as suppression of REM sleep and REM sleep fragmentation. Frequent moving between sleep stages occurs, with awakenings due to headaches, polyuria, dehydration and diaphoresis. Glutamine rebound also plays a role as when someone is drinking, alcohol inhibits glutamine, one of the body's natural stimulants. When the person stops drinking, the body tries to make up for lost time by producing more glutamine than it needs. The increase in glutamine levels stimulates the brain while the drinker is trying to sleep, keeping them from reaching the deepest levels of sleep. Stopping chronic alcohol use can also lead to severe insomnia with vivid dreams. During withdrawal REM sleep is typically exaggerated as part of a rebound effect.
Opioids

Opioid medications such as hydrocodone, oxycodone, and morphine are used for insomnia which is associated with pain due to their analgesic properties and hypnotic effects. Opioids (also referred to as opiates) can fragment sleep and decrease REM and stage 2 sleep. By producing analgesia and sedation, opioids may be appropriate in carefully selected patients with pain-associated insomnia.

Antidepressants

Some antidepressants such as amitriptyline, doxepin, mirtazapine, and trazodone can often have a very strong sedative effect, and are prescribed off label to treat insomnia. The major drawback of these drugs is that they have properties which can lead to many side effects, for example; amitriptyline and doxepin both have antihistaminergic, anticholinergic and antiadrenergic properties which contribute to their side effect profile, while mirtazapines side effects are primarily antihistaminergic, and trazadones side effects are primarily antiadrenergic. Some also alter sleep architecture. As with benzodiazepines, the use of antidepressants in the treatment of insomnia can lead to withdrawal effects; withdrawal may induce rebound insomnia.

Mirtazapine is known to decrease sleep latency, promoting sleep efficiency and increasing the total amount of sleeping time in patients suffering from both depression and insomnia.

Melatonin and melatonin agonists

The hormone and supplement melatonin is effective in several types of insomnia. Melatonin has demonstrated effectiveness equivalent to the prescription sleeping tablet zopiclone in inducing sleep and regulating the sleep/waking cycle.[47] One particular benefit of melatonin is that it can treat insomnia without altering the sleep pattern which is altered by many prescription sleeping tablets. Another benefit is it does not impair performance related skills.

Melatonin agonists, including ramelteon (Rozerem) and tasimelteon, seem to lack the potential for misuse and dependence. This class of drugs has a relatively mild side effect profile and lower likelihood of causing morning sedation. While these drugs show good effects for the treatment of insomnia due to jet lag, the results for other forms of insomnia are less promising.¹

Natural substances such as 5-HTP and L-Tryptophan have been said to fortify the serotonin-melatonin pathway and aid people with various sleep disorders including insomnia.
Antihistamines

The antihistamine diphenhydramine is widely used in nonprescription sleep aids such as Benadryl. The antihistamine doxylamine is used in nonprescription sleep aids such as Unisom (USA) and Unisom 2 (Canada). In some countries, including Australia, it is marketed under the names Restavit and Dozile. It is the most effective over-the-counter sedative currently available in the United States, and is more sedating than some prescription hypnotics.

While the two drugs mentioned above are available over the counter in most countries, the effectiveness of these agents may decrease over time and the incidence of next-day sedation is higher than for most of the newer prescription drugs. Anticholinergic side effects may also be a draw back of these particular drugs. Dependence does not seem to be an issue with this class of drugs.

Cyproheptadine is a useful alternative to benzodiazepine hypnotics in the treatment of insomnia. Cyproheptadine may be superior to benzodiazepines in the treatment of insomnia because cyproheptadine enhances sleep quality and quantity whereas benzodiazepines tend to decrease sleep quality.

Atypical antipsychotics

Low doses of certain atypical antipsychotics such as quetiapine, olanzapine and risperidone are also prescribed for their sedative effect but the danger of neurological and cognitive side effects make these drugs a poor choice to treat insomnia. Over time, quetiapine may lose its effectiveness as a sedative. The ability of quetiapine to produce sedation is determined by the dosage. Higher doses (300 mg - 900 mg) are usually taken for its use as an antipsychotic, while lower doses (25 mg - 200 mg) have a marked sedative effect, e.g. if a patient takes 300 mg, he/she will more likely benefit from the drug’s antipsychotic effects, but if the dose is brought down to 100 mg, it will leave the patient feeling more sedated than at 300 mg, because it primarily works as a sedative at lower doses.

Eplivanserin is an investigational drug with a mechanism similar to these antipsychotics, but probably with less side effects.

Other substances

Some insomniacs use herbs such as valerian, chamomile, lavender, hops, and passion-flower. Valerian has undergone multiple studies and appears to be modestly effective..

Insomnia may be a symptom of magnesium deficiency, or low magnesium levels, but this has not yet been proven. A healthy diet containing magnesium can help to improve sleep in individuals without an adequate intake of magnesium.
Narcolepsy

Narcolepsy is a chronic sleep disorder, or dyssomnia, characterized by excessive daytime sleepiness (EDS) in which a person experiences extreme fatigue and possibly falls asleep at inappropriate times, such as while at work or at school. Narcoleptics usually experience disturbed nocturnal sleep and an abnormal daytime sleep pattern, which is often confused with insomnia. When a narcoleptic falls asleep they generally experience the REM stage of sleep within 10 minutes; whereas most people do not experience REM sleep until after 30 minutes. There is little evidence to suggest that narcoleptics tend to have a shorter life span.

Another problem that some narcoleptics experience is cataplexy, a sudden muscular weakness brought on by strong emotions (though many people experience cataplexy without having an emotional trigger). It often manifests as muscular weaknesses ranging from a barely perceptible slackening of the facial muscles to the dropping of the jaw or head, weakness at the knees, or a total collapse. Usually only speech is slurred, vision is impaired (double vision, inability to focus), but hearing and awareness remain normal. In some rare cases, an individual’s body becomes paralyzed and muscles become stiff.

Narcolepsy is a neurological sleep disorder. It is not caused by mental illness or psychological problems. It is most likely affected by a number of genetic abnormalities that affect specific biologic factors in the brain, combined with a set off from environment, such as a virus.

The term narcolepsy derives from the French word narcolepsie created by the French physician Jean-Baptiste-Édouard Gélineau by combining the Greek (narkē, "numbness" or "stupor"), and (lepsis), "attack" or "seizure").

Signs and symptoms

The main characteristic of narcolepsy is excessive daytime sleepiness (EDS), even after adequate nighttime sleep. A person with narcolepsy is likely to become drowsy or fall asleep or just be very tired throughout the day, often at inappropriate times and places. Daytime naps may occur with little warning and may be physically irresistible. These naps can occur several times a day. They are typically refreshing, but only for a few hours. Drowsiness may persist for prolonged periods of time. In addition, nighttime sleep may be fragmented with frequent awakenings.

Four of the other classic symptoms of the disorder, often referred to as the "tetrad of narcolepsy," are cataplexy, sleep paralysis, hypnagogic hallucinations, and automatic behavior. These symptoms may not occur in all patients. Cataplexy is an episodic condition featuring loss of muscle function, ranging from slight weakness (such as limpness at the neck or knees, sagging facial muscles, or inability to speak clearly) to complete body collapse. Episodes may be triggered by sudden emotional reactions such as laughter, anger, surprise, or fear, and may last from a few seconds to several minutes. The person remains conscious throughout the episode. In some cases,
cataplexy may resemble epileptic seizures. Sleep paralysis is the temporary inability to talk or move when waking (or less often, when falling asleep). It may last a few seconds to minutes. This is often frightening but is not dangerous. Hypnagogic hallucinations are vivid, often frightening, dreamlike experiences that occur while dozing, falling asleep and/or while awakening.

Automatic behavior means that a person continues to function (talking, putting things away, etc.) during sleep episodes, but awakens with no memory of performing such activities. It is estimated that up to 40 percent of people with narcolepsy experience automatic behavior during sleep episodes. Sleep paralysis and hypnagogic hallucinations also occur in people who do not have narcolepsy, but more frequently in people who are suffering from extreme lack of sleep. Cataplexy is generally considered to be unique to narcolepsy and is analogous to sleep paralysis in that the usually protective paralysis mechanism occurring during sleep is inappropriately activated. The opposite of this situation (failure to activate this protective paralysis) occurs in rapid eye movement behavior disorder.

In most cases, the first symptom of narcolepsy to appear is excessive and overwhelming daytime sleepiness. The other symptoms may begin alone or in combination months or years after the onset of the daytime naps. There are wide variations in the development, severity, and order of appearance of cataplexy, sleep paralysis, and hypnagogic hallucinations in individuals. Only about 20 to 25 percent of people with narcolepsy experience all four symptoms. The excessive daytime sleepiness generally persists throughout life, but sleep paralysis and hypnagogic hallucinations may not.

Although these are the common symptoms of narcolepsy, many people with narcolepsy also suffer from insomnia for extended periods of time. The symptoms of narcolepsy, especially the excessive daytime sleepiness and cataplexy, often become severe enough to cause serious problems in a person's social, personal, and professional life. Normally, when an individual is awake, brain waves show a regular rhythm. When a person first falls asleep, the brain waves become slower and less regular. This sleep state is called non-rapid eye movement (NREM) sleep. After about an hour and a half of NREM sleep, the brain waves begin to show a more active pattern again. This sleep state, called REM sleep (rapid eye movement sleep), is when most remembered dreaming occurs. Associated with the EEG-observed waves during REM sleep, muscle atonia is present (called REM atonia).

In narcolepsy, the order and length of NREM and REM sleep periods are disturbed, with REM sleep occurring at sleep onset instead of after a period of NREM sleep. Thus, narcolepsy is a disorder in which REM sleep appears at an abnormal time. Also, some of the aspects of REM sleep that normally occur only during sleep—lack of muscular control, sleep paralysis, and vivid dreams—occur at other times in people with narcolepsy. For example, the lack of muscular control can occur during wakefulness in a cataplexy episode; it is said that there is intrusion of REM atonia during wakefulness. Sleep paralysis and vivid dreams can occur while falling asleep or waking up. Simply put, the brain does not pass through the normal stages of
dozing and deep sleep but goes directly into (and out of) rapid eye movement (REM) sleep.

This has several consequences. Night time sleep does not include as much deep sleep, so the brain tries to "catch up" during the day, hence EDS. People with narcolepsy may visibly fall asleep at unpredicted moments (such motions as head bobbing are common). People with narcolepsy fall quickly into what appears to be very deep sleep, and they wake up suddenly and can be disoriented when they do (dizziness is a common occurrence). They have very vivid dreams, which they often remember in great detail. People with narcolepsy may dream even when they only fall asleep for a few seconds.

**Causes**

Although the cause of narcolepsy was not determined for many years after its discovery, scientists had discovered conditions that seemed to be associated with an increase in an individual's risk of having the disorder. Specifically, there appeared to be a strong link between narcoleptic individuals and certain genetic conditions. One factor that seemed to predispose an individual to narcolepsy involved an area of Chromosome 6 known as the HLA complex. There appeared to be a correlation between narcoleptic individuals and certain variations in HLA genes, although it was not required for the condition to occur. Certain variations in the HLA complex were thought to increase the risk of an auto-immune response to protein-producing neurons in the brain. The protein produced, called hypocretin or orexin, is responsible for controlling appetite and sleep patterns. Individuals with narcolepsy often have reduced numbers of these protein-producing neurons in their brains. In 2009 the autoimmune hypothesis was supported by research carried out at Stanford University School of Medicine.

The neural control of normal sleep states and the relationship to narcolepsy are only partially understood. In humans, narcoleptic sleep is characterized by a tendency to go abruptly from a waking state to REM sleep with little or no intervening non-REM sleep. The changes in the motor and proprioceptive systems during REM sleep have been studied in both human and animal models. During normal REM sleep, spinal and brainstem alpha motor neuron depolarization produces almost complete atonia of skeletal muscles via an inhibitory descending reticulospinal pathway. Acetylcholine may be one of the neurotransmitters involved in this pathway. In narcolepsy, the reflex inhibition of the motor system seen in cataplexy is believed to be identical to that seen in normal REM sleep.

In 2004 researchers in Australia induced narcolepsy-like symptoms in mice by injecting them with antibodies from narcoleptic humans. The research has been published in the Lancet providing strong evidence suggesting that some cases of narcolepsy might be caused by autoimmune disease. Narcolepsy is strongly associated with HLA-DQB1*0602 genotype. There is also an association with HLA-DR2 and HLA-DQ1. This may represent linkage disequilibrium. Despite the experimental evidence in human narcolepsy that there may be an inherited basis for
at least some forms of narcolepsy, the mode of inheritance remains unknown. Some cases are associated with genetic diseases such as Niemann-Pick disease\[13\] or Prader-Willi syndrome.

**Diagnosis**

Diagnosis is relatively easy when all the symptoms of narcolepsy are present, but if the sleep attacks are isolated and cataplexy is mild or absent, diagnosis is more difficult. It is also possible for cataplexy to occur in isolation. Two tests that are commonly used in diagnosing narcolepsy are the polysomnogram and the multiple sleep latency test (MSLT). These tests are usually performed by a sleep specialist. The polysomnogram involves continuous recording of sleep brain waves and a number of nerve and muscle functions during nighttime sleep. When tested, people with narcolepsy fall asleep rapidly, enter REM sleep early, and may awaken often during the night. The polysomnogram also helps to detect other possible sleep disorders that could cause daytime sleepiness.

For the multiple sleep latency test, a person is given a chance to sleep every 2 hours during normal wake times. Observations are made of the time taken to reach various stages of sleep (sleep onset latency). This test measures the degree of daytime sleepiness and also detects how soon REM sleep begins. Again, people with narcolepsy fall asleep rapidly and enter REM sleep early.

**Treatment**

Treatment is tailored to the individual, based on symptoms and therapeutic response. The time required to achieve optimal control of symptoms is highly variable, and may take several months or longer. Medication adjustments are also frequently necessary, and complete control of symptoms is seldom possible. While oral medications are the mainstay of formal narcolepsy treatment, lifestyle changes are also important.

The main treatment of excessive daytime sleepiness in narcolepsy is with central nervous system stimulant drugs such as methylphenidate, racemic - amphetamine, dextroamphetamine, and methamphetamine, or modafinil (Provigil), a new stimulant with a different pharmacologic mechanism, and more recently, armodafinil (Nuvigil). In Fall 2007 an alert for severe adverse skin reactions to modafinil was issued by the FDA. Other medications used are codeine and selegiline.\[17\] Another drug that is used is atomoxetine (Strattera), a non-stimulant and norepinephrine reuptake inhibitor (NRI), that has little or no abuse potential. In many cases, planned regular short naps can reduce the need for pharmacological treatment of the EDS to a low or non-existent level.

Cataplexy and other REM-sleep symptoms are frequently treated with tricyclic antidepressants such as clomipramine, imipramine, or protriptyline, as well as other drugs that suppress REM sleep. Venlafaxine (branded as Effexor XR by Wyeth Pharmaceuticals), an antidepressant which blocks the reuptake of serotonin and
norepinephrine, has shown usefulness in managing symptoms of cataplexy, however, it has notable side-effects including sleep disruption.

Gamma-hydroxybutyrate (GHB), more commonly known on the pharmaceutical market as Sodium Oxybate, or Xyrem (branded by Jazz Pharmaceuticals), is the only medication specifically indicated and approved for narcolepsy and cataplexy. Gamma-hydroxybutyrate has been shown to reduce symptoms of EDS associated with narcolepsy. While the exact mechanism of action is unknown, GHB is thought to improve the quality of nocturnal sleep by increasing the prevalence of slow wave (delta) sleep (as this is the time when the brain is least active and therefore most at rest and able to rebuild and repair itself physiologically). GHB appears to help sufferers much more effectively than the hypnotic class of medications typically used for insomnia (hypnotics tend to obstruct delta wave sleep), so it can be vital to be properly diagnosed as narcoleptic rather than insomniac. GHB was previously available on the open market as a dietary supplement but was reclassified a controlled substance in the United States due to pressure associated with the abuse of the chemical (it is infamously known as the date rape drug). It can currently only be legally acquired through prescription, after very specific diagnoses (typically for narcolepsy itself). Many healthcare providers, such as Welfare prescription plans in the US, are unwilling to pay for the expensive drug and will instead present patients with stimulants.

Using stimulants to mask daytime sleepiness does not address the actual cause of the problem. Stimulants may provide some assistance with daytime activity, but the underlying cause will remain and potentially worsen over time due to the stimulant itself becoming an obstruction to delta wave sleep periods. Lifestyle changes involving reduced stress, more exercise (especially for overweight persons experiencing narcolepsy caused by sleep apnea and snoring) and less stimulant intake (such as coffee and nicotine) are likely to be ideal forms of assistive treatment. Some people with narcolepsy have a nocturnal body clock and are helped by selecting an occupation that properly coincides with their body's natural sleep cycle (such as sleeping in the day and working at night). This allows sufferers to avoid the need to force themselves into the more common 9 to 5 schedule that their body is unable to maintain, and avoids the need to take stimulants to remain active during the times when their bodies are inclined to rest.

In addition to drug therapy, an important part of treatment is scheduling short naps (10 to 15 minutes) two to three times per day to help control excessive daytime sleepiness and help the person stay as alert as possible. Daytime naps are not a replacement for nighttime sleep, especially if a person's body is natively inclined towards a nocturnal life cycle. Ongoing communication between the health care provider, patient, and the patient's family members is important for optimal management of narcolepsy.

Finally, a recent study reported that transplantation of hypocretin neurons into the pontine reticular formation in rats is feasible, indicating the development of alternative therapeutic strategies in addition to pharmacological interventions.
SEX

In biology, sex is a process of combining and mixing genetic traits, often resulting in the specialization of organisms into a male or female variety (known as a sex). Sexual reproduction involves combining specialized cells (gametes) to form offspring that inherit traits from both parents. Gametes can be identical in form and function (known as isogametes), but in many cases an asymmetry has evolved such that two sex-specific types of gametes (heterogametes) exist: male gametes are small, motile, and optimized to transport their genetic information over a distance, while female gametes are large, non-motile and contain the nutrients necessary for the early development of the young organism.

An organism's sex is defined by the gametes it produces: males produce male gametes (spermatozoa, or sperm) while females produce female gametes (ova, or egg cells); individual organisms which produce both male and female gametes are termed hermaphroditic. Frequently, physical differences are associated with the different sexes of an organism; these sexual dimorphisms can reflect the different reproductive pressures the sexes experience.

Sexual reproduction

Sexual reproduction is a process where organisms form offspring that combine genetic traits from both parents. Chromosomes are passed on from one parent to another in this process. Each cell has half the chromosomes of the mother and half of the father. Genetic traits are contained within the deoxyribonucleic acid (DNA) of chromosomes — by combining one of each type of chromosomes from each parent, an organism is formed containing a doubled set of chromosomes.

The life cycle of sexually reproducing organisms cycles through haploid and diploid stages.
This double-chromosome stage is called "diploid", while the single-chromosome stage is "haploid". Diploid organisms can, in turn, form haploid cells (gametes) that randomly contain one of each of the chromosome pairs, via a process called meiosis. Meiosis also involves a stage of chromosomal crossover, in which regions of DNA are exchanged between matched types of chromosomes, to form a new pair of mixed chromosomes. Crossing over and fertilization (the recombining of single sets of chromosomes to make a new diploid) result in the new organism containing a different set of genetic traits from either parent.

In many organisms, the haploid stage has been reduced to just gametes specialized to recombine and form a new diploid organism; in others, the gametes are capable of undergoing cell division to produce multicellular haploid organisms. In either case, gametes may be externally similar, particularly in size (isogamy), or may have evolved an asymmetry such that the gametes are different in size and other aspects (anisogamy). By convention, the larger gamete (called an ovum, or egg cell) is considered female, while the smaller gamete (called a spermatozoon, or sperm cell) is considered male. An individual that produces exclusively large gametes is female, and one that produces exclusively small gametes is male. An individual that produces both types of gametes is a hermaphrodite; in some cases hermaphrodites are able to self-fertilize and produce offspring on their own, without a second organism.

**Animal**

Most sexually reproducing animals spend their lives as diploid organisms, with the haploid stage reduced to single cell gametes. The gametes of animals have male and female forms—spermatozoa and egg cells. These gametes combine to form embryos which develop into a new organism.

The male gamete, a spermatozoan (produced within a testicle), is a small cell containing a single long flagellum which propels it. Spermatozoa are extremely reduced cells, lacking many cellular components that would be necessary for embryonic development. They are specialized for motility, seeking out an egg cell and fusing with it in a process called fertilization.

Female gametes are egg cells (produced within ovaries), large immobile cells that contain the nutrients and cellular components necessary for a developing embryo. Egg cells are often associated with other cells which support the development of the embryo, forming an egg. In mammals, the fertilized embryo instead develops within the female, receiving nutrition directly from its mother.

Animals are usually mobile and seek out a partner of the opposite sex for mating. Animals which live in the water can mate using external fertilization, where the eggs and sperm are released into and combine within the surrounding water. Most animals that live outside of water, however, must transfer sperm from male to female to achieve internal fertilization.
In most birds, both excretion and reproduction is done through a single posterior opening, called the cloaca—male and female birds touch cloaca to transfer sperm, a process called "cloacal kissing". In many other terrestrial animals, males use specialized sex organs to assist the transport of sperm—these male sex organs are called intromittent organs. In humans and other mammals this male organ is the penis, which enters the female reproductive tract (called the vagina) to achieve insemination—a process called sexual intercourse. The penis contains a tube through which semen (a fluid containing sperm) travels. In female mammals the vagina connects with the uterus, an organ which directly supports the development of a fertilized embryo within (a process called gestation).

Because of their motility, animal sexual behavior can involve coercive sex. Traumatic insemination, for example, is used by some insect species to inseminate females through a wound in the abdominal cavity - a process detrimental to the female's health.

**Evolution**

Sexual reproduction first appeared about a billion years ago, evolved within ancestral single-celled eukaryotes. The reason for the initial evolution of sex, and the reason(s) it has survived to the present, are still matters of debate. Some of the many plausible theories include: that sex creates variation among offspring, sex helps in the spread of advantageous traits, and that sex helps in the removal of disadvantageous traits.

Sexual reproduction is a process specific to eukaryotes, organisms whose cells contain a nucleus and mitochondria. In addition to animals, plants, and fungi, other eukaryotes (e.g. the malaria parasite) also engage in sexual reproduction. Some bacteria use conjugation to transfer genetic material between bacteria; while not the same as sexual reproduction, this also results in the mixture of genetic traits.

What is considered defining of sexual reproduction is the difference between the gametes and the binary nature of fertilization. Multiplicity of gamete types within a species would still be considered a form of sexual reproduction. However, no third gamete is known in multicellular animals.

**Human reproduction**

This article is intended to focus on the biological aspects of sex. If you are interested in articles specifically related to humans and sexuality please see the above links.
Sex determination

The most basic sexual system is one in which all organisms are hermaphrodites, producing both male and female gametes—this is true of some animals (e.g. snails) and the majority of flowering plants. In many cases, however, specialization of sex has evolved such that some organisms produce only male or only female gametes. The biological cause for an organism developing into one sex or the other is called sex determination.

In the majority of species with sex specialization organisms are either male (producing only male gametes) or female (producing only female gametes). Exceptions are common—for example, in the roundworm C. elegans the two sexes are hermaphrodite and male (a system called androdioecy).

Sometimes an organism's development is intermediate between male and female, a condition called intersex. Sometimes intersex individuals are called "hermaphrodite"; but, unlike biological hermaphrodites, intersex individuals are unusual cases and are not typically fertile in both male and female aspects.

Genetic

In genetic sex determination systems, an organism's sex is determined by the genome it inherits. Genetic sex determination usually depends on asymmetrically inherited sex chromosomes which carry genetic features that influence development; sex may be determined either by the presence of a sex chromosome or by how many the organism has. Genetic sex determination, because it is determined by chromosome assortment, usually results in a 1:1 ratio of male and female offspring.

Humans and other mammals have an XY sex determination system: the Y chromosome carries factors responsible for triggering male development. The default sex, in the absence of a Y chromosome, is female. Thus, XX mammals are female and XY are male. XY sex determination is found in other organisms, including the common fruit fly and some plants. In some cases, including in the fruit fly, it is the number of X chromosomes that determines sex rather than the presence of a Y chromosome.

In birds, which have a ZW sex-determination system, the opposite is true: the W chromosome carries factors responsible for female development, and default development is male. In this case ZZ individuals are male and ZW are female. The majority of butterflies and moths also have a ZW sex-determination system. In both XY and ZW sex determination systems the sex chromosome carrying the critical factors is often significantly smaller, carrying little more than the genes necessary for triggering the development of a given sex.
Like humans and other mammals, the common fruit fly has an XY sex determination system.

Many insects use a sex determination system based on the number of sex chromosomes. This is called XX/XO sex determination—the O indicates the absence of the sex chromosome. All other chromosomes in these organisms are diploid, but organisms may inherit one or two X chromosomes. In field crickets, for example, insects with a single X chromosome develop as male, while those with two develop as female. In the nematode *C. elegans* most worms are self-fertilizing XX hermaphrodites, but occasionally abnormalities in chromosome inheritance regularly give rise to individuals with only one X chromosome—these XO individuals are fertile males (and half their offspring are male).

Other insects, including honey bees and ants, use a haplodiploid sex-determination system. In this case diploid individuals are generally female, and haploid individuals (which develop from unfertilized eggs) are male. This sex-determination system results in highly biased sex ratios, as the sex of offspring is determined by fertilization rather than the assortment of chromosomes during meiosis.

**Nongenetic**

For many species sex is not determined by inherited traits, but instead by environmental factors experienced during development or later in life. Many reptiles have temperature-dependent sex determination: the temperature embryos experience during their development determines the sex of the organism. In some
turtles, for example, males are produced at lower incubation temperatures than females; this difference in critical temperatures can be as little as 1-2°C.

Many fish change sex over the course of their lifespan, a phenomenon called sequential hermaphroditism. In clownfish, smaller fish are male, and the dominant and largest fish in a group becomes female. In many wrasses the opposite is true—most fish are initially female and become male when they reach a certain size. Sequential hermaphrodites may produce both types of gametes over the course of their lifetime, but at any given point they are either female or male.

In some ferns the default sex is hermaphrodite, but ferns which grow in soil that has previously supported hermaphrodites are influenced by residual hormones to instead develop as male.

**Sexual dimorphism**

Many animals have differences between the male and female sexes in size and appearance, a phenomenon called sexual dimorphism. Sexual dimorphisms are often associated with sexual selection - the competition between individuals of one sex to mate with the opposite sex.

Antlers in male deer, for example, are used in combat between males to win reproductive access to female deer. In many cases the male of a species is larger in size; in mammals species with high sexual size dimorphism tend to have highly polygynous mating systems—presumably due to selection for success in competition with other males.

Other animals, including most insects and many fish, have larger females. This may be associated with the cost of producing egg cells, which requires more nutrition than producing sperm—larger females are able to produce more eggs. Occasionally this dimorphism is extreme, with males reduced to living as parasites dependent on the female.

In birds, males often have a more colourful appearance and may have features (like the long tail of male peacocks) that would seem to put the organism at a disadvantage (e.g. bright colors would seem to make a bird more visible to predators). One proposed explanation for this is the handicap principle. This hypothesis says that, by demonstrating he can survive with such handicaps, the male is advertising his genetic fitness to females—traits that will benefit daughters as well, who will not be encumbered with such handicaps.

Sex differences in humans include, generally, a larger size and more body hair in men; women have breasts, wider hips, and a higher body fat percentage.
DYNAMICS OF SEXUAL BEHAVIOUR

In lower animals we speak about sexual motivation as a "drive." That is, we state that some internal, innate force pushes the animal to engage in reproductive behavior. Humans don't simply give in to an internal push towards sexual behavior. Instead, human motivation to engage in sexual behavior is due to a complex relationship among several factors.

Most theorists refer to motivation as an inferred need, desire or impulse which initiates, directs and sustains behavior (e.g., Coon, 1997; Wood & Wood, 1996). One group of psychologists calls motivation a factor which explains the relations between stimuli and behavior (Bernstein, Clarke-Stewart, Roy, & Wickens, 1997). By combining these two definitions and applying them to human sexual behavior we could say that sexual motivation is an inferred, internal state influenced by several factors which determines engagement in sexual activity.

Collecting Data on Human Sexuality

Problems with data - Before discussing the elements of sexual behavior, it is important to understand the methods of collecting data that are involved in studies on human sexual behavior. Due to the private nature of the subject matter, most research is performed using surveys, self-reports and volunteers. Self-reports and surveys can be riddled with errors. For example, individuals make errors either intentionally, to give socially-acceptable responses, or accidentally, by forgetting, or even unintentionally because what they think motivates their behavior doesn't (see, e.g., Walster, Aronson, Abrahams, & Rottman, 1966). Finally, volunteers in sex studies are not typically subjects from which one can generalize. Take, for example, the question, "how often do you masturbate?" Volunteers who are willing to answer questions like this are probably more outgoing than the general population. Another important fact to keep in mind is that most studies of sexual behavior are correlational. Studies which show behaviors differentially produced by men and women, heterosexuals versus homosexuals, or members of different nations, are only descriptive since they cannot control for all potential variables. In other words, it is rare that we can assume causation from any of the variables examined in studies of human sexual behavior.

Two landmark studies - With the above information in mind, it is important to introduce two early sources of data on sexual attitudes and behavior. One primary source of self-reported data which has greatly influenced the field of human sexual behavior comes from the Kinsey studies (Kinsey, Pomeroy & Martin, 1948; Kinsey, Pomeroy, Martin, & Gebhard, 1953). These reports were highly influential due to the nature of the questions asked and the large number (several thousand) of subjects who were polled. Kinsey's studies sought to identify, among other facts, what sexual behaviors people engaged in, what age they were when they began engaging in them, and how often they were currently engaging in them. They also indicated that women and men were not very different from each other in terms of sexual physiology. This information raised a furor in the conservative decade of the 1950s (Wade & Tavris, 1996). However, the Kinsey studies also stated that sexual
differences were due to women's lesser sexual capacity. Herein lies the error in descriptive studies that are used to imply causation. Kinsey and associates completely disregarded the effects of culture and learning on their subjects' behavior.

Another landmark study, due to the methodology used, involved actual physiological measurement of sexual responses in male and female volunteers (Masters & Johnson, 1966). This study dispelled the myth that women's sexual response to intercourse was vastly different from men's and indeed showed that both sexes had very similar physiological responses. Their results would indicate that differential subjective responses to sexual intercourse between the sexes were indeed more likely associated with culture and learning.

The data collected in these studies are now rather outdated. Furthermore, critics of the studies state the information is not generalizable since the participants were primarily white, middle-class volunteers (Bernstein, et al., 1997; Wood & Wood, 1996). It was with this information in mind that two recent studies were conducted, one in the United States and one in Great Britain, which gathered data from non-volunteers using extensive interviews (Laumann, Gagnon, Michael, & Michaels, 1994; Wellings, Field, Johnson, & Wadsworth, 1994). These studies were designed to include a representative sample and also allow participants to give in-depth, and anonymous answers (due to the sensitive nature of some of the questions) (Laumann, et al., 1994; Wellings, et al., 1994). Laumann and his associates found a more conservative pattern of sexual behavior than did the Kinsey studies indicating that volunteers are not, in fact, representative of the general population (Bernstein, et al., 1997).

In summary of the method of data collection, there are difficulties associated with collection of data from volunteers and generalization is limited. Superior studies should attempt to choose broader samples and provide participants an opportunity to produce honest, confidential answers. Further, those who analyze studies of human sexual motivation need to beware of drawing causal conclusions where none are warranted.

Factors in Human Sexual Motivation

It is common to try to organize various psychological topics by placing the factors involved into environmental and physiological categories. For example, you would place hormones, a known component of sexual motivation, into the physiological category. But where would you place something like desire for physical pleasure, a frequently cited element in sexual motivation (Abramson & Pinkerton, 1995; Cofer, 1972; Hatfield & Rapson, 1993)? Physical pleasure has both a physiological component (the physical sensations associated with touch) and a subjective psychological component. Where does something subjective like pleasure fit in our breakdown into physiological and environmental components? Pleasure is an emotion (Cofer, 1972), which, according to the Schacter-Singer theory, is a subjective feeling based upon physiological arousal and interpretations of the stimuli that are linked to the arousal (Cornelius, 1996). Thus emotions are both physiologically- and
Physiological psychology – IV Semester

Physiological correlates. This indicates that another category exists into which we might place sexual motivators, but to state this would be to miss the larger issue. The larger issue is that pleasure is influenced by both our cognitions and our physiological functioning. As a factor involved in sexual motivation, it is not unusual to be associated with motivation and to simultaneously be associated with other variables that are themselves identified as related to sexual motivation and which may or may not belong to the same category. Thus, identifying categories and then placing the elements of sexual motivation into discrete categories is a difficult, if not impossible task. Rather than attempting to do so, the current author will identify the variables that have been linked to sexual motivation and identify, where possible, any mediating variables.

Physiological correlates - An analysis of human sexual motivation couldn't proceed without first discussing physiological factors, in particular, hormones. The influence of hormones in sexual behavior is well-supported by research. Both men and women produce estrogens, progestins and androgens, though women produce far more estrogens and progestin and men more androgens (Hokanson, 1969; Leger, 1992). In lower species, hormone levels are almost directly correlated with sexual behavior, however, as one moves up the phylogenetic scale, other elements become involved (Fisher, 1993; Hokanson, 1969). In humans, hormones are also related to sexual desire, but are not the entire story.

In males, a minimum level of testosterone is necessary to maintain normal sexual motivation in males (Leger, 1992). If males' testosterone levels fall below the threshold, sexual motivation is greatly reduced. However, once the threshold level is reached, it no longer predicts sexual behavior. Women's studies also show correlations between hormones and sexual desire (Leger, 1992; Sherwin & Gelfan, 1987; Sherwin, Gelfan, & Brender, 1985), however, the results are inconsistent (Leger, 1992). Since neither increases nor decreases in hormones in either males or females are perfectly correlated with sexual desire, it stands to reason that there must be other factors involved. As Hokanson (1969) concludes, hormones serve the primary purpose of readying the individual for action, but other factors determine whether the individual actually engages in sexual activity.

Another physiological factor in sexual motivation may well be odor and sense of smell. Of all the elements researched, odor and sense of smell have received the least attention, probably because, as Kohl and Francoeur (1995) state, their influence on sexual behavior is difficult to ascertain. However, body odor (i.e., airborne hormones) definitely influences our behaviors. In their review of numerous studies such as synchronization of menstrual cycles of women who live together, and the influence of hormone-scented masks on individuals' ratings of others, Kohl and Francoeur (1995) state that odor must be involved in our sexual behaviors also. Helen Fisher (1993) also agrees that odors may influence sexual behavior and cites that some men in Greece swear by body-odor scented handkerchiefs which they use to lure women into relationships.

Sexual orientation - Our desire to engage in sexual behavior with someone is also influenced by sexual orientation. Sexual orientation refers to the direction of an
individual's sexual attraction (Wood, et al., 1996). Most individuals are heterosexual (Laumann, 1994; Wellings, et al., 1994) which means they are primarily attracted to the opposite sex. Homosexuals are individuals who are attracted to the same sex and bisexuals are attracted to both sexes.

Why are individuals attracted to one sex rather than another? LeVay (1995) believes that most researchers of the topic agree it is a combination of multiple factors including genetic makeup, hormones and social experiences. He further believes that newer studies (e.g., Bailey & Pillard, 1991; Bailey, Pillard, Neale, & Agyei, 1993) indicate that genes are perhaps more influential than the other factors. Studies indicate that the percentage of individuals who call themselves homosexual is quite small, ranging from about .5% to 2.8% (Laumann, 1994; Wellings, et al., 1994). This estimate is significantly lower than the rates given in the problematic Kinsey Reports (1948; 1953).

In his review of several studies on the prevalence of homosexuality, LeVay (1995) states that it is best to keep an open mind towards reviewing new evidence since changing attitudes and beliefs appear to be linked to self-stated homosexuality. What he was referring to was the indication that individuals are more likely to express their gay behavior within their own culture as that culture becomes more accepting of homosexuality. Thus it is apparent that culture influences the expression of one's sexual orientation which in turn influences sexual motivation.

Pleasure - As mentioned earlier, pursuit of erotic pleasure is a primary reason to engage in sexual behavior (Abramson et al., 1995; Hatfield et al., 1993). Kinsey and colleagues (1948; 1953) found that children between the ages of 2 and 5 years of age spontaneously touch their genitals. At this age, one could not argue that this sexual behavior is learned or designed to contribute to reproduction. Abramson and Pinkerton (1995) point out that the pleasure of sexual behavior is physiologically and psychologically-based and that the sex organs do not exist merely to guarantee reproductive behavior. As an example, they cite the female orgasm, uncommon during vaginal penetration, but very common by more direct means of clitoral stimulation. In other words, sexual pleasure does not occur merely to ensure procreation. We engage in sexual behavior because it is enjoyable. However, as will be reviewed later, what is considered pleasurable, may well be influenced by one's interpretation of the stimuli.

Cognitions - How a stimulus is interpreted influences how individuals respond to that stimulus. Zellman and Goodchild (1983) surveyed 400 teenagers and found that the behaviors girls felt conveyed romantic interest were the same actions boys considered invitations to sex. Since societies create very different gender roles for men and women, differences in interpretation of the same data are bound to occur (Wade, et al., 1996). Wade’s comments indicate that culture influences sexual behaviors, not only through performance of behaviors that are considered appropriate, but also through interpretation of those behaviors.

Cognitions and arousal - Based upon the results of surveys such as the Kinsey studies (1948; 1953), men have been considered to be more sexually responsive than
women. Early studies comparing men and women's subjective responses to erotic films supported that theory. However, when studies were conducted comparing male and female physiological responses to male-produced, male-intended erotic films, researchers found that men and women actually experienced the same physiological arousal (Laan, Everaerd, Van Bellen, & Hanewald; 1994). When participants were asked to express their feelings about the stimuli, men reported sexual arousal and positive affect, yet women reported disgust and lack of arousal. In other words, both men and women experienced the same physiological arousal but different subjective arousal. When women viewed an erotic film produced by women for women, the female participants showed the same physiological arousal as they did to male-produced films, but reported significantly greater sexual arousal, interest and positive affect. As interpreted by the researchers, the difference was due to how women interpreted the content of the film. Essentially, this study indicated that interpretation of the stimuli is of great importance in subjective feelings of sexual arousal. Cognitions affect sexual arousal in another fashion. According to Kalat (1996), inhibition of arousal can occur in individuals who believe that sex is shameful. These individuals experience sexual arousal, but have difficulties achieving sexual orgasm because of their thoughts.

Palace and Gorzalka (1992) studied sexually functional and dysfunctional women and found that cognitions and physiological arousal were simultaneously important in sexual arousal. They hypothesized that cognitions and physiological arousal comprise a feedback loop to determine overall sexual arousal. These many studies indicate that the thoughts individuals have regarding various stimuli impact individuals sexual motivation through influencing their arousal or their interpretations of behavior.

Attraction - Numerous elements have been identified as playing a role in attraction. For example, attraction is a function of proximity (how frequently you cross paths with someone), familiarity and similarity (e.g. in looks, or attitudes) (Kalat, 1996). This has been supported both with studies of attraction to friends and to romantic partners.

Playing hard-to-get also contributes to human's attraction to one another (Hatfield, Walster, Piliavin & Schmidt, 1988). Apparently individuals make attributions about potential significant others based upon how quickly that person returns a show of interest. Those who are easily attained are less attractive than those who are more difficult too attain due to the traits the relationship-seeker attributes to her. For example, relationship seekers fear that easy-to-get women might display inappropriate behaviors in public. However, a hard-to-get woman who indicates interest in the relationship-seeker has positive traits attributed to her such as warmth and friendliness.

Another overwhelmingly important element in attraction is physical attractiveness. As stated previously, research between attitudes and behaviors are not always consistent. Research on what individuals find attractive in potential dates provides further evidence for this inconsistency in human sexual behavior. Although subjects stated that physical attractiveness was one of the least important elements in their
attraction to someone else, in actual experiments using blind dates, the only factor which predicted whether subjects desired a second date with the same person was the attractiveness of the blind date (Walster, Aronson, Abrahams, & Rottman, 1966). This was true for both male and female participants of the study. In a study on physical attractiveness and relationship length, the factor which best predicted whether couples would remain together nine months after they began dating was the similarity in their physical attractiveness (White, 1980). This "matching" phenomenon in which people tend to select mates that match them in terms of physical attractiveness, has been replicated and expanded upon with consistent results (Feingold, 1988). It might seem that we learn to appreciate beauty from the culture that we are born into, yet studies of pre-school children indicate that they too, prefer attractive classmates and also make attributions based on classmates' physical characteristics (Dion & Berscheid, 1971).

Attraction to others is yet another element of sexual motivation that has its roots in both nature and nurture -- it is obviously innate to seek out attractive others, yet we still lean towards mates who are more similar to us, an apparent influence of culture and learning in addition to an inherited predisposition.

Learning - Learning is, of course, highly influential in sexual motivation. We copy the behaviors of those we respect and admire. We learn to repeat behaviors that are rewarded (and sexual behavior is rewarding for most) and we learn to discontinue behaviors that have negative outcomes.

Conditioning is believed to influence sexual motivation. Certain stimuli may increase sexual arousal. For example, one might become sexually aroused by candlelight due to the learned association with sexual pre-encounters such as a romantic, candlelight dinner. It has also been proposed that conditioning accounts for sexually dysfunctional behaviors and sexual deviance (O'Donohue & Plaud, 1994). For example, a pedophile (person sexually aroused by children) might have been accidentally sexually aroused in the presence of a child. Principles of conditioning indicate he would seek this same combination of factors in the future in order to achieve the same pleasurable circumstances again. In her study of sexual motivators, Barbara Leigh (1989) states that fear of rejection, a learned component, is indeed the reason most often given by single men for not engaging in sex.

Matching theory (Carli, Ganley, & Pierce-Otay, 1991), which states that individuals within couples are frequently very similar in attractiveness ratings, is easily understood using the principles of conditioning. For example, an average-looking man who is rebuffed whenever he approaches beautiful females should reduce his attempts to interact with beautiful women. Similarly, he should rebuff less-attractive women if he could interact with more attractive women. Who he ultimately couples with should be very similar in looks due to the conditioning of each person's partner-choosing behaviors.

Conditioning as a theory to explain sexual deviance and dysfunction is not without its critics. O'Donohue and Plaud (1994) examined several studies which used behavioral and aversion therapy to change sexual behaviors. Due to methodological
problems in the studies they examined, they believe that conditioning plays a much smaller role in sexual motivation than previously believed. Thus conditioning may play some role in the sexual motivation, but how much of a role it plays is not clear.

Culture - As mentioned throughout this essay, culture determines what behaviors are gender appropriate, what behaviors may or may not be performed in public, and what behaviors are considered sexually arousing. Yet culture and learning are inextricably tied together. An individual could not acquire his or her culture's norms without learning taking place. Conversely, there is very little one could learn which is not influenced by culture. For example, when we model the behaviors of individuals from our own society, we are copying behaviors that are more than likely already societally-influenced. If we view behaviors performed by individuals from another culture, we do so through lenses already colored by our society's influence. Hence any learning we might acquire from a culturally-different person is mediated by our own culture first.

Attitudes and Culture - Attitudes are defined as relatively stable evaluations of a person, object, situation or issue (Wood et al., 1996). Studies have shown that behaviors normally considered proper in one culture, may be improper or unarousing in another. In other words, attitudes towards sexual behaviors are culturally learned. For example, some cultures find kissing repulsive (Tiefer, 1995) while other cultures insist on same-gender sex as a rite of passage into adulthood (Herdt, 1984).

It is still noted, even in newer surveys in the United States (e.g., Laumann et al., 1994), that men and women have different attitudes toward sexual behaviors. For example, men are more interested in a variety of sexual behaviors, such as group sex, than are women. These divergences are undoubtedly, as mentioned earlier, a function of the gender roles each society impresses upon its members. A comparison of Swedish and American college students sought to examine if indeed the difference in men's and women's attitudes could be definitively tied to culture, rather than inherent gender differences (Weinberg, Lottes, Shaver, 1995). Specifically, it was believed that men and women in Sweden would have more convergent and relaxed attitudes toward sexual behaviors than the American participants. Sweden is generally known to have more relaxed sexual standards. It is believed that this is due, in part, to several years of mandatory sex education and the relatively equal power that women have in society. The study indeed showed that Swedish men and women had very similar attitudes towards sexual behaviors. Americans, as expected, had very different attitudes about what constituted appropriate sexual behaviors. While the current author cautioned earlier against drawing causal conclusions from a descriptive study such as this, the information further indicates that culture is associated with differences in sexual attitudes.

The influence of learning on sexual motivation is quite profound. Attraction, cognitions, and sexual orientation, variables mentioned previously, are also influenced by learning. Thus a key component which determines the level of our sexual motivation is learning.
HORMONES AND SEXUAL BEHAVIOUR

Sex hormones are steroids (fat soluble compounds) that control sexual maturity and reproduction. These hormones are produced mainly by the endocrine glands. The endocrine glands in females are ovaries and those in males are testes. While both males and females have all types of hormones present in their bodies, females produce the majority of two types of hormones, estrogens and progesterone, while males produce mainly androgens such as testosterone. Most androgens produced by females are converted to estrogens and some androgens in males are also converted to estrogens. Sex hormones are synthesized from cholesterol (a fatty acid) and other compounds and secreted throughout a person's lifetime at different levels. Their production increases at puberty and normally decreases in old age.

Hormone Production

The production of hormones is a complex process. At puberty, the brain's hypothalamus gland produces increased amounts of gonadotropin-releasing hormone. This hormone stimulates the nearby pituitary gland to release two other hormones: follicle-stimulating hormone (FSH) and luteinizing hormone (LH). Finally, these two hormones signal the sex glands (gonads) to produce the sex hormones.

Female Reproductive Cycle

Females produce three estrogens: estradiol, estriol, and estrone. These estrogens stimulate growth of the ovaries and begin preparing the uterus for pregnancy. Estrogens also control the body's secondary sex characteristics, including breast and pelvic development and the distribution of fat and muscle. Progesterone maintains uterine conditions during pregnancy. It also acts on the central nervous system in a way that isn't yet understood.

During the monthly reproductive cycle, FSH stimulates growth of an ovarian body called the graafian follicle. The follicle encloses the egg. LH aids in the rupture of the follicle, sending the egg to the fallopian tubes. LH also promotes growth of the corpus luteum (a yellow, progesterone-secreting mass of cells that forms from an ovarian follicle after the release of a mature egg) as the ovary prepares to release the egg into the uterus.

If no pregnancy occurs within 10-12 days, the corpus luteum withers and the uterus sheds the blood supply that was formed to nourish a fetus. This shedding of the uterine lining and blood supply is called menstruation (the period). The production of estrogens and progesterone drops dramatically, and the cycle begins again.

Male Reproduction

In males, LH stimulates the development of the testes. The testes produce the androgens testosterone and androsterone. When FSH activates the testes' sperm-
forming cells, testosterone maintains the process of forming sperm. This is the ten-week process results in sperm constantly ready for release by ejaculation from the penis. The androgens also promote the secondary sex characteristics of muscle growth, lowered voice range, the Adam's apple, and increased body hair.

THE DEVELOPMENTAL ASPECTS OF SEXUAL BEHAVIOR

Adult human sexual behavior results from a long, complex, and often hazardous development. Until about the beginning of our century, sex was believed to be largely instinctive, i.e., the result of biological heredity. Most people simply assumed that, at some time after puberty, sexual desire and sexual activity "came naturally" to every male and female, and that no social conditioning was involved. Sexuality was a "force of nature" which appeared suddenly and then, all by itself, found its full "natural" expression. Society could suppress this force, but had no part in shaping it.

The first serious challenge of this traditional view came from Sigmund Freud (1856-1939) and his followers. In his practice as a physician, Freud encountered many patients suffering from what was then called hysteria, i.e., a severe disability, such as paralysis or blindness, for which no physical cause could be found. Indeed, according to all standard medical tests, the patients should have been able to function normally. After interviewing these men and women over long periods of time, Freud noticed that their disabilities seemed somehow related to painful or disturbing childhood experiences. He further discovered that these early experiences, of which the patients were no longer consciously aware, were of a sexual nature. Finally, he found that once the experiences were again clearly remembered and understood by the suffering adults, their mysterious disabilities disappeared.

On the basis of these and other findings, Freud gradually developed his psychoanalytic theory which since then has had a profound influence on European and American thought. However, when it was first proposed the theory was greeted with outcries of public indignation. It was plainly inconceivable to most people that a long forgotten childhood experience should continue to have any decisive influence on a person's adult life, and they were positively outraged at the suggestion that such experiences were sexual. In their view, children were "innocent" and "by nature" utterly incapable of sexual feelings or responses. For Freud, on the other hand, the sexuality of children and, indeed, infants was an indisputable fact of the utmost importance.

According to psychoanalytic thinking, there is a basic sexual instinct or drive present universally in all human beings from the moment of birth. This instinct, which strives for sensual pleasure, is at first diffuse and attains its eventual proper direction and focus only through a process of "psychosexual maturation". Human infants first seek their gratification in a direct, unhampered, and undiscriminating way, until they learn to modify and control their instinctual urges through social conditioning. Human sexuality thus unfolds under the influence of two opposing forces: the "pleasure principle" and the "reality principle". In other words, a child's
personality development can be described as a contest between biological drive and cultural constraint. This contest proceeds in three major steps, which are coordinated with the child's physiological maturation: the oral, anal, and phallic phases.

In the oral phase (from Latin os: mouth), the chief source of pleasure is the mouth. As it sucks the mother's breast, the infant finds not only nourishment, but deep physical and psychological satisfaction. In this phase, the mouth also serves as an organ of exploration. The infant puts everything in its mouth in order to get to know it. "Taking in" the world is the first attempt at mastering it.

In the following anal phase (from Latin anus: the rectal opening), the main source of sensual gratification shifts from the mouth to the anal area. The child now begins to gain control over the bowel movements and thereby, indirectly, over the attending adults, whom it can now please or displease by eliminating or withholding feces. At the same time, the child learns to grant or withhold affection, say yes or no, in short, to master the world by "holding back" and "letting go."

While the oral and anal phases, which extend roughly through the first three years of life, are the same for both sexes, the now following phallic phase (from Greek phallos: penis) brings an increasing awareness of sexual differences and of the male and female sex organs. The most pleasurable zones of the body are no longer the mouth or the anus, but the penis (for boys) and the clitoris (for girls). This is the phase in which children become actively curious about their surroundings, poke their fingers into things, look inside their toys by taking them apart, and also investigate their own and each other's bodies. The most important aspect of this phase, however, is the development of the so-called Oedipus complex, i.e., the child's erotic attachment to the parent of the opposite sex and a feeling of rivalry toward the parent of the same sex. (The term "Oedipus complex" alludes to the legendary Greek king Oedipus who unknowingly killed his father and married his mother.) For example, it is the rule for a four-year-old boy to be deeply in love with his mother. She is, for him, the only woman he knows and cares to know. However, this woman already has a husband—the father. The boy is jealous of him and would like to push him aside in order to assume his position. This desire is usually expressed openly and spontaneously, as for instance when the boy climbs into his mother's bed announcing: "When I grow up, I'll marry you". Obviously, this situation can be compared to that of King Oedipus, although there is one important difference: Oedipus actually did remove his father forever from his mother's side, and he did marry her. The normal development of a child takes another course. The boy replaces his desire to marry his mother with the wish to marry a woman like his mother, and his urge to take the place of his father turns into the determination to become a man like his father. The boy can make this transition easily, if the father provides an attractive model to follow, and if he actively encourages his son to become a man. At the same time, it is the mother's task to help her son realize that she has already chosen and is no longer available as a sexual object. These parental attitudes will lead the boy to seek his sexual gratification elsewhere. (In the case of a girl, the development takes the opposite course: she loves her father and is jealous of
her mother. The respective psychoanalytic term is "Electra complex", after Electra, a legendary Greek princess who, after the death of her beloved father, helped kill her mother who had murdered him. [It must be pointed out, however, that the notion of an Electra complex was advanced by some of Freud's followers, not by Freud himself, who did not subscribe to it.]

Freud believed that every child normally progressed from the oral to the anal and finally to the phallic phase, unless some negative influence interfered with this development. However, if the particular needs of any one of these phases were either unfulfilled or gratified to excess, the child could become "fixated" and thus hampered in its psychosexual growth. For example, a child's too rigid or overindulgent toilet training could lead to a fixation at the anal level of satisfaction. As an adult, such a child would then turn into an "anal character", i.e., a person who is obsessed with discipline, order, and cleanliness, who hoards money (the unconscious equivalent of feces, which can be "withheld" from others) or who prefers anal stimulation to all other forms of sexual intercourse. An "oral character," on the other hand, would continue to depend mainly on his mouth even for sexual satisfaction, or he might become a compulsive eater, smoker, or drinker.

Children who do not become fixated in this manner eventually reach "genital maturity." That is to say, after a so-called latency period, during which obvious sexual interests seem largely suspended, the sexual instinct reawakens with puberty and seeks satisfaction through genital intercourse. Oral and anal stimulation may still be enjoyed to a limited extent, but they now take second place to coitus which, for adults, is the one truly "mature" form of sexual expression.

As can be gathered from this brief and superficial sketch, Freud's concept of human sexuality is extraordinarily broad. Indeed, he stretches this concept to cover responses and activities that, before him, were considered to be completely nonsexual. Even today, the average layman may find it difficult to see any sexual implications in a baby's suckling on the mother's breast, or in an adult's compulsive eating habits. As a matter of fact, many scientists also continue to challenge the psychoanalytic view. For example, anthropologists who have studied various primitive cultures suggest that the Oedipal conflict may not be a universal human experience. Social psychologists have raised serious doubts as to whether an innate sexual drive or instinct even exists at all. Finally, many behaviorists and learning theorists maintain that Freud's whole theory is unnecessarily complex and that there are simpler (and therefore more convincing) explanations of human behavior. Moreover, the fact remains that this theory has never been scientifically tested on a sufficient scale to be proven or disproven.

It is therefore obvious that Freud's teachings cannot simply be accepted as dogma, but have to be studied and evaluated within the cultural context of his particular time. Eventually, such a critical evaluation may even lead to a better understanding of our own post-Freudian culture. Freud was one of history's most brilliant and uncompromising thinkers as well as a great writer, and his works (which comprise
24 volumes in their English language edition) contain deep insights not only into human sexuality, but also into the history and character of Western civilization.

Some of Freud's disciples and followers, however, have shown little allegiance to his critical spirit, but instead have converted elements of his theory into convenient tools of social control. As a consequence, the liberating impulse of psychoanalytic thinking has often been obscured and perverted.

This tendency has been particularly noticeable in America where, contrary to Freud's own intentions, some of his hypotheses have been used to justify the persecution and oppression of sexual minorities.

The scope of the present book does not permit a detailed discussion of the various psychoanalytic schools or even of Freud's original theory. On the other hand, experience has shown that this theory does not lend itself to simplification and popularization. Where such simplifications have been attempted, they have all too often led to serious misunderstandings. It is true that Freudian terms have long since entered our everyday language, and that today we can read about the "Oedipus complex" and "the subconscious" in newspapers and popular magazines. We hear of "Freudian slips", "ego," "superego", "libido", and "sublimation" in movies, on radio, and on television. Nevertheless, when taken out of their theoretical context, these words can create considerable confusion, and, among laymen, they are usually misapplied.

Fortunately, in the meantime, it has become very well possible to describe the development of sexual behavior without any reference to psychoanalytic concepts. Recent empirical sex research has provided us with a great deal of new information as to how people learn to act the way they do. We have also gained some understanding of the statistical frequency of certain behaviors. This, in turn, has forced us to reexamine many traditional assumptions about the "nature" of human sexuality. As a result, we are now able to take another entirely fresh look at the subject.

Around the middle of our century, Alfred C. Kinsey and his associates of the Institute for Sex Research in Bloomington, Indiana, published two monumental studies of human sexual behavior which were based on personal interviews with thousands of individuals from all age groups and all walks of life. Previously, such studies had always been forced to rely on small samples of medical patients or sex offenders, and the full range of "normal" sexuality was therefore largely unknown. Kinsey's work provided the first reliable statistical data on the behavior of healthy, average men and women. (Sexual Behavior in the Human Male, 1948, and Sexual Behavior in the Human Female, 1953.)

At about the same time, Clellan S. Ford and Frank A. Beach, an anthropologist and a psychologist, wrote a cross-cultural study in which they compared the patterns of sexual behavior in 191 different societies. (Patterns of Sexual Behavior, 1951.) More recently, John Money of Johns Hopkins University and some fellow researchers have
conducted extensive research into sexual malformations and the problems of gender identity. (Sex Errors of the Body, 1968; Man and Woman, Boy and Girl, 1973; and Sexual Signatures, 1975.) In addition, William H. Masters and Virginia E. Johnson of the Reproductive Biology Research Foundation in St. Louis, Missouri, have carried out a thorough scientific investigation of human sexual functioning and malfunctioning. (Human Sexual Response, 1966; Human Sexual Inadequacy, 1970; and The Pleasure Bond, 1975.)

These and many other new studies of human sexuality owe little or nothing to psychoanalytic theory, and on certain issues they sharply disagree with Freud. Nevertheless, they confirm at least some of his basic contentions. For example, it is today generally accepted that sexual behavior does not "come naturally" to human beings, but is, in fact, shaped by social conditioning. It is further quite obvious that this conditioning has different goals and produces different results in different societies. There is also no longer any doubt that children are capable of sexual responses, and that certain early childhood experiences can have a crucial influence on a person's later sexual development.

Unfortunately, it is less clear than ever what all this social conditioning really means. The physician Freud had been mainly concerned with helping his patients, and for him and his followers sexual childhood experiences could easily be defined as either beneficial or harmful according to a single criterion: they were beneficial if they furthered the individual's "genital maturity," and they were harmful if they hindered or prevented it. Sexual behavior was thus described in terms of maturity and immaturity, health and sickness, norm and deviation.

In the meantime, however, sex researchers have become much more cautious. They now realize that sexual norms change a great deal from one time and place to another and that, in regard to human behavior, terms like "maturity" and "health" are value judgments rather than judgments of fact. In Freud's time, sexual health and maturity were believed to manifest themselves in a monogamous marriage devoted to the procreation of children. Sex, love, marriage, and procreation were therefore seen as inseparable. Indeed, sexual activity without any of its "socially redeeming" features was considered evil: sex without love (masturbation and prostitution), sex without marriage (premarital and extramarital intercourse), sex without procreation (childhood sex play, sex after the menopause, homosexuality). Today, we know that this particular value system is far from universal, and that it was typical only of the Western middle classes during a certain historical period. Medieval farmers or feudal lords, for example, lived by an entirely different value system, and the same must be said for people in the traditional African and Asian cultures. Finally, we see that in our own society more and more men and women are breaking away from their inherited middle class morality and are searching for new values. Under these circumstances, we have to be very careful about establishing any specific goals, norms, or standards for sexual behavior. Our first obligation is simply to understand it, and we therefore need an objective description in morally neutral terms.
Objectivity is not the only requirement, however. The description also has to be clear and precise, and this is a difficult task in itself. Nowhere is the terminological confusion greater than in the area of human sexuality. In fact, this confusion already begins with the very concept of sex.

We know that the term "sex" somehow refers to the difference and the attraction between males and females, but the extent of this difference and the character of this attraction are still largely disputed. Nevertheless, modern research has done a great deal to clarify the issues, and particularly the study of childhood development has provided us with some very valuable clues. It has been observed, for instance, that hermaphroditic children (i.e., children who are "sexually unfinished") may be raised as either boys or girls and develop all the "appropriate" attitudes, including their choice of sexual partner. To put it another way, children whose sex is misdiagnosed at birth learn to identify with the sex that is assigned to them. Furthermore, once a certain critical period has passed, this identification is permanent. Even if the mistake is later discovered, it cannot be corrected. After a certain age, a boy raised as a girl will continue to consider himself female and, in most cases, feel sexually attracted to males, while a girl raised as a boy will continue to consider herself male and, in most cases, feel sexually attracted to females. In other words, if "sex" has to do with the contrast between male and female, then a person's "sexual" development has at least three aspects:

1. The male or female characteristics of the body (physical sex),
2. the social role as male or female (gender role), and
3. the preference for male or female sexual partners (sexual orientation).

A great deal of confusion can be avoided if these three aspects of human sexuality are considered separately, and it seems useful, therefore, to keep the following definitions firmly in mind:

**Physical Sex**

Physical sex is defined as a person's maleness or femaleness. It is determined on the basis of five physical criteria: chromosomal sex, gonadal sex, hormonal sex, internal accessory reproductive structures, and external sex organs. People are male or female to the degree in which they meet the physical criteria for maleness or femaleness. Most individuals are clearly male or female by all five physical criteria. However, a minority fall somewhat short of this test, and their physical sex is therefore ambiguous (hermaphroditism).

**Gender Role**

Gender role is defined as a person's masculinity or femininity. It is determined on the basis of certain psychological qualities that are nurtured in one sex and discouraged in the other. People are masculine or feminine to the degree in which
they conform to their gender roles. Most individuals clearly conform to the gender role appropriate to their biological sex. However, a minority partially assume a gender role that contradicts their biological sex (transvestism), and for an even smaller minority such a role inversion is complete (transsexualism).

**Sexual Orientation**

Sexual orientation is defined as a person's heterosexuality or homosexuality. It is determined on the basis of preference for sexual partners. People are heterosexual or homosexual to the degree in which they are erotically attracted to partners of the other or same sex. Most individuals develop a clear erotic preference for partners of the other sex (heterosexuality). However, a minority are erotically attracted to both men and women (ambisexuality), and an even smaller minority are attracted mainly to partners of their own sex (homosexuality). It is important to realize that not only physical sex but also gender role and sexual orientation are matters of degree, and that they may be independent of each other. Thus, they may appear in different combinations in different individuals. A few examples of physical males may illustrate the point:

- **Male — Masculine — Heterosexual**

  A person of male sex usually adopts the masculine gender role and develops a heterosexual orientation. Such an individual then conforms to our image of the "typical" male.

- **Male — Masculine — Homosexual**

  A person of male sex who has adopted the masculine gender role may very well develop a homosexual orientation. Such an individual may then look and behave like any other "typical" male in all respects but one—his choice of sexual partner.

- **Male — Feminine — Heterosexual**

  A person of male sex may adopt the feminine gender role. Such an individual may then try everything possible (including a "sex change operation") to make the body conform to the feminine self-image. In this case, an erotic preference for males, would, of course, have to be considered heterosexual.

- **Male — Feminine — Homosexual**

  A person of male sex may adopt the feminine gender role and try everything possible to make the body conform to the feminine self-image. If such an individual then also developed an erotic preference for females this sexual orientation could only be called homosexual.

Obviously, the last two examples represent rather extreme cases, and it should be remembered that even where a man identifies with the feminine gender role, this
identification does not have to be complete. He may adopt that role only partially or occasionally, and he may not consider himself female at all. He may only cultivate feminine mannerisms and prefer feminine clothes or feminine occupations. It should further be noted that, in any or all of these cases, he may be heterosexual, ambisexual, or homosexual. In short, the four examples given here are not meant to establish new norms, classifications, or human stereotypes. They should simply be taken as a hint at the wide range and astonishing variety of human life. We must never forget that each individual person is unique, that few people ever fall into tidy sexual categories, and that there are countless shades and gradations.

Indeed, the very distinction between physical sex, gender role, and sexual orientation can help us to avoid hasty judgments and unwarranted generalizations. It can remind us, for instance, that not every effeminate man is a homosexual, and that not all homosexuals are effeminate. It also makes clear why somebody can think of himself as less than a "real man" when he knows very well that he is male. Finally, it shows us the possible extent and the limitations of a "sex change".

Once we realize how social conditioning influences our development as males and females, we have taken the first step toward understanding the development of our "sexual" behavior. Moreover, we can now make another useful distinction. In the preceding text, we have used the term "sexual orientation" very broadly to indicate an erotic preference for male or female partners. However, most people know that erotic preferences are usually much more specific. For example, a "typical" male is by no means attracted to all females, but only to those of a certain age, height, weight, hair color, etc. In fact, he may prefer not only a special type of female, but a special type of sexual intercourse under special conditions. These particular preferences and tastes within the general framework of a person's sexual orientation are best described as personal sexual interests. They too are the result of conditioning.

It is, of course, true that all human beings are born with the capacity to respond to many kinds of sensual stimulation. We also know that erections of the penis, the lubrication of the vagina, muscular contractions, and rhythmic pelvic movements can be observed in very young infants. In short, nobody has to learn the physiological responses that lead to orgasm. Still, everybody does learn under which specific circumstances these responses may be triggered. From their first years of life, children learn to react positively to certain stimuli and negatively to certain others. As a result of their personal experiences, they then acquire their individual behavior patterns. Thus, as already mentioned, human beings learn to be masculine or feminine, heterosexual or homosexual. They also learn to masturbate, to engage in coitus, and to feel happy or guilty about sex. They learn to prefer younger or older partners, blondes or brunettes, Europeans, Africans, or Asians. Some persons develop a strong attachment to one particular partner and are unable to respond to anyone else; others change their partners frequently. Some like variety in their erotic techniques; others stick to a single approach throughout their lives. Some men and women depend on complete privacy for their sexual responsiveness; others find additional stimulation in the knowledge that they are being watched. There are
people whose sexual advances are passionate, inconsiderate, and even brutal, and there are others who enjoy making love slowly, gently, and deliberately. Certain individuals may ever prefer solitary masturbation to any sexual intercourse, and certain others may seek sexual contact with animals.

Since these and many other personal sexual interests, choices, and preferences are developed through learning, they may appear natural, reasonable and, indeed, inevitable to the person involved. Even behavior which seems outrageous, fantastic, meaningless, or absurd to most people may be meaningful and rewarding to a certain individual because of the way in which he has been conditioned. A man who becomes sexually excited at the sight of a wooden horse may merely reflect some early experience in which sexual pleasure was associated with a merry-go-round, and his behavior may be no more difficult to explain than that of another man who becomes aroused while watching a striptease show. The latter response may have a certain advantage over the former, but neither of them should be of any social concern. A great number of people, however, seem to find comfort in the assumption that there is only one right way of doing anything. They take no joy in the infinite variety of human sexual behavior, but instead see it as an affront to their sense of stability and order. Such people are always tempted to set up their own preferences as universal norms, and to condemn everybody who disagrees with them.

On the other hand, it is clear that every society has a right to protect itself against sexual acts that involve force or violence, or which take place in front of unwilling witnesses. Such acts may be satisfying to the person who commits them, but since they obviously violate fundamental rights of others, they are socially unacceptable. Traditionally, they have always been treated as serious crimes which deserved severe punishment. However, in modern times there has been a growing tendency to view such acts as symptoms of mental illness rather than crimes. By the 19th century, psychiatrists began to argue in court that certain sexual offenders should not be sent to prison but to a mental hospital, and that they should not be punished but cured. In support of this argument, numerous attempts were made to classify sexual acts as normal or abnormal, healthy or sick. The best known of these attempts is perhaps that of Richard von Krafft-Ebing, a Viennese psychiatrist. In his book Psychopathia Sexualis (1886), he presented a long list of supposedly pathological sexual interests, for which he invented a number of rather fanciful special terms. Since then many other psychiatrists have followed his example, the lists have grown longer, and the special terms have become even more outlandish and exotic. Unfortunately, these lists usually do not restrict themselves to socially harmful acts, but include many types of behavior that are merely uncommon, unconventional, or disliked by the writer. Indeed, to this very day studies on "sexual psychopathology" have rarely been more than moralistic tracts in scientific disguise. They are important mainly as historical documents which reflect the sexual standards and moral obsessions of a particular time. (For further details, see "Conformity and Deviance.")
Nevertheless, it cannot be denied that some people develop behavior patterns which are unacceptable even to themselves. For example, a man may realize that his sexual acts are harmful to others, but he may have great difficulty controlling himself. In another case, such compulsive behavior may not be antisocial, but since it creates a sense of helplessness in the individual, he may still find it highly disturbing. There are also some men and women who feel guilty and apprehensive about any kind of sexual activity, and some others are so self-conscious and inhibited that their sexual responses are inadequate.

It is fair to say that all of these people are sexually maladjusted. In other words, their particular learning experiences have rendered them incapable of full sexual communication. They either have become insensitive to the needs of others, or are unable to fulfill them. They cannot relate to their sexual partners as complete persons, or adapt their own desires to different circumstances and situations. Instead, they seem condemned to repeat the same frustrating and self-defeating acts. In short, they fail to achieve the full amount of physical and emotional satisfaction of which most human beings are capable.
MODULE 2
THE PHYSIOLOGICAL BASIS OF EMOTION

THE NEURAL BASIS OF EMOTION- THE LIMBIC SYSTEM

Emotion involves the entire nervous system, of course. But there are two parts of the nervous system that are especially significant: The limbic system and the autonomic nervous system.

The Limbic System

This is the part of the brain that appears to be most directly involved in human emotion-regulation problems. The limbic system is a complex set of structures that lies on both sides of the thalamus, just under the cerebrum. It includes the hypothalamus, the hippocampus, the amygdala, and several other nearby areas. It appears to be primarily responsible for our emotional life, and has a lot to do with the formation of memories. In this drawing, you are looking at the brain cut in half, but with the brain stem intact. The part of the limbic system shown is that which is along the left side of the thalamus (hippocampus and amygdala) and just under the front of the thalamus (hypothalamus):

Hypothalamus

The hypothalamus is a small part of the brain located just below the thalamus on both sides of the third ventricle. (The ventricles are areas within the cerebrum that are filled with cerebrospinal fluid, and connect to the fluid in the spine.) It sits just inside the two tracts of the optic nerve, and just above (and intimately connected with) the pituitary gland.

The hypothalamus is one of the busiest parts of the brain, and is mainly concerned with homeostasis. Homeostasis is the process of returning something to some “set point.” It works like a thermostat: When your room gets too cold, the thermostat conveys that information to the furnace and turns it on. As your room warms up and the temperature gets beyond a certain point, it sends a signal that tells the furnace to turn off.

The hypothalamus is responsible for regulating your hunger, thirst, response to pain, levels of pleasure, sexual satisfaction, anger and aggressive behavior, and more. It also regulates the functioning of the autonomic nervous system (see below), which in turn means it regulates things like pulse, blood pressure, breathing, and arousal in response to emotional circumstances.

The hypothalamus receives inputs from a number of sources. From the vagus nerve, it gets information about blood pressure and the distension of the gut (that is, how
full your stomach is). From the reticular formation in the brainstem, it gets information about skin temperature. From the optic nerve, it gets information about light and darkness. From unusual neurons lining the ventricles, it gets information about the contents of the cerebrospinal fluid, including toxins that lead to vomiting. And from the other parts of the limbic system and the olfactory (smell) nerves, it gets information that helps regulate eating and sexuality. The hypothalamus also has some receptors of its own, that provide information about ion balance and temperature of the blood.

In one of the more recent discoveries, it seems that there is a protein called leptin which is released by fat cells when we overeat. The hypothalamus apparently senses the levels of leptin in the bloodstream and responds by decreasing appetite. It would seem that some people have a mutation in a gene which produces leptin, and their bodies can’t tell the hypothalamus that they have had enough to eat.

The hypothalamus sends instructions to the rest of the body in two ways. The first is to the autonomic nervous system. This allows the hypothalamus to have ultimate control of things like blood pressure, heartrate, breathing, digestion, sweating, and all the sympathetic and parasympathetic functions.

The other way the hypothalamus controls things is via the pituitary gland. It is neurally and chemically connected to the pituitary, which in turn pumps hormones called releasing factors into the bloodstream. As you know, the pituitary is the so-called “master gland,” and these hormones are vitally important in regulating growth and metabolism.

**Hippocampus**

The hippocampus consists of two “horns” that curve back from the amygdala. It appears to be very important in converting things that are “in your mind” at the moment (in short-term memory) into things that you will remember for the long run (long-term memory). If the hippocampus is damaged, a person cannot build new memories, and lives instead in a strange world where everything they experience just fades away, even while older memories from the time before the damage are untouched! This very unfortunate situation is fairly accurately portrayed in the wonderful movie Memento, as well as in a more light-hearted movie, 50 First Dates. But there is nothing light-hearted about it: Most people who suffer from this kind of brain damage end up institutionalized.

**Amygdala**

The amygdalas are two almond-shaped masses of neurons on either side of the thalamus at the lower end of the hippocampus. When it is stimulated electrically, animals respond with aggression. And if the amygdala is removed, animals get very tame and no longer respond to things that would have caused rage before. But there is more to it than just anger: When removed, animals also become indifferent to stimuli that would have otherwise have caused fear and even sexual responses.
Related areas

Besides the hypothalamus, hippocampus, and amygdala, there are other areas in the structures near to the limbic system that are intimately connected to it:

The cingulate gyrus is the part of the cerebrum that lies closest to the limbic system, just above the corpus collosum. It provides a pathway from the thalamus to the hippocampus, seems to be responsible for focusing attention on emotionally significant events, and for associating memories to smells and to pain.

The ventral tegmental area of the brain stem (just below the thalamus) consists of dopamine pathways that seem to be responsible for pleasure. People with damage here tend to have difficulty getting pleasure in life, and often turn to alcohol, drugs, sweets, and gambling.

The basal ganglia (including the caudate nucleus, the putamen, the globus pallidus, and the substantia nigra) lie over and to the sides of the limbic system, and are tightly connected with the cortex above them. They are responsible for repetitive behaviors, reward experiences, and focusing attention. If you are interested in learning more about the basal ganglia, click here.

The prefrontal cortex, which is the part of the frontal lobe which lies in front of the motor area, is also closely linked to the limbic system. Besides apparently being involved in thinking about the future, making plans, and taking action, it also appears to be involved in the same dopamine pathways as the ventral tegmental area, and plays a part in pleasure and addiction.

The Autonomic Nervous System

The second part of the nervous system to have a particularly powerful part to play in our emotional life is the autonomic nervous system. The autonomic nervous system is composed of two parts, which function primarily in opposition to each other. The first is the sympathetic nervous system, which starts in the spinal cord and travels to a variety of areas of the body. Its function appears to be preparing the body for the kinds of vigorous activities associated with “fight or flight,” that is, with running from danger or with preparing for violence.

*Activation of the sympathetic nervous system has the following effects:*

- dilates the pupils
- opens the eyelids
- stimulates the sweat glands
- dilates the blood vessels in large muscles
constricts the blood vessels in the rest of the body

increases the heart rate

opens up the bronchial tubes of the lungs

inhibits the secretions in the digestive system

One of its most important effects is causing the adrenal glands (which sit on top of the kidneys) to release epinephrine (aka adrenalin) into the blood stream. Epinephrine is a powerful hormone that causes various parts of the body to respond in much the same way as the sympathetic nervous system. Being in the blood stream, it takes a bit longer to stop its effects. This is why, when you get upset, it sometimes takes a while before you can calm yourself down again.

The sympathetic nervous system also takes in information, mostly concerning pain from internal organs. Because the nerves that carry information about organ pain often travel along the same paths that carry information about pain from more surface areas of the body, the information sometimes get confused. This is called referred pain, and the best known example is the pain some people feel in the left shoulder and arm when they are having a heart attack.

The other part of the autonomic nervous system is called the parasympathetic nervous system. It has its roots in the brainstem and in the spinal cord of the lower back. Its function is to bring the body back from the emergency status that the sympathetic nervous system puts it into.

Some of the details of parasympathetic arousal include...

pupil constriction

activation of the salivary glands

stimulating the secretions of the stomach

stimulating the activity of the intestines

stimulating secretions in the lungs

constricting the bronchial tubes

decreasing heart rate

The parasympathetic nervous system also has some sensory abilities: It receives information about blood pressure, levels of carbon dioxide in the blood, and so on.
There is actually one more part of the autonomic nervous system that we don't mention too often: The enteric nervous system. This is a complex of nerves that regulate the activity of the stomach.

AGGRESSIVE BEHAVIOUR

The most apparent type of aggression is that seen in the interaction between a predator and its prey. An animal defending itself against a predator becomes aggressive in order to survive and to ensure the survival of its offspring. Because aggression against a much larger enemy or group of enemies would lead to the death of an animal, animals have developed a good sense of when they are outnumbered. This ability to gauge the strength of other animals gives animals a “fight or flight” response to predators; depending on how strong they gauge the predator to be, animals will either become aggressive or flee.

The need to survive and the viability of cooperative behavior as a survival strategy leads to a phenomenon known as altruism. An example of an altruistic act is the alarm call that is given when a predator is approaching. While this call will inform the community of a predator’s presence, it will also inform the predator of the whereabouts of the animal that gave the alarm call. While this would appear to give the alarm caller an evolutionary disadvantage, it would facilitate the continuation of this animal’s genes because its relatives and progeny would be more able to avoid predators.

Aggression within a species

Aggression against conspecifics serves a number of purposes having to do with breeding. One of the most common of these purposes is the establishment of a dominance hierarchy. When certain types of animals are first placed in a common environment, the first thing they do is fight to assert their role in the dominance hierarchy. In general, the more dominant animals will be more aggressive than their subordinates. The majority of conspecific aggression ceases about 24 hours after the introduction of the animals being tested.

There are many different theories that try to explain how males and females developed these different aggressive tendencies. One theory states that in species where one sex makes a higher parental investment than the other, the higher investing sex is a resource for which the other sex competes: in the majority of species, females are the higher investing sex. It also holds that reproductive success is cardinal to the perpetuation an organism’s lineage and hereditary characteristics. For males, it is of crucial importance to establish dominance and resource holding to obtain reproductive opportunities in order to pass on their genetics. Unlike females, whose reproductive success is constrained by long gestation and lactation periods, male reproductive success is constrained by the number of partners they can mate with. As a result, males employ physical aggression more often than females; they
take more risks in order to compete with other males and gain an elevation of status. Males even go as far as killing one another, although this is rare. Males demonstrate less concern for their physical welfare in such competitions. In contrast, females compete with one another for resources, which can be converted to offspring. The establishment of dominance is more costly for females than for males and females have less to gain from achieving status. The female presence is more critical to the offspring’s survival and hence her reproductive success than is the father’s. It is only logical then that the health and well being of females would cause them to use less aggressive, low risk, and indirect strategies to acquire resources. As a result, in the majority of female-female conflicts, females rarely inflict serious damage to one another over resources. When translated to human, these facts suggest that women should be expected to show less evidence of dominance hierarchies than men do. In society, aggression in boys becomes increasingly motivated by issues of social status and self-esteem, which are usually decided by varying degrees of aggressive reactivity to personal challenge. Aggression in girls, focusing mainly on resource acquisition and not status, is more likely to take less physically dangerous and more covert forms of indirect aggression. There are, however, extensive critiques of the use of animal behavior to explain human behavior and the application of evolutionary explanations of contemporary human behavior.

In humans

Although humans share aspects of aggression with non-human animals, they differ from most of them in the complexity of their aggression because of factors such as culture, morals, and social situations. A wide variety of studies have been done on these situations.

Culture

Culture is a distinctly human factor that plays a role in aggression. Kung Bushmen were described as the "harmless people" by Elizabeth Marshall Thomas (1958). Other researchers, however, have countered this point of view, calculating that the homicide rate among Bushmen is actually higher than that of most modern industrial societies (Keeley, 1996). Lawrence Keeley argues that the "peaceful savage" is a myth that is unsupported by the bulk of anthropological and archeological evidence. Hunter gatherer societies do not have possessions to fight over, but they may still come to conflict over status and mating opportunities.

Empirical cross-cultural research has found differences in the level of aggression between cultures. In one study, American men resorted to physical aggression more readily than Japanese or Spanish men, whereas Japanese men preferred direct verbal conflict more than their American and Spanish counterparts (Andreu et al. 1998). Within American culture, southerners were shown to become more aroused and to respond more aggressively than northerners when affronted (Bowdle et al. 1996). There is also a higher homicide rate among young white southern men than among white northern men in the United States (Nisbett 1993). Changes in dominant behavior or in social status causes changes in testosterone levels. Reports of changes
in testosterone of young men during athletic events, which involve face-to-face competition with a winner and a loser, reveal that testosterone rises shortly before their matches, as if in anticipation of the competition. Also, one to two hours after the competitive match, the testosterone levels of the winners are high relative to those levels of the losers. It is also important to take into account the type of conflict that is occurring when assessing aggression. Is the conflict between groups, within a group, within a family? The sex of those involved in the conflict is also critical. Male-male, male-female and female-female encounters should all be clearly distinguished from one another. Same sex encounters are more frequent than inter-sex encounters and this could affect the level of aggression present.

Media

Behaviors like aggression can be learned by watching and imitating the behavior of others. A considerable amount of evidence suggests that watching violence on television increases the likelihood of short-term aggression in children (Aronson, Wilson, & Akert, 2005), though for a dissenting viewpoint, see Freedman (2002). Individuals may differ in how they respond to violence. The greatest impact is on those who are already prone to violent behavior. Adults may be influenced by violence in media as well. A long-term study of over 700 families found "a significant association" between the amount of time spent watching violent television as a teenager and the likelihood of committing acts of aggression later in life. The results remained the same in spite of factors such as family income, parental education and neighborhood violence (Aronson, Wilson, & Akert, 2005).

Although exposure to violence in media is associated with likelihood of short-term increases in aggression, none of these studies provide evidence for a definitive causal mechanism. Instead, violence in media may be one of many factors, or it may play a maintenance role since violent media tend to be selected by people who are prone to violence.

Situational factors

Alcohol impairs judgment, making people much less cautious than they usually are (MacDonald et al. 1996). It also disrupts the way information is processed (Bushman 1993, 1997; Bushman & Cooper 1990). A drunk person is much more likely to view an accidental event as a purposeful one, and therefore act more aggressively.

Pain and discomfort also increase aggression. Even the simple act of placing one's hands in warm water can cause an aggressive response. Hot temperatures have been implicated as a factor in a number of studies. One study completed in the midst of the civil rights movement found that riots were more likely on hotter days than cooler ones (Carlsmith & Anderson 1979). Students were found to be more aggressive and irritable after taking a test in a hot classroom (Anderson et al. 1996, Rule, et al. 1987). Drivers in cars without air conditioning were also found to be more likely to honk their horns (Kenrick & MacFarlane 1986[clarification needed]).
Frustration is another major cause of aggression. The Frustration aggression theory states that aggression increases if a person feels that he or she is being blocked from achieving a goal (Aronson et al. 2005). One study found that the closeness to the goal makes a difference. The study examined people waiting in line and concluded that the 2nd person was more aggressive than the 12th one when someone cut in line (Harris 1974). Unexpected frustration may be another factor. In a separate study, a group of students were collecting donations over the phone. Some of them were told that the people they would call would be generous and the collection would be very successful. The other group was given no expectations. The group with high expectations was much more upset and became more aggressive when no one was pledging.

There is some evidence to suggest that the presence of violent objects such as a gun can trigger aggression. In a study done by Leonard Berkowitz and Anthony Le Page (1967), college students were made angry and then left in the presence of a gun or badminton racket. They were then led to believe they were delivering electric shocks to another student, as in the Milgram experiment. Those who had been in the presence of the gun administered more shocks. It is possible that a violence-related stimulus increases the likelihood of aggressive cognitions by activating the semantic network.

A new proposal links military experience to anger and aggression, thus creating serial killers. Castle and Hensley state, “The military provides the social context where servicemen learn aggression, violence, and murder”. Post Traumatic Stress Disorder (PTSD) is also a serious issue in the military, also believed to lead to aggression in soldiers who are suffering from what they witnessed in battle. They come back to the civilian world and are still haunted by flash backs and nightmares, causing severe stress. This can be contributed to serial killing, as well; however, these studies are still being further investigated.

**Gender**

Gender is a factor that plays a role in both human and animal aggression. Males are historically believed to be generally more physically aggressive than females (Coie & Dodge 1997, Maccoby & Jacklin 1974), and men commit the vast majority of murders (Buss 2005). This is one of the most robust and reliable behavioral sex differences, and it has been found across many different age groups and cultures. There is evidence that males are quicker to aggression (Frey et al. 2003) and more likely than females to express their aggression physically (Bjorkqvist et al. 1994). When considering indirect forms of non-violent aggression, such as relational aggression and social rejection, some scientists argue that females can be quite aggressive although female aggression is rarely expressed physically (Archer, 2004; Card, Stucky, Sawalani, & Little, 2008).

Although females are less likely to initiate physical violence, they can express aggression by using a variety of non-physical means. Exactly which method women use to express aggression is something that varies from culture to culture. On
Bellona Island, a culture based on male dominance and physical violence, women tend to get into conflicts with other women more frequently than with men. When in conflict with males, instead of using physical means, they make up songs mocking the man, which spread across the island and humiliate him. If a woman wanted to kill a man, she would either convince her male relatives to kill him or hire an assassin. Although these two methods involve physical violence, both are forms of indirect aggression, since the aggressor herself avoids getting directly involved or putting herself in immediate physical danger.

**In children**

The frequency of physical aggression in humans peaks at around 2–3 years of age. It then declines gradually on average.[19] These observations suggest that physical aggression is mostly not a learned behavior and that development provides opportunities for the learning of self-regulation. However, a small subset of children fails to acquire the necessary self-regulatory abilities and tends to show atypical levels of physical aggression across development. These may be at risk for later violent behavior. It is often noted that obese children are more aggressive than their normal weight counterparts.

Aggressive behavior can impede learning as a skill deficit, while assertive behavior can facilitate learning. However, with young children, aggressive behavior is developmentally appropriate and can lead to opportunities of building conflict resolution and communication skills.

By school age, children should learn more socially appropriate forms of communicating such as expressing themselves through verbal or written language; if they have not, this behavior may signify a disability or developmental delay.

**What triggers aggressive behavior in children?**

- Physical fear of others
- Family difficulties
- Learning, neurological, or conduct/behavior disorders
- Emotional trauma
- Corporal punishment such as spanking increases subsequent aggression in children.

The Bobo doll experiment was conducted by Albert Bandura in 1961. In this work, Bandura found that children exposed to aggressive adult model acted more aggressively than those who were exposed to a nonaggressive adult model. This experiment suggests that anyone who comes in contact with and interacts with children can have an impact on the way they react and handle situations.
Biology

Aggression is directed to and often originates from outside stimuli, but has a very distinct internal character. Using various techniques and experiments, scientists have been able to explore the relationships between various parts of the body and aggression.

In the brain

Many researchers focus on the brain to explain aggression. The areas involved in aggression in mammals include the amygdala, hypothalamus, prefrontal cortex, cingulate cortex, hippocampus, septal nuclei, and periaqueductal gray of the midbrain. Because of the difficulties in determining the intentions of animals, aggression is defined in neuroscience research as behavior directed at an object or animal which results in damage or harm to that object or animal.

In many animals, aggression is encoded by pheromones. In mice, Major urinary proteins (Mups) have been demonstrated to promote innate aggressive behavior in behavior males. Mups were demonstrated to activate olfactory sensory neurons in the vomeronasal organ (VNO), a subsystem of the nose known to detect pheromones via specific sensory receptors, of mice [38] and rats.

The hypothalamus and periaqueductal gray of the midbrain are the most critical areas controlling aggression in mammals, as shown in studies on cats, rats, and monkeys. These brain areas control the expression of all the behavioral and autonomic components of aggression in these species, including vocalization. They have direct connections with both the brainstem nuclei controlling these functions and areas such as the amygdala and prefrontal cortex.

Electrical stimulation of the hypothalamus causes aggressive behavior the hypothalamus expresses receptors that help determine aggression levels based on their interactions with the neurotransmitters serotonin and vasopressin.

The amygdala is also critically involved in aggression. Stimulation of the amygdala results in augmented aggressive behavior in hamsters, while lesions of an evolutionarily homologous area in the lizard greatly reduce competitive drive and aggression Bauman et al. 2006). Several experiments in attack-primed Syrian Golden Hamsters support the claim of the amygdala being involved in control of aggression. Using expression of c-fos as a neuroanatomically localized marker of activity, the neural circuitry involved in the state of “attack readiness” in attack primed hamsters was studied. The results showed that certain structures of the amygdala were involved in aggressiveness: the medial nucleus and the cortical nuclei showed distinct differences in involvement as compared to other structures such as the lateral and basolateral nuclei and central nucleus of the amygdala, which were not associated with any substantial changes in aggressiveness. In addition, c-fos expression was found most clearly in the most dorsal and caudal aspects of the corticomedial amygdala (CMA). In the same study, it was also shown that lesions of
the CMA significantly reduced the number of aggressive behaviors. Eight of eleven subjects failed to attack. Also a correlation between lesion site and attack latency was determined: the more anterior the lesion, the longer mean elapsed time to the aggressive behavior.

The prefrontal cortex (PFC) has been implicated in aggressive psychopathology. Reduced activity of the prefrontal cortex, in particular its medial and orbitofrontal portions, has been associated with violent/antisocial aggression. Specifically, regulation of the levels of the neurotransmitter serotonin in the PFC has been connected with a particular type of pathological aggression, induced by subjecting genetically predisposed, aggressive, wild-type mice to repeated winning experience; the male mice selected from aggressive lines had lower serotonin tissue levels in the PFC than the low-aggressive lines in this study.

**Neurotransmitters and hormones**

Various neurotransmitters and hormones have been shown to correlate with aggressive behavior. The most often mentioned of these is the hormone testosterone. In one source, it was noted that concentration of testosterone most clearly correlated with aggressive responses involving provocation. In adulthood, it is clear that testosterone is not related to any consistent methods of measuring aggression on personality scales, but several studies of the concentration of blood testosterone of convicted male criminals who committed violent crimes compared to males without a criminal record or who committed non-aggressive crimes revealed in most cases that men who were judged aggressive/dominant had higher blood concentrations of testosterone than controls. However, a correlation between testosterone levels and aggression does not prove a causal role for testosterone. Studies of testosterone levels of male athletes before and after a competition revealed that testosterone levels rise shortly before their matches, as if in anticipation of the competition, and are dependent on the outcome of the event: testosterone levels of winners are high relative to those of losers. Interestingly, testosterone levels in female criminals versus females without a criminal record mirror those of males: testosterone levels are higher in women who commit aggressive crimes or are deemed aggressive by their peers than non-aggressive females. However, no specific response of testosterone levels to competition was observed in female athletes, although a mood difference was noted. Testosterone has been shown to correlate with aggressive behavior in mice and in some humans, but in contrast to some long-standing theories, various experiments have failed to find a relationship between testosterone levels and aggression in humans. The possible correlation between testosterone and aggression could explain the "roid rage" that can result from anabolic steroid use, although an effect of abnormally high levels of steroids does not prove an effect at physiological levels.

Another line of research has focused more on the effects of circulating testosterone on the nervous system mediated by local metabolism within the brain. Testosterone can be metabolized to 17b-estradiol by the enzyme aromatase or to 5a-
Dihydrotestosterone by 5a-reductase. Aromatase is highly expressed in regions involved in the regulation of aggressive behavior, such as the amygdala and hypothalamus. In studies using genetic knock out techniques in inbred mice, male mice that lacked a functional aromatase enzyme displayed a marked reduction in aggression. Long-term treatment of these mice with estradiol partially restored aggressive behavior, suggesting that the neural conversion of circulating testosterone to estradiol and its effect on estrogen receptors affects inter-male aggression. Also, two different estrogen receptors, ERa and ERb, have been identified as having the ability to exert different effects on aggression. In studies using estrogen receptor knockout mice, individuals lacking a functional ERa displayed markedly reduced inter-male aggression while male mice that lacked a functional ERb exhibited normal or slightly elevated levels of aggressive behavior. These results imply that ERa facilitates male-male aggression, whereas ERb may inhibit aggression. However, different strains of mice show the opposite pattern in that aromatase activity is negatively correlated with aggressive behavior. Also, in a different strain of mice the behavioral effect of estradiol is dependent on daylength: under long-days (16h of light) estradiol reduces aggression, and under short-days (8h of light) estradiol rapidly increases aggression.

Glucocorticoids also play an important role in regulating aggressive behavior. In adult rats, acute injections of corticosterone promote aggressive behavior and acute reduction of corticosterone decreases aggression; however, a chronic reduction of corticosterone levels can produce abnormally aggressive behavior. In addition, glucocorticoids affect development of aggression and establishment of social hierarchies. Adult mice with low baseline levels of corticosterone are more likely to become dominant than are mice with high baseline corticosterone levels.

Dehydroepiandrosterone (DHEA) is the most abundant circulating androgen and can be rapidly metabolized within target tissues into potent androgens and estrogens. Gonadal steroids generally regulate aggression during the breeding season, but non-gonadal steroids may regulate aggression during the non-breeding season. Castration of various species in the non-breeding season has no effect on territorial aggression. In several avian studies, circulating DHEA has been found to be elevated in birds during the non-breeding season. These data support the idea that non-breeding birds combine adrenal and/or gonadal DHEA synthesis with neural DHEA metabolism to maintain territorial behavior when gonadal testosterone secretion is low. Similar results have been found in studies involving different strains of rats, mice, and hamsters. DHEA levels also have been studied in humans and may play a role in human aggression. Circulating DHEAS (its sulfated ester) levels rise during adrenarche (~7 years of age) while plasma testosterone levels are relatively low. This implies that aggression in pre-pubertal children with aggressive conduct disorder might be correlated with plasma DHEAS rather than plasma testosterone, suggesting an important link between DHEAS and human aggressive behavior.
Another chemical messenger with implications for aggression is the neurotransmitter serotonin. In various experiments, serotonin action was shown to be negatively correlated with aggression[55](Delville et al. 1997). This correlation with aggression helps to explain the aggression-reducing effects of selective serotonin reuptake inhibitors such as fluoxetine (Delville et al. 1997), aka prozac.

While serotonin and testosterone have been the two most researched chemical messengers with regards to aggression, other neurotransmitters and hormones have been shown to relate to aggressive behavior as well. The neurotransmitter vasopressin causes an increase in aggressive behavior when present in large amounts in the anterior hypothalamus (Delville et al. 1997). The effects of norepinephrine, cortisol, and other neurotransmitters are still being studied.

Genetics

In a nonmammalian example, the fruitless gene in Drosophila melanogaster is a critical determinant for how fruit flies fight. Patterns of aggression can be switched, with males using female patterns of aggression or females using male patterns, by manipulating either the fruitless or transformer genes in the brain. Candidate genes for differentiating aggression between the sexes are the Sry (sex determining region Y) gene, located on the Y chromosome and the Sts (steroid sulfatase) gene. The Sts gene encodes the steroid sulfatase enzyme, which is pivotal in the regulation of neurosteroid biosynthesis. It is expressed in both sexes, is correlated with levels of aggression among male mice, and increases dramatically in females after parturition and during lactation, corresponding to the onset of maternal aggression.

Alcohol

There has been some links between those who prone to violence and their alcohol use. Those who are prone to violence and use alcohol are more likely to carry out violent acts.[56] For example, Ted Bundy, an inherently violent individual, became more violent with his murders after much alcohol abuse.
MODULE 3

LEARNING, MEMORY, AND LOCALIZATION OF HIGHER ORDER FUNCTIONS

LEARNING AND NERVOUS SYSTEM

Neuroscience is the study of the human nervous system, the brain, and the biological basis of consciousness, perception, memory, and learning.

The nervous system and the brain are the physical foundation of the human learning process. Neuroscience links our observations about cognitive behavior with the actual physical processes that support such behavior. This theory is still “young” and is undergoing rapid, controversial development.

Some of the key findings of neuroscience are:

The brain has a triad structure. Our brain actually contains three brains: the lower or reptilian brain that controls basic sensory motor functions; the mammalian or limbic brain that controls emotions, memory, and biorhythms; and the neocortex or thinking brain that controls cognition, reasoning, language, and higher intelligence.

The brain is not a computer. The structure of the brain’s neuron connections is loose, flexible, “webbed,” overlapping, and redundant. It’s impossible for such a system to function like a linear or parallel-processing computer. Instead, the brain is better described as a self-organizing system.

The brain changes with use, throughout our lifetime. Mental concentration and effort alters the physical structure of the brain. Our nerve cells (neurons) are connected by branches called dendrites. There are about 10 billion neurons in the brain and about 1,000 trillion connections. The possible combinations of connections is about ten to the one-millionth power. As we use the brain, we strengthen certain patterns of connection, making each connection easier to create next time. This is how memory develops.

How Neuroscience Impacts Education

When educators take neuroscience into account, they organize a curriculum around real experiences and integrated, “whole” ideas. Plus, they focus on instruction that promotes complex thinking and the “growth” of the brain. Neuroscience proponents advocate continued learning and intellectual development throughout adulthood.
**CORTEX AND LEARNING**

The psychological processes through which humans learn to categorize stimuli have been studied extensively (Smith et al., 1998). Considerable interest surrounds the proposal that people abstract the rules that define category membership unconsciously, through simple exposure to exemplars of the categories (Reber, 1967). This proposal remains controversial however (Shanks, 1995). Firstly, much of the evidence that claims to demonstrate abstract rule learning can equally be explained in terms of categorization on the basis of superficial similarity, either between whole exemplars [instance-based categorization (Nosofsky, 1986)] or exemplar parts [fragment-based categorization (Perruchet and Pacteau, 1990)]. Secondly, the situations that provide the most robust evidence for abstract rule induction are those that involve explicit (conscious) hypothesis testing rather than passive stimulus exposure (Shanks and St John, 1994).

Despite a need for rule learning in everyday life, the brain regions involved in explicit rule induction remain undetermined. Here we use event-related functional magnetic resonance imaging to measure learning-dependent neuronal responses during an explicit categorization task. Subjects made category decisions, with feedback, to exemplar letter strings for which the rule governing category membership was periodically changed. Bilateral fronto-polar prefrontal cortices were selectively engaged following rule change. This activation pattern declined with improving task performance reflecting rule acquisition. The vocabulary of letters comprising the exemplars was also periodically changed, independently of rule changes. This exemplar change modulated activation in left anterior hippocampus. Our finding that fronto-polar cortex mediates rule learning supports a functional contribution of this region to generic reasoning and problem-solving behaviours.

**LEARNING AND HIPPOCAMPUS**

One of the most influential views on the hippocampal function suggests that this brain region is critically involved in relational memory processing, that is, binding converging inputs to mediate the representation of relationships among the constituents of episodes. It has been proposed that this binding is automatic and obligatory during learning and remembering. In addition, neuroimaging studies have highlighted the importance of the prefrontal cortex in learning, memory, and language processing. However, the posited importance of hippocampal–prefrontal interaction remains to be empirically tested. In the present study we used functional magnetic resonance imaging to examine in detail this interaction by assessing learning-related changes in hemodynamic activity during artificial language acquisition. It has been shown previously that artificial grammar systems might be learned by evaluating pattern-based relations in word sequences and generalizing beyond specific word order, that is, rule abstraction. During scanning, participants learned an artificial language whose miniature grammar meets the universal
principles of a natural language. Increased proficiency level of the artificial language is associated with decreased left hippocampal activity.

THE SYNAPTIC BASIS OF LEARNING

Synaptic plasticity is the change in synaptic connections between two neurons due to the activity of one or both of these neurons. It is believed to be the basis of learning memory and some forms of brain development. The course will study both abstract models and biophysical models of synaptic plasticity. Abstract models of synaptic plasticity demonstrate how the concept of synaptic plasticity can contribute to different forms of learning, memory and development and how this might contribute to machine learning. Biophysical models of synaptic plasticity are based on actual cellular and molecular mechanisms observed in neurons and demonstrate how synaptic plasticity can arise from real biological mechanisms.

Hebbian theory

Hebbian theory describes a basic mechanism for synaptic plasticity where in an increase in synaptic efficacy arises from the presynaptic cell's repeated and persistent stimulation of the postsynaptic cell. Introduced by Donald Hebb in 1949, it is also called Hebb's rule, Hebb's postulate, and cell assembly theory, and states:

Let us assume that the persistence or repetition of a reverberatory activity (or "trace") tends to induce lasting cellular changes that add to its stability.... When an axon of cell A is near enough to excite a cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A's efficiency, as one of the cells firing B, is increased.

The theory is often summarized as "cells that fire together, wire together", although this is an oversimplification of the nervous system not to be taken literally, as well as not accurately representing Hebb's original statement on cell connectivity strength changes. The theory is commonly evoked to explain some types of associative learning in which simultaneous activation of cells leads to pronounced increases in synaptic strength. Such learning is known as Hebbian learning.

Hebbian engrams and cell assembly theory

Hebbian theory concerns how neurons might connect themselves to become engrams. Hebb's theories on the form and function of cell assemblies can be understood from the following:

"The general idea is an old one, that any two cells or systems of cells that are repeatedly active at the same time will tend to become 'associated', so that activity in one facilitates activity in the other."
"When one cell repeatedly assists in firing another, the axon of the first cell develops synaptic knobs (or enlarges them if they already exist) in contact with the soma of the second cell." (Gordon Allport posits additional ideas regarding cell assembly theory and its role in forming engrams, along the lines of the concept of auto-association, described as follows:

"If the inputs to a system cause the same pattern of activity to occur repeatedly, the set of active elements constituting that pattern will become increasingly strongly interassociated. That is, each element will tend to turn on every other element and (with negative weights) to turn off the elements that do not form part of the pattern. To put it another way, the pattern as a whole will become 'auto-associated'. We may call a learned (auto-associated) pattern an engram."

Hebbian theory has been the primary basis for the conventional view that when analyzed from a holistic level, engrams are neuronal nets or neural networks.

Work in the laboratory of Eric Kandel has provided evidence for the involvement of Hebbian learning mechanisms at synapses in the marine gastropod Aplysia californica.

Experiments on Hebbian synapse modification mechanisms at the central nervous system synapses of vertebrates are much more difficult to control than are experiments with the relatively simple peripheral nervous system synapses studied in marine invertebrates. Much of the work on long-lasting synaptic changes between vertebrate neurons (such as long-term potentiation) involves the use of non-physiological experimental stimulation of brain cells. However, some of the physiologically relevant synapse modification mechanisms that have been studied in vertebrate brains do seem to be examples of Hebbian processes. One such study reviews results from experiments that indicate that long-lasting changes in synaptic strengths can be induced by physiologically relevant synaptic activity working through both Hebbian and non-Hebbian mechanisms.

**MEMORY CONSOLIDATION**

**Memory consolidation** is a category of processes that stabilize a memory trace after the initial acquisition. Consolidation is distinguished into two specific processes, *synaptic consolidation*, which occurs within the first few hours after learning, and *system consolidation*, where hippocampus-dependent memories become independent of the hippocampus over a period of weeks to years. Recently, a third process has become the focus of research, *reconsolidation*, in which previously consolidated memories can be made labile again through reactivation of the memory trace.
History

Memory consolidation was first referred to in the writings of the renowned Roman teacher of rhetoric Quintillian. He noted the “curious fact... that the interval of a single night will greatly increase the strength of the memory,” and presented the possibility that “… the power of recollection .. undergoes a process of ripening and maturing during the time which intervenes.” The process of consolidation was later proposed based on clinical data illustrated in 1882 by Ribot’s Law of Regression, “progressive destruction advances progressively from the unstable to the stable”. This idea was elaborated on by William H. Burnham a few years later in a paper on amnesia integrating findings from experimental psychology and neurology. Coining of the term “consolidation” is credited to the German researchers Müller and Alfons Pilzecker who rediscovered the concept that memory takes time to fixate or undergo “Konsolidierung” in their studies conducted between 1892 and 1900.

Systematic studies of retrograde amnesia started to emerge in the 1960s and 1970s. These were accompanied by the creation of animal models of human amnesia in an effort to identify brain substrates critical for slow consolidation. Meanwhile, neuropharmacological studies of selected brain areas began to shed light on the molecules possibly responsible for fast consolidation. In recent decades, advancements in cellular preparations, molecular biology, and neurogenetics have revolutionized the study of consolidation.

Synaptic Consolidation

Synaptic consolidation is one form of memory consolidation seen across all species and long-term memory tasks. Long-term memory, when discussed in the arena of synaptic consolidation, is memory that lasts for at least 24 hours. An exception to this 24-hour rule is long-term potentiation, or LTP, a model of synaptic plasticity related to learning, in which an hour is thought to be sufficient. Synaptic consolidation is achieved faster than systems consolidation, within only minutes to hours of learning. LTP, one of the best understood forms of synaptic plasticity, is thought to be a possible underlying process in synaptic consolidation.

Standard Model

The standard model of synaptic consolidation suggests that alterations of synaptic protein synthesis and changes in membrane potential are achieved through activating intracellular transduction cascades. These molecular cascades trigger transcription factors that lead to changes in gene expression. The result of the gene expression is the lasting alteration of synaptic proteins, as well as synaptic remodeling and growth. In a short time-frame immediately following learning, the molecular cascade, expression and process of both transcription factors and immediate early genes, are susceptible to disruptions. Disruptions caused by specific drugs, antibodies and gross physical trauma can block the effects of synaptic consolidation.
Long-term Potentiation

LTP can be thought of as the prolonged strengthening of synaptic transmission, and is known to produce increases in the neurotransmitter production and receptor sensitivity, lasting minutes to even days. The process of LTP is regarded as a contributing factor to synaptic plasticity and in the growth of synaptic strength, which are suggested to underlie memory formation. LTP is also considered to be an important mechanism in terms of maintaining memories within brain regions, and therefore is thought to be involved in learning. There is compelling evidence that LTP is critical for Pavlovian fear conditioning in rats suggesting that it mediates learning and memory in mammals. Specifically, NMDA-receptor antagonists appear to block the induction of both LTP and fear conditioning and that fear conditioning increases amygdaloidal synaptic transmission that would result in LTP.

Timeline of Consolidation

Synaptic consolidation, when compared to systems consolidation; which is said to take weeks to months to years to be accomplished, is considerably faster. There is evidence to suggest that synaptic consolidation takes place within minutes to hours of memory encoding or learning, and as such is considered the ‘fast’ type of consolidation. As soon as six hours after training, memories become impervious to interferences that disrupt synaptic consolidation and the formation of long-term memory.

Spacing Effect

Distributed learning has been found to enhance memory consolidation, specifically for relational memory. Experimental results suggest that distributing learning over the course of 24 hours decreases the rate of forgetting compared to massed learning, and enhances relational memory consolidation. When interpreted in the context of synaptic consolidation, mechanisms of synaptic strengthening may depend on the spacing of memory reactivation to allow sufficient time for protein synthesis to occur, and thereby strengthen long-term memory.

Protein Synthesis

Protein synthesis has been suggested to play a critical role in the formation of new memories. Studies have shown that protein synthesis inhibitors administered after learning, weaken memory, suggesting that protein synthesis is required for memory consolidation. Additionally, reports have suggested that the effects of protein synthesis inhibitors also inhibit LTP. However, it should be noted that other results have shown that protein synthesis may not in fact be necessary for memory consolidation, as it has been found that the formation of memories can withstand vast amounts of protein synthesis inhibition, suggesting that this criterion of protein synthesis as necessary for memory consolidation is not unconditional.
Dietary Flavanoids

There is evidence to suggest that dietary flavanoids have effects on encouraging LTP and synaptic plasticity, therefore affecting memory. Specifically, it was found that dietary-derived flavanoids might protect neurons, enhance neuronal function, and stimulate neuronal regeneration. Additionally, these dietary phytochemicals interact with several neuronal signaling cascade pathways that are responsible for alterations in LTP, and consequently, learning and human memory. Flavanoids may trigger certain events, including the activation of the CREB transcription factor, which is important to the enhancement of short-term and long-term memory. This activation then triggers the synthesis of important proteins related to LTP, ultimately leading to synapse growth and eventually long-term memory.

System Consolidation

System Consolidation is the second form of memory consolidation. It is a reorganization process in which memories from the hippocampal region where memories are first encoded are moved to the neo-cortex in a more permanent form of storage. System consolidation is a slow dynamic process that can take from one to two decades to be fully formed in humans, unlike synaptic consolidation that only takes minutes to hours for new information to stabilize into memories.

Standard Model

The Standard model of systems consolidation was first developed by Paul W. Frankland; it states that when novel information is originally encoded and registered, memory of these new stimuli becomes retained in both the hippocampus and cortical regions. Later the hippocampus’ representations of this information become active in explicit (conscious) recall or implicit (unconscious) recall like in sleep and ‘offline’ processes.

Memory is retained in the hippocampus for up to one week after initial learning, representing the hippocampus-dependent stage. During this stage the hippocampus is ‘teaching’ the cortex more and more about the information and when the information is recalled it strengthens the cortico-cortical connection thus making the memory hippocampus-independent. Therefore from one week and beyond the initial training experience, the memory is slowly transferred to the neo-cortex where it becomes permanently stored.

Semantic vs. Episodic Memory

Nadel and Moscovitch argued that when studying the structures and systems involved in memory consolidation, semantic memory and episodic memory need to be treated as different types of memory. This additional distinction expands the Standard Model by Frankland, which does not consider the types of memory as separate. Evidence from extensive neuro-imaging research on the different function of cortical and hippocampus memory traces have found that the hippocampus
provides temporal and spatial context, whereas the cortical traces are primarily context-free. Episodic memory, no matter whether new or old, relies on hippocampus-cortical networks whereas remote semantic memories can be retrieved independent of the hippocampus.

Multiple Trace Theory

Multiple Trace Theory (MTT) builds on the distinction between semantic memory and episodic memory, arguing that semantic memories are created by multiple traces left in the neo-cortex in the process of consolidation, separate from the hippocampus. Hence, while proper hippocampus functioning is necessary for the retention and retrieval of episodic memories, it is less necessary for semantic memories.

REM Sleep

Rapid eye movement (REM) sleep has been implicated in the overnight learning in humans by the re-organization of novel information in the hippocampal and cortical regions of the brain. REM sleep elicits an increase in neuronal activity following an enriched or novel waking experience, thus increasing neuronal plasticity and therefore playing an essential role in the consolidation of memories.

In particular studies have been done on sensory and motor related tasks. In one study testing finger-tapping, people were split into two groups and tested post-training with or without intervening sleep; results concluded that sleep post-training increases both speed and accuracy in this particular task, while increasing the activation of both cortical and hippocampal regions; whereas the post-training awake group had no such improvements.

Zif268 & REM Sleep

Zif268 is an Immediate Early Gene (IEG) thought to be involved in neuroplasticity by an up-regulation of the transcription factor during REM sleep after pre-exposure to an enriched environment. Results from studies testing the effects of zif268 on mice brains postmortem, suggest that a waking experience prior to sleep can have an enduring effect in the brain, due to an increase of neuroplasticity.

Reconsolidation

Memory reconsolidation is the process of previously consolidated memories being recalled and actively consolidated. It is a distinct process that serves to maintain, strengthen and modify memories that are already stored in the long-term memory. Once memories undergo the process of consolidation and become part of long-term memory, they are thought of as stable. However, the retrieval of a memory trace can cause another labile phase that then requires an active process to make the memory stable after retrieval is complete. It is believed that post-retrieval stabilization is different and distinct from consolidation, despite its overlap in function (e.g. storage).
and its mechanisms (e.g. protein synthesis). Memory modification needs to be demonstrated in the retrieval in order for this independent process to be valid.

History

The theory of reconsolidation has been debated for many years and has become quite controversial. Reconsolidation was first conceptualized after studies were done on elimination of phobias with electroconvulsive shock therapy; the disruption of the consolidated fear memory after shock administration led to further investigation into the concept. In many early studies electroconvulsive shock therapy was used to test for reconsolidation, as it was a known amnesic agent, and lead to memory loss if administered directly after the retrieval of a memory. Later research using Pavlovian fear conditioning on rats found that a consolidated fear memory can return to a labile state, with immediate amygdala infusions of the protein synthesis inhibitor anisomycin, but not infusions made six hours afterwards. It was concluded that consolidated fear memory, when reactivated, enters a changeable state that requires de novo protein synthesis for new consolidation or reconsolidation of the old memory. Since these break through studies many more have been done testing the theory of reconsolidation. Studies have been done on numerous subjects including; crabs, chicks, honeybees, medaka fish, lymnaea, humans and rodents.

Criticisms

Some studies have supported this theory, while others have failed to demonstrate disruption of consolidated memory after retrieval. It is important to note that negative results may be examples of conditions where memories are not susceptible to a permanent disruption, thus a determining factor of reconsolidation. After much debate and a detailed review of this field it had been concluded that reconsolidation was a real phenomenon. More recently Tronson and Taylor compiled a lengthy summary of multiple reconsolidation studies, noting a number of studies were unable to show memory impairments due to blocked reconsolidation. However the need for standardized methods was underscored as in some learning tasks such as fear conditioning, certain forms of memory reactivation could actually represent new extinction learning rather than activation of an old memory trace. Under this possibility, traditional disruptions of reconsolidation might actually maintain the original memory trace but preventing the consolidation of extinction learning.

Reconsolidation experiments are more difficult to run then typical consolidation experiments as disruption of a previously consolidated memory must be shown to be specific to the reactivation of the original memory trace. Furthermore, it is important to demonstrate that the vulnerability of reactivation occurs in a limited time frame, which can be assessed by delaying infusion till six hours after reactivation. It is also useful to show that the behavioral measure used to assess disruption of memory is not just due to task impairment caused by the procedure, which can be demonstrated by testing control groups in absence of the original learning. Finally, it is important to rule out alternative explanations, such as extinction learning by lengthening the reactivation phase.
Distinctions from Consolidation

Questions arose if reconsolidation was a unique process or merely another phase of consolidation. Both consolidation and reconsolidation can be disrupted by pharmacological agents (e.g. the protein synthesis inhibitor anisomycin) and both require the transcription factor CREB. However, recent amygdala research suggests that BDNF is required for consolidation (but not reconsolidation) whereas the transcription factor and immediate early gene Zif268 is required for reconsolidation but not consolidation[13]. A similar double dissociation between Zif268 for reconsolidation and BDNF for consolidation was found in the hippocampus for fear conditioning. However not all memory tasks show this double dissociation, such as object recognition memory.

MEMORY IN BRAIN DAMAGED INDIVIDUALS

Why does brain damage impair memory? Object recognition is thought to be the canonical test of declarative memory, the type of memory putatively impaired after damage to the temporal lobes. Studies of object recognition memory have helped to elucidate the specific anatomical structures involved in declarative memory implicating, in particular, the perirhinal cortex (Zola-Morgan et al., 1989b; Gaffan and Murray, 1992; Meunier et al., 1993; Mumby and Pinel, 1994; Aggleton et al., 1997; Baxter and Murray, 2001; Málková et al., 2001; Winters et al., 2004). Furthermore, electrophysiological data have identified properties of neurons that seem likely to form part of the mechanism underlying recognition memory (Brown and Aggleton, 2001). However, no full mechanistic account has been provided that explains why impairments after damage to perirhinal cortex should be exacerbated not only by lengthening the delay between presentation of to-be-remembered items and test (Meunier et al., 1993; Mumby and Pinel, 1994) but also by lengthening the list of to-be-remembered items (Meunier et al., 1993), or why such impairments are only revealed when stimuli are trial unique rather than repeatedly presented (Eacott et al., 1994).

Object recognition is the canonical test of declarative memory, the type of memory putatively impaired after damage to the temporal lobes. Studies of object recognition memory have helped elucidate the anatomical structures involved in declarative memory, indicating a critical role for perirhinal cortex. We offer a mechanistic account of the effects of perirhinal cortex damage on object recognition memory, based on the assumption that perirhinal cortex stores representations of the conjunctions of visual features possessed by complex objects. Such representations are proposed to play an important role in memory when it is difficult to solve a task using representations of only individual visual features of stimuli, thought to be stored in regions of the ventral visual stream caudal to perirhinal cortex. The account is instantiated in a connectionist model, in which development of object representations with visual experience provides a mechanism for judgment of previous occurrence. We present simulations addressing the following empirical findings: (1) that impairments after damage to perirhinal cortex (modeled by removing the "perirhinal cortex" layer of the network) are exacerbated by...
lengthening the delay between presentation of to-be-remembered items and test, (2) that such impairments are also exacerbated by lengthening the list of to-be-remembered items, and (3) that impairments are revealed only when stimuli are trial unique rather than repeatedly presented. This study shows that it may be possible to account for object recognition impairments after damage to perirhinal cortex within a hierarchical, representational framework, in which complex conjunctive representations in perirhinal cortex play a critical role.

Any brain function can be disrupted by brain trauma resulting in inattention, difficulty concentrating, excessive sleepiness, faulty judgment, depression, irritability, emotional outbursts, and slowed thinking. However, memory loss is one of the most common cognitive side effects of traumatic brain injury (TBI). Even in mild TBI, memory loss is still very common. The more severe the victim's memory loss after the TBI, the more significant the brain damage will most likely be.

Some TBI-related amnesia such as patients unable to recall what happened just before, during and after the head injury is temporary. Temporary memory loss is often caused by swelling of the brain in response to the damage it sustained. But because the brain is pressed against the skull, even parts that were not injured are still not able to work. The patient's memory typically returns as the swelling goes down over a period of weeks or even months. Temporary memory loss may also be an emotional response to the stressful events surrounding a TBI.

Damage to the nerves and axons (connection between nerves) of the brain may also result in memory loss. The brain cannot heal itself like an arm or a leg, so any function that is damaged during a TBI is permanently impaired unless the brain learns how to perform that function differently. Fixed amnesia may include the loss of meanings of certain common, everyday objects or words, or a person may not remember skills he had before the TBI.

A different kind of memory loss is called anterograde amnesia, which is an inability to form memories of events that happened after the injury. Doctors are not sure, exactly, why this happens, but some research has shown that it may have something to do with the fact that TBI's reduce the levels of a protein in the brain that helps the brain balance its activity. Without enough of that particular protein, the brain can easily overload and memory formation is affected.

In general, symptoms of brain injury should lessen over time as the brain heals but sometimes the symptoms worsen because the patient's inability to adapt to the brain injury. It is not uncommon for psychological symptoms to arise and worsen after a brain injury.

At the current time, there is no treatment for memory loss following TBI; if the memory does not come back on its own, it will be lost permanently. There is a great deal of research in the field of TBI and memory loss, but, sadly, there are no cures for TBI-related amnesia at this time.
FORGETTING

Forgetting (retention loss) refers to apparent loss of information already encoded and stored in an individual's long term memory. It is a spontaneous or gradual process in which old memories are unable to be recalled from memory storage. It is subject to delicately balanced optimization that ensures that relevant memories are recalled. Forgetting can be reduced by repetition and/or more elaborate cognitive processing of information. Reviewing information in ways that involve active retrieval seems to slow the rate of forgetting.

CORTICAL LOCALIZATION

One of the oldest controversies in psychology and neurology concerns localization of function, the notion that different aspects of behaviour are mediated by different parts of the brain. The issue of mental localization was debated by classical thinkers from 400 BC to AD 200 and Aristotle even argued that the soul (i.e. the mind) occupied the heart. Only after several hundred years did Greek writers such as Alcmaeon finally prevail in their arguments that the faculties of the mind lay in the watery ventricles of the brain. The emphasis then shifted to the number of mental faculties and by AD 400 the Church Fathers, including St Augustine, proposed the cell doctrine of the mind, the cells being the ventricles and the faculties of sensation, imagination, reasoning, movement, and memory residing in separate cells, with some sharing since there were only three cells. Although the number of faculties eventually rose to seven or eight, little then changed for another thousand years — making the cell doctrine easily the most enduring theory of the physical basis of mind. But 18th-century anatomists like Sylvius were busy undermining it, convincing their contemporaries that the convolutions of the cerebral cortex were far too complex to be mere cooling pipes for the blood. However, the idea of cortical localization of function had to wait for Franz Joseph Gall in the early 19th century. From first observing that the mental characteristics of his school friends appeared to be related to the shape of their heads, Gall believed that traits like cautiousness and mirthfulness — he announced 27 in all — were localized and that their magnitude was reflected in the size of a particular region, which in turn was indicated by the size of the overlying skull. Gall’s phrenology enjoyed a brief ascendancy until about 1820 when Flourens, noting that damage to different parts of the brain often had similar and diffuse effects on behaviour, concluded that the brain acts as a whole. It was much later that localization of function acquired scientific respectability when Broca showed in 1861 that speech impairment followed damage to a restricted part of the left frontal lobe, and Gustav Fritsch and J. L. Hitzig reported their observations on the effects of electrically stimulating different parts of the exposed brain, first in soldiers with head injuries and then in animals. They found that stimulating discrete parts of what is now known as the motor cortex produced movements of different regions of the body. Interestingly, the doyen of Scottish phrenology George Coombe had observed similar patients in the 1830s and noted that the exposed brain swelled and reddened when the patient became excited. Coombe had stumbled on changes in cerebral blood flow in relation to particular mental activity, which formed the basis of late 20th-century functional imaging techniques.
neuroimaging, whereby the localized changes in blood flow that correlate with particular mental events can be registered and pinpointed from outside the head. Much later, in 1950, W. G. Penfield and Theodore Rasmussen published the results of similar observations made on fully conscious patients awaiting brain surgery under local anaesthetic. By electrically stimulating small regions along the central fissure, they showed that there was a map of bodily movements in front of the fissure and a map of sensation behind it (see Fig. 1). Meanwhile Gordon Holmes had discovered that the eye is mapped onto the back of the brain. By charting small areas of blindness in the visual field of patients with gunshot wounds at the back of the head he found that the part of the eye that was blind depended on the part of the visual cortex that was damaged. Thus were sensory and motor maps established.

Despite this apparently irrefutable evidence of regional specialization in the brain in connection with speech, movement, seeing, and touch, the American psychologist Karl Lashley produced evidence that Flourens' position remained tenable with respect to some forms of behaviour. By studying maze learning in rats, Lashley showed that the deleterious effects of removing parts of the cerebral cortex depended on the amount of tissue removed rather than on its exact location, a finding enshrined in the principles of mass action and equipotentiality. Lashley's views struck a sympathetic chord with many psychologists of the mid-20th century, who likened the brain to a complex electronic device which can become increasingly unreliable as more of its components are damaged, but which rarely suffers a severe breakdown when a small number of specific localized components are removed.

With hindsight, the often bitter controversy was unnecessary. The view that the brain acts as a whole stems from investigation of complex phenomena, such as learning and remembering complicated tasks involving several of the senses. It is small wonder that a good deal of the brain is involved in such behaviour and, therefore, that damage to any part of it has some effect. The evidence for regional specificity stemmed, by contrast, from investigations of relatively simple actions such as moving a finger, seeing a light in one part of space, or detecting that a particular part of the skin had been touched. The latter are all examples of simple perception or voluntary movements, the former of higher-level cognitive and intellectual behaviour. Even so, the mediation of some complex cognitive abilities can be surprisingly localized. For example, the modern techniques of functional neuroimaging by positron emission tomography (PET) or magnetic resonance imaging (MRI) (see brain imaging), both depending on changes in regional cerebral blood flow, have shown that spatial memory is concentrated in the hippocampus and the recognition of faces in the fusiform gyrus. But let us not forget that this simple view of localization conceals the fact, stressed by Hughlings Jackson in 1879, that localizing the lesion that leads to a 'selective' disturbance of behaviour is not the same as understanding how that bit of the brain works. Jackson's logical argument is just as true today with respect to focal changes in blood flow revealed by functional brain imaging.
The acceptance of the idea of localization of function had one unfortunate effect. It came to be taken for granted that the senses of touch and vision and hearing were mapped on the surface of the brain and that there was a similarly orderly representation of the muscles, as shown in Fig. 1. But why there is a map at all was not recognized as a question of fundamental importance, despite the fact that nature went to enormous trouble to evolve genetic instructions which ensured that the retina of the eye and the surface of the body are represented on the surface of the brain in an orderly map and not higgledy-piggledy. Furthermore, a computer programmed to recognize patterns does not need within its components anything like a geographical map of the original scene. So why does the brain have one?

It became increasingly difficult to sidestep this question with the demonstration from 1970 onwards of multiple maps of the eye in the brain. A map is demonstrated by recording the electrical activity of clusters of nerve cells, determining where a visual stimulus must lie on the retina for it to excite these particular cells, and then moving the recording electrode to another group of cells. Using this procedure in anaesthetized animals, it was shown that the retina is mapped not once but many times in the cortex. The macaque monkey has at least ten mapped representations of the retina, and about twenty others where it is the nature of the stimulus rather than its position that is computed. At least a third of the cerebral cortex in the owl monkey is concerned with the multiple mapped representations of visual space.

What is the purpose of such an arrangement, which is not confined to vision, for there are now known to be several topological representations of the surface of the body and the musculature in monkeys? A plausible explanation concerns a well-known physiological phenomenon called lateral inhibition. In the eye itself, adjacent differences in the brightness of colour of the image are given prominence in the nerve signals that leave the eye. This is accomplished by a system of lateral inhibitory connections in the retina which ensure that nerve cells tend to inhibit their immediate neighbours. In an area of uniform illumination or colour, all cells are equally excited by the light and equally inhibited by their neighbours. But where there is a sharp difference in illumination, as at the image of a contour, the highly illuminated cells exert a powerful inhibition on their neighbours in the shade, and the difference in signals sent by the two groups of cells is enhanced. Lateral inhibition cannot create something out of nothing, but it can enhance one feature of the visual image at the expense of another. Lateral inhibition of this kind ensures that edges and contours are prominently coded in the signals from the eye.

There is now incontrovertible evidence from physiology and anatomy that lateral inhibition works in the brain as well as in the eye, and this provides the major reason for the existence of a map of the eye on the cortex of the brain. If the differences in illumination of adjacent parts of the eye are to be accentuated in the cortex, the sensory connections between the nerve cells concerned with the two adjacent parts of the image should be close together. In a map they are as close together as possible, and lateral interactions will be maximally efficient. If there were no map, so that nerve cells concerned with adjacent parts of the image were often far apart in the
relevant cortical area, the problem of interconnecting the cells becomes formidable and the average length of a connection would be much greater, about 20 to 30 times greater in visual area 1 of man and monkey. In a map of the sensory surface the lateral interconnections between cells can all be local, and anatomy has shown this to be so.

But why are there many maps for each of the senses rather than just one? The answer is really the same. Inhibitory connections between neighbouring nerve cells of the cortex are now believed to be involved in coding many attributes of the visual image, such as colour, movement, disparity, orientation, size, and spatial periodicity. If all of these were to be attempted within one map, the local interconnections would again have to be longer and the problem of interconnecting the right cells would increase. By having many maps, each small and containing nerve cells concerned only with one or a few of the stimulus attributes just mentioned, the lateral interconnections can be kept as short as possible and the problem of interconnecting the right type of cell is minimized.

This simple idea has much to support it. First, although there are long fibre connections from one part of the brain to another, microscopy has shown that the connections within a particular map are short and predominantly inhibitory. Second, physiology has shown that nerve cells within a particular cortical representation of the eye tend to be concerned with a restricted range of stimulus qualities, such as orientation, distance, size, colour, or movement. Different maps deal with different stimulus qualities. Third, the human corpus callosum contains about 600 million nerve fibres connecting the two sides of the brain. They are grouped from front to back according to destination and function; if they were not, their average length would have to be longer. Fourth, there are many examples of very selective effects on visual perception of localized brain damage. Although they are rare, some patients suffer a highly selective disturbance of the perception of colour or position or depth or motion, as would be expected when the damage is occasionally restricted to one of the visual maps. Functional maps keep connections short and, therefore, keep the brain (and skull) small enough to be born through a narrow birth canal.

Although the different sensory qualities of the visual scene are initially coded in separate visual areas, our visual perception is unitary not fragmented, which means that the timing of the activity of cells in different visual areas must be precisely coordinated. If we look at a moving, spinning, coloured object and the nervous signals in one visual area are out of phase with all the others, some distortion should occur in what is seen. Indeed, fever, toxicosis, and brain damage can all lead to temporary visual perceptual dislocations. For example, in one part of the visual field objects may appear too large or too small, smooth movement may look jerky, contours may be multiplied, position and orientation be greatly misperceived.

Multiple brain maps of sensory and motor systems are now established. They permit the maximum efficiency and economy in the myriad interconnections between nerve cells responsible for analysing sensory signals. Their existence also throws light on
what is now seen as an unwarranted controversy about localization of function. The cortical representations of the sensory attributes of stimuli, such as colour, may be confined to a few areas. The cortical events underlying certain complex and cognitive actions are probably so widely dispersed that no brain damage, however great, can either destroy them entirely or leave them wholly unimpaired. See also neuropsychology.

LOCALISATION OF LANGUAGE

Language localization (from the English term "locale" and abbreviated in the numeronym "L10N", the 10 being a way of replacing the middle 10 letters of the word) can be defined as the second phase of a larger process (Internationalization and localization) of product translation and cultural adaptation (for specific countries, regions, groups) to account for differences in distinct markets. Thus, it is important not to reduce it to a mere translation activity because it involves a comprehensive study of the target culture in order to correctly adapt the product.

The localisation process is most generally related to cultural adaptation and translation of software, video games and websites, and less frequently to any written translation (although these also involve cultural adaptation processes). The process of localising can be done for regions or countries where people speak different languages, or where the same language is spoken. Just recall the language differences in countries where Spanish is natively spoken (for instance, in South America), or where English is the official language (e.g., in the United States, the United Kingdom, and the Philippines).

The overall process: internationalization, globalization and localization

As everyone know, globalization "can best be thought of as a cycle rather than a single process". To globalize is to plan in advance the way the product or the website should be designed and developed in order to avoid costs from going up and quality problems from emerging, to save time, and eventually to smooth the localizing effort for each region/country. Localization is one phase, but an integral part, of the overall process called globalization.

In this view, there are two primary technical processes that comprise globalization, internationalization and localization, which make up a double-phase process

The first phase, internationalization, «encompasses the planning and preparation stages for a product in which it is built by design to support global markets. This process means that all cultural assumptions are removed and any country or language-specific content is stored externally to the product so that it can be easily adapted». If this is not done during this phase, they must be fixed during localization, though, adding time and expense to the project. It is important to acknowledge that in extreme cases, products that were not internationalized may not even be localizable.
The second phase, localization, «refers to the actual adaptation of the product for a specific market». The localization phase involves, among other things (see below and Internationalization and localization), the four issues describes as linguistic, physical, business and cultural, and technical issues.

At the end of each phase, a testing and a quality assurance (QA) test are done to ensure that product works properly and to deliver it according to the client's quality expectations.

**Translation versus localization**

Localization is often treated as a mere "high-tech translation", but this view does not capture its importance, its complexity or what it encompasses. Though it is sometimes somehow difficult to draw the limits between translation and localization, in general localization addresses significant, non-textual components of products or services. In addition to strict translation (and, therefore, grammar and spelling issues that vary from place to place or from country to country where the same language is spoken), the localization process might include adaptation of graphics, adoption of local currencies, use of proper forms for dates, addresses and phone numbers, the choices of colours and many other details, including rethinking the physical structure of a product. All these changes aim to recognize local
sensitivities, avoid conflict with local culture and habits and to enter the local market by merging into its needs and desires.

**BRAIN LATERALITY**

The human brain is divided into two hemispheres—left and right. Scientists continue to explore how some cognitive functions tend to be dominated by one side or the other, that is, how they are lateralized.

A longitudinal fissure separates the human brain into two distinct cerebral hemispheres, connected by the corpus callosum. The sides resemble each other and each hemisphere's structure is generally mirrored by the other side. Yet despite the strong similarities, the functions of each cortical hemisphere are different.

![Image of a brain](image)

Broad generalizations are often made in popular psychology about certain function (e.g., logic, creativity) being lateralised, that is, located in the right or left side of the brain. These ideas need to be treated carefully because the popular lateralizations are often distributed across both sides.

Many differences between the hemispheres have been observed, from the gross anatomical level to differences in dendritic structure or neurotransmitter distribution. For example, the lateral sulcus generally is longer in the left hemisphere than in the right hemisphere. However, experimental evidence provides little, if any, consistent support for correlating such structural differences with functional differences. The extent of specialized brain function by area remains under investigation. If a specific region of the brain or even an entire hemisphere is either injured or destroyed, its functions can sometimes be assumed by a neighboring region, even in the opposite hemisphere, depending upon the area damaged and the patient's age. Injury may also interfere with a pathway from one area to another. In this case, alternative (indirect) connections may exist which can be used to transmit the information to the target area. Such transmission may not be as efficient as the original pathway.
While functions are lateralized, the lateralizations are functional trends, which differ across individuals and specific function. Short of having undergone a hemispherectomy (removal of a cerebral hemisphere), no one is a "left-brain only" or "right-brain only" person.

Brain function lateralization is evident in the phenomena of right- or left-handedness and of right or left ear preference, but a person's preferred hand is not a clear indication of the location of brain function. Although 95% of right-handed people have left-hemisphere dominance for language, only 18.8% of left-handed people have right-hemisphere dominance for language function. Additionally, 19.8% of the left-handed have bilateral language functions. Even within various language functions (e.g., semantics, syntax, prosody), degree (and even hemisphere) of dominance may differ.

**Left versus right**

Linear reasoning and language functions such as grammar and vocabulary often are lateralized to the left hemisphere of the brain. Dyscalculia is a neurological syndrome associated with damage to the left temporo-parietal junction. This syndrome is associated with poor numeric manipulation, poor mental arithmetic skill, and the inability to either understand or apply mathematical concepts.

In contrast, prosodic language functions, such as intonation and accentuation, often are lateralized to the right hemisphere of the brain. Functions such as the processing of visual and audiological stimuli, spatial manipulation, facial perception, and artistic ability seem to be functions of the right hemisphere.

There is some evidence that the right hemisphere is more involved in processing novel situations, while the left hemisphere is most involved when routine or well rehearsed processing is called for.

Other integrative functions, including arithmetic, binaural sound localization, and emotions, seem more bilaterally controlled.

<table>
<thead>
<tr>
<th><strong>Left hemisphere functions</strong></th>
<th><strong>Right hemisphere functions</strong></th>
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<tbody>
<tr>
<td>numerical computation (exact calculation, numerical comparison, estimation)</td>
<td>numerical computation (approximate calculation, numerical comparison, estimation)</td>
</tr>
<tr>
<td>left hemisphere only: direct fact retrieval</td>
<td>language: intonation/accentuation, prosody, pragmatic, contextual</td>
</tr>
<tr>
<td>language: grammar/vocabulary, literal</td>
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History

Speech and language

Broca

One of the first indications of brain function lateralization resulted from the research of French physician Pierre Paul Broca, in 1861. His research involved the male patient nicknamed "Tan", who suffered a speech deficit (aphasia); "tan" was one of the few words he could articulate, hence his nickname. In Tan's autopsy, Broca determined he had a syphilitic lesion in the left cerebral hemisphere. This left frontal lobe brain area (Broca's Area) is an important speech production region. The motor aspects of speech production deficits caused by damage to Broca’s Area are known as Broca’s aphasia. In clinical assessment of this aphasia, it is noted that the patient cannot clearly articulate the language being employed.

Wernicke

German physician Karl Wernicke continued in the vein of Broca’s research by studying language deficits unlike Broca aphasias. Wernicke noted that not every deficit was in speech production; some were linguistic. He found that damage to the left posterior, superior temporal gyrus (Wernicke's area) caused language comprehension deficits rather than speech production deficits, a syndrome known as Wernicke's aphasia.

Advance in imaging technique

These seminal works on hemispheric specialization were done on patients and/or postmortem brains, raising questions about the potential impact of pathology on the research findings. New methods permit the in vivo comparison of the hemispheres in healthy subjects. Particularly, magnetic resonance imaging (MRI) and positron emission tomography (PET) are important because of their high spatial resolution and ability to image subcortical brain structures.

Handedness and language

Broca's Area and Wernicke’s Area are linked by a white matter fiber tract, the arcuate fasciculus. This axonal tract allows the neurons in the two areas to work together in creating vocal language. In more than 95% of right-handed men, and more than 90% of right-handed women, language and speech are subserved by the brain's left hemisphere. In left-handed people, the incidence of left-hemisphere language dominance has been reported as 73% and 61%.

There are ways of determining hemispheric dominance in a person. The Wada Test introduces an anesthetic to one hemisphere of the brain via one of the two carotid arteries. Once the hemisphere is anesthetized, a neuropsychological examination is effected to determine dominance for language production, language comprehension, verbal memory, and visual memory functions. Less invasive (sometimes costlier)
techniques, such as functional magnetic resonance imaging and Transcranial magnetic stimulation, also are used to determine hemispheric dominance; usage remains controversial for being experimental.

Movement and sensation

In the 1940s, Canadian neurosurgeon Wilder Penfield and his neurologist colleague Herbert Jasper developed a technique of brain mapping to help reduce side effects caused by surgery to treat epilepsy. They stimulated motor and somatosensory cortices of the brain with small electrical currents to activate discrete brain regions. They found that stimulation of one hemisphere's motor cortex produces muscle contraction on the opposite side of the body. Furthermore, the functional map of the motor and sensory cortices is fairly consistent from person to person; Penfield and Jasper's famous pictures of the motor and sensory homunculi were the result.

Split-brain patients

Research by Michael Gazzaniga and Roger Wolcott Sperry in the 1960s on split-brain patients led to an even greater understanding of functional laterality. Split-brain patients are patients who have undergone corpus callosotomy (usually as a treatment for severe epilepsy), a severing of a large part of the corpus callosum. The corpus callosum connects the two hemispheres of the brain and allows them to communicate. When these connections are cut, the two halves of the brain have a reduced capacity to communicate with each other. This led to many interesting behavioral phenomena that allowed Gazzaniga and Sperry to study the contributions of each hemisphere to various cognitive and perceptual processes. One of their main findings was that the right hemisphere was capable of rudimentary language processing, but often has no lexical or grammatical abilities. Eran Zaidel, however, also studied such patients and found some evidence for the right hemisphere having at least some syntactic ability.

For example: Patients with brain damage from surgery, stroke or infection sometimes develop a syndrome in which they can feel sensations in their hand, but they don't feel responsible for nor able to control its movements. In patients with a corpus callostomy, alien hand syndrome most often manifests as uncontrolled but purposeful movements of the nondominant hand.

Exaggeration

Hines states that the research on brain lateralization is valid as a research program, though commercial promoters have applied it to promote subjects and products far outside the implications of the research. For example, the implications of the research have no bearing on psychological interventions such as EMDR and neurolinguistic programming, brain training equipment, or management training.
Nonhuman brain lateralization

Specialization of the two hemispheres is general in vertebrates including fish, frogs, reptiles, birds and mammals with the left hemisphere being specialized to categorize information and control everyday, routine behavior, with the right hemisphere responsible for responses to novel events and behavior in emergencies including the expression of intense emotions. An example of a routine left hemisphere behavior is feeding behavior whereas as a right hemisphere is escape from predators and attacks from conspecifics.

FUNCTIONS OF CORPUS CALLOSUM

The corpus callosum (Latin: tough body) is a structure of the eutherian brain in the longitudinal fissure that connects the left and right cerebral hemispheres. It facilitates communication between the two hemispheres. It is the largest white matter structure in the brain, consisting of 200-250 million contralateral axonal projections. It is a wide, flat bundle of axons beneath the cortex. Much of the inter-hemispheric communication in the brain is conducted across the corpus callosum.

Review

The posterior portion of the corpus callosum is called the splenium; the anterior is called the genu (or "knee"); between the two is the truncus, or "body", of the corpus callosum.
callosum. The rostrum is the portion of the corpus callosum that projects posteriorly following from the anteriormost genu.

Thinner axons in the genu interconnect prefrontal cortex areas between the two sides of the brain. Those in the posterior body of the corpus callosum interconnect parietal lobe areas. Thicker axons in the midbody of the corpus callosum and in the splenium interconnect areas of the motor, somatosensory, and visual cortex.

Using magnetic resonance diffusion tensor imaging, the studies of Hofer and Frahm suggest that the anterior sixth of the corpus callosum interconnect the prefrontal parts of the brain; the next third, the premotor and supplementary motor regions; the following sixth, the motor areas; then the next twelfth deals with the sensory areas; and the final quarter, the parietal, temporal, and occipital lobes.

**Evolution**

In primates, axon diameter, and hence its conduction velocity, has increased in the corpus callosum with increased brain size and so maintained the speed of communication between the two cerebral hemispheres particularly between its primary motor and sensory areas. However, this scaling between increased brain size and increased myelination of corpus callosum axons has not occurred between chimpanzees and humans. This has resulted in humans having double the delay time of communication between the two sides of the brain compared to that of macaques.

**Sexual dimorphism**

There are disputed claims about the difference of the size of the human corpus callosum in men and women and the relationship of any such differences to gender differences in human behaviour and cognition.

R. B. Bean, a Philadelphia anatomist, suggested in 1906 that the "exceptional size of the corpus callosum may mean exceptional intellectual activity" and claimed differences in size between males and females and between races, although these were refuted by Franklin Mall, the director of his own laboratory.

Of much more substantial popular impact was a 1982 *Science* article claiming to be the first report of a reliable sex difference in human brain morphology, and arguing for relevance to cognitive gender differences. This paper appears to be the source of a large number of lay explanations of perceived male-female difference in behaviour: For example *Time* magazine was reported to state in 1992 that the corpus callosum is "Often wider in the brains of women than in those of men, it may allow for greater cross-talk between the hemispheres—possibly the basis for women’s intuition."

There is scientific dispute not only about the implications of anatomical difference, but whether such a difference actually exists. A substantial review paper performed a meta-analysis of 49 studies and found, contrary to de Lacoste-Utamsing and Holloway, that males have a larger corpus callosum, a relationship that is true
whether or not account is taken of larger male brain size. Bishop and Wahlstein found that "the widespread belief that women have a larger splenium than men and consequently think differently is untenable." However, more recent studies using new analysis and imaging techniques (e.g. diffusion-tensor imaging) revealed morphological and microstructural sex differences in human corpus callosum. A 2006 Serbian study found variations in morphology correlated with sex, but in ways too complex for simple direct comparison. Whether, and to what extent, these morphological differences are associated with behavioural and cognitive differences between men and women remains unclear.

Other correlations

The front portion of the corpus callosum has been reported to be significantly larger in musicians than non-musicians, and to be 11% larger in left-handed and ambidextrous people than right-handed people.

Epilepsy

The symptoms of refractory epilepsy can be reduced by cutting the corpus callosum in an operation known as a corpus callosotomy.

Pathology

- Alien hand syndrome
- A complete or partial absence of it in humans is called agenesis of the corpus callosum.
- Split-brain
- Septo-optic dysplasia (deMorsier syndrome)
- Alexia without agraphia (seen with damage to splenium of corpus callosum)