

Biopsychology 2012 – sec 001

Study Guide for Section 4 (last section)

Psychoactive Drugs and Addiction

What are psychoactive drugs? Substances that influence subjective experience and behavior by acting on the nervous system.

What are some of the most common psychoactive drugs?

1. Sedative hypnotics and anxiolytics (antianxiety drugs)
2. Antipsychotic drugs
3. Antidepressant drugs
4. Opiates (analgesics)
5. Stimulants

I. Sedative hypnotics and anxiolytics:

- Most common:
1. Alcohol
 2. Barbiturates (ex. pentobarbital, sodium amytal – *truth serum*)
 3. Benzodiazepines (ex., valium™, librium™)

Also known as “mild tranquilizers”

How do sedative hypnotics and antianxiety drugs work? They bind to the GABA_A receptor complex and facilitate the action of the endogenous neurotransmitter GABA.

II. Antipsychotic drugs: used to treat psychotic conditions such as schizophrenia, paranoia, etc.

- Most common
1. Phenothiazines (ex., chlorpromazine - Thorazine™)
 2. Butyrophenones (ex., haloperidol - Haldol™)

Also known as “major tranquilizers”

How do antipsychotics work? They block dopamine receptors, especially the D₂ receptor subtype.

III. Antidepressant drugs: used to treat depressive illnesses

- Most common
1. Monoamine oxidase inhibitors (MAOI)
 2. Tricyclic antidepressants (ex., imipramine - Tofranil™)
 3. Serotonin-specific reuptake inhibitors (SSRIs ex., fluoxetine - Prozac™)

How do antidepressants work? MAOIs and tricyclics/SSRIs work through different mechanisms:

- MAOIs block the breakdown of monoamine neurotransmitters (especially serotonin and noradrenaline)
- Tricyclic antidepressants and SSRIs block the reuptake of monoamines (especially serotonin and noradrenaline – with the SSRIs being more specific for serotonin)
- Overall then, all antidepressant drugs increase the amount of monoamine neurotransmitters in the synapses

IV. Opiates (analgesics): clinically used in the treatment of pain – high potential for addiction

- Most common:
1. Opium poppy derivatives (ex., morphine, codeine)
 2. Derivatives of morphine (ex., heroin)
 3. Endogenous morphine (endorphins) = made in the body (ex., enkephalins, dynorphin, β -endorphin)

How do opiates work? All work by binding opiate receptors in the nervous system (mu, delta, and kappa subtypes of opiate receptors)

V. Stimulants: in general, increase the activity of the nervous system

- Several classes of stimulants:
1. Behavioral stimulants (ex., cocaine, “crack”, amphetamine)
 2. Convulsant stimulants (ex., pentalenetetrazol, bicuculline)
 3. General stimulants (ex., caffeine)
 4. Psychedelics (ex., lysergic acid diethylamide [LSD], mescaline, marijuana, ecstasy, psilocybin [from some mushrooms])

How do stimulants work? Each subtype has different mechanism of action:

- Behavioral stimulants generally work by blocking dopamine reuptake at the synapse and some even produce dopamine release (amphetamine).
- Convulsants block GABA receptors.
- A general stimulant such as caffeine works by blocking one subtype of adenosine receptor
- Psychedelic drugs have various mechanisms of action which involve the serotonin system (LSD, ecstasy, mescaline, psilocybin) or other specific neurotransmitter receptors (the cannabinoid receptor for marijuana).

What is addiction? Someone addicted to a drug is, in a way, sentenced to a term of involuntary servitude, being obliged to fulfill the demands of their drug dependency

What is drug tolerance? Decreased susceptibility to a drug that develops as a result of repeated exposure to the drug; mostly mediated by compensatory mechanisms that oppose the initial drug effect (ex., if drug causes hypothermia, opposing mechanism of hyperthermia is produced)

What is cross-tolerance? tolerance that develops to one drug carries over to other drugs (often of the same family) suggesting that they act through the same target (mechanism)

What are the 3 different types of tolerance that we discussed in class?

1. Metabolic tolerance: reduced sensitivity to a drug that results from the increased ability of the body to metabolize the drug (ex., up-regulation of liver enzymes)
2. Cellular tolerance: a change that takes place in nerve cells in which the activity of neurons adjust to the excitatory or inhibitory effects of a drug (ex., receptor downregulation)
3. Learned tolerance: behavior change acquired through associative learning.

What is physical dependence? State in which discontinuation of drug taking will induce withdrawal syndrome (illness)

What is the withdrawal syndrome? Illness induced by the elimination or absence from the body of a drug on which a person is physically dependent.

What is psychological dependence? The most important factor in addictive behavior – includes several cues associated (conditioned) with pleasurable effects of drugs that are difficult to eliminate; mostly responsible for “compulsive” drug taking behaviors.

What is sensitization? Increased behavioral response to the same dose of a drug
- for example, the behavioral activity of animals in response to repeated injections of amphetamine increases over time.

What is the role of learning in addiction? Involved in the development of psychological dependence.

1. Associations of places and cues with drug taking produces both **conditioned drug tolerance** and **conditioned withdrawal effects** (Siegel).

Example: Rats that are injected with morphine repeatedly in context A will develop conditioned tolerance and withdrawal only in context A, not in their homecage. Thus, if they get injected with a high dose of morphine in their homecage, they are much more vulnerable to die from an overdose, than if they received the injection in context A.

What is reinforcement? Process by which there is an increase in the likelihood of a behavior immediately preceding the reinforcement (positive or negative). Reinforcement is most effective upon behaviors that have just happened – it’s effects wane very quickly with time (example of rats preferring a small reward immediately rather than a much larger reward, with a delay).

Who discovered reinforcement? In a classic study, Olds & Milner (1954) implanted electrodes in the brain of rodents that were aimed for the reticular formation, but accidentally implanted some animals in the medial forebrain bundle (MFB). They observed that the rats with MFB electrodes would do everything to get more stimulation. They argued that the MFB was a region involved in pleasure and reinforcement. (rats would die of starvation in order to obtain electrical stimulation of the MFB)

What are the neural systems of reinforcement? Several additional studies have shown that neurons from the ventral tegmental area, which mainly contain dopamine as a neurotransmitter, project their axons through the MFB to the nucleus accumbens, where dopamine is released.

- If the effect of dopamine is blocked by injecting dopamine receptor antagonists in the nucleus accumbens, electrical self-stimulation of the MFB and drug taking behavior can be blocked in rodents.

What is the role of reinforcement in addiction? Most addictive drugs studied so far have strong reinforcing properties. Thus, the behaviors associated with drug taking become more likely (reinforced). This occurs through:

1. **Positive reinforcement:** Pleasurable effects of drugs that can be produced, but not always, consciously (remember the example of the detoxicated heroin addicts and their willingness to work hard for morphine injections that they consciously reported as “worthless”). Increases the likelihood of behavior just preceding reinforcement.
2. **Negative reinforcement:** Increase in the likelihood of a response that reduces or removes an aversive stimulus (in the case of addiction, attempts to stop withdrawal syndrome by injecting drug).

What is the theory of incentive sensitization? Why do humans and animals keep injecting drugs even if the drugs are no longer pleasurable? The incentive sensitization theory (Robinson & Berridge) suggests that the stimuli associated with drug taking (conditioned stimuli) become “attached” with motivational properties, which become “sensitized” (stronger) with repeated drug taking. So even if drugs lose their direct “pleasurable” qualities, the conditioned incentive stimuli “replace” the primary drug effects, being themselves very pleasurable.

- As a matter of fact, dopamine release in the nucleus accumbens is triggered by situational cues (in addicted rats) more than by the drug itself in addicted animals.

What are there genetic influences on susceptibility to substance abuse? In alcoholism, the most studied of abused substances, there is a genetic link for at least one type of addict.

1. Steady drinkers: personality traits include antisocial personalities, with lifelong histories of impulsiveness and aggressiveness, with inclination for seeking novel and exciting experiences.
2. Binge drinkers: personality traits include emotionally dependent, rigid, perfectionist, introverted, without an inclination for novelty seeking.

- Monozygotic twin and cross-fostering studies indicate that the children of steady drinkers are seven times more likely to drink themselves (only in sons, not in daughters).
- Binge drinkers have no significant associations with genetic factors.
- Animal studies indicate that alcohol preferring strains of rats have lower dopamine levels in nucleus accumbens compared to most other strains of rats; suggests that these individuals “need” additional exciting events to achieve comparable dopamine levels observed in “normal” strains.

How are drug dependence problems treated? In general, the physical dependence and withdrawal symptoms that accompany discontinuation of drug taking can be monitored and slowly reduced by systematically reducing drug taking in a clinical setting (clinical drug rehabilitation programs – example of nicotine patches in individuals trying to stop smoking). At most, a few months are normally sufficient to stop drug taking and avoid serious withdrawal symptoms. Unfortunately, the psychological dependence is much more difficult to deal with, and often, individuals who have suffered drug dependence and find themselves in situations (cues) previously associated with drug taking will relapse into their drug problem.

What is ecstasy? It is a derivative of amphetamine (3,4-methylenedioxymethamphetamine – MDMA) that shares some similarities with mescaline.

What are the acute effects of ecstasy? (beginning about 20 min after ingestion and lasts on average 4 hrs)

- euphoria, increased energy, elevated arousal and self-confidence, heightened sensory awareness
- feelings of intimacy and closeness, increased depth of emotion, and decreased appetite

Some Acute physiological adverse effects:

- tachycardia, jaw-clenching, pupillary dilation, gait instability, and nausea

What are the subacute effects of ecstasy? (up to 48 hrs after ingestion) - carry over of many acute subjective effects

- additional effects related to “crash” phenomenon associated with psychostimulants: muscle aches, fatigue, depression, irritability, difficulty in concentrating, and headaches
- depression ratings reaching clinical depression up to 4 days after ingestion!

What are the some of the chronic effects of ecstasy? (defined loosely as 50 tablets or more in a lifetime)

- leads to higher incidence of clinical depression, anxiety, and sleep disorders
- higher incidence of impulsiveness/aggressiveness and novelty seeking
- higher incidence of learning and memory impairments
- relatively moderate doses of ecstasy can lead to a relatively permanent reduction in serotonin terminals and axons in many brain regions (i.e., cortex, hippocampus, amygdala), as determined in non-human primates

Hormones and Behavior

What is the neuroendocrine system? It is the sum of the glands, hormones, and target tissues/organs involved in the control of bodily functions (including behavior).

What are glands? They are specific cell masses throughout the body that produce and secrete a variety of hormones (chemicals).

There are two types of glands:

1. Exocrine glands: they secrete their chemicals into ducts, which are carried to the surface of the body (ex. sweat and tear [lacrimal] glands).
2. Endocrine glands: ductless glands that secrete “hormones” into the general circulation (ex. pituitary and gonadal glands).

What are hormones? Chemicals released by the endocrine glands into the general circulation. Hormones can be of several general types:

- I. Amino acid derivatives (ex. adrenaline, produced from tyrosine);
- II. Short peptides and proteins (adrenocorticotropin hormone, ACTH);
- III. Steroids (ex. cortisol, estradiol; synthesized from cholesterol).

What are some examples of endocrine glands and their hormones?

- pineal gland: melatonin;
- hypothalamus: vasopressin, oxytocin, prolactin;
- pituitary gland: luteinizing hormone, adrenocorticotropin hormone, follicle stimulating hormone;
- thyroid gland: thyroxin hormone;
- thymus gland: lymphokines (involved in immune responses);
- adrenal glands: cortisol;
- pancreas: insulin, glucagon;
- ovaries: estradiol, testosterone;
- testes: testosterone, estradiol.

As an example of endocrine regulation, how are the gonads controlled?

The pituitary gland (“master gland”) produces and secretes tropic hormones, which in turn control the release of hormones from other glands, including the gonads.

In the case of the gonads, gonadotropins (follicle-stimulating hormone and luteinizing hormone) are secreted by the anterior pituitary in the general circulation and target the gonads to induce secretion of gonadal steroids (androgens and estrogens).

What controls the pituitary gland?

Different nuclei of the hypothalamus produce *releasing factors*, which control the production and secretion of tropic hormones from the anterior pituitary.

- neurons of the hypothalamus that produce releasing hormones (ex. paraventricular nucleus) secrete their hormones in the median eminence.

- the portal blood system that bathes the median eminence transports the releasing hormones to the anterior pituitary, which produces the secretion of tropic hormones from anterior pituitary cells (secretagogues) into the general circulation (and eventually reaches the gonads and other glands throughout the body).

- example: gonadotropin-releasing hormone from the hypothalamus produces the release of follicle-stimulating hormone and luteinizing hormones from the anterior pituitary, which target the gonads.

The posterior pituitary, on the other hand, is directly innervated by axons and terminals from neurons of the hypothalamus, which directly secrete hormones in the general circulation.

- example: oxytocin is released from the hypothalamus (supraoptic nucleus) into the posterior pituitary, and is involved in uterine contraction during child birth and milk ejection during suckling.

What is negative feedback in the neuroendocrine system? A signal (usually a hormone in the endocrine system) from a change in one direction that results in a compensatory effect in the other direction. Practically, when a hormone is released, it goes back to several body areas (pituitary, hypothalamus) involved in its release to terminate further release.

- recall analogy with heating system at home, with the thermostat controlling the temperature, and high temperature shutting down the furnace.

What are regulatory behaviors? Behaviors controlled by a homeostatic mechanism. Examples are temperature regulation, eating and drinking, salt appetite, waste elimination, etc.

What are homeostatic mechanisms? Mechanisms that keep some body functions within a narrow, fixed range.

What are non-regulatory behaviors? Behaviors that are not controlled by homeostatic mechanisms – all behaviors excluding those regulated by homeostatic processes. Examples are sexual behavior, parental behaviors, aggression, playing sports, etc. Both regulatory and non-regulatory behaviors are controlled by the hypothalamus.

Example of non-regulatory behaviors – Sex!

What are steroid hormones? lipid soluble molecules characterized by 3 six carbon rings and 1 five carbon ring produced primarily in the adrenals and gonads

What are releasing hormones? Hormones from the hypothalamus that stimulate the production and release of hormones from the anterior pituitary

What are gonadal hormones? They include two main classes of steroid hormones (derived from the fat molecule cholesterol) known as androgens and estrogens, and a third class known as the progestins (the most common of which is progesterone)

What are androgens? The class of steroid hormones that includes testosterone

What are estrogens? The class of steroid hormones that includes estradiol

How is the brain of males and females different?

Some brain structures differ between males and females; these structures are referred to as sexually dimorphic.

- the suprachiasmatic nucleus and parts of the preoptic nuclei (medial nucleus) are generally larger in males.

- this is produced by the organizational effects of testosterone around or shortly after birth (that is, if testosterone is present, facilitates the development of the “male” brain).

Is there a genetic link to sexual orientation and preferences?

According to studies performed in monozygotic twins, the chance of homosexual preference of one twin given that the other one is homosexual is 50%; the figure in dizygotic twins is only about 20%.

- the “homosexual” gene is clustered near the end of the X-chromosome.

Example of regulatory behaviors – Eating and Drinking

How is eating (feeding) controlled? Eating is partly controlled by the digestive tract, the hypothalamus, and cognitive factors

What is the role of the digestive tract in the control of eating? It functions as a reservoir where a variety of chemicals and enzymes released (ex., hydrochloric acid, pepsin, etc.) help breakdown and absorb essential nutrients and energy molecules from food.

What are the 3 classes of molecules ingested by our body?

1. Lipids (fats – provides majority of energy stores – 85%)
2. Amino acids (essential building blocks of proteins – provides about 14% of energy)
3. Glycogens (starches and sugars – glucose – provides about 1% of energy stored)

What are the brain areas involved in the long-term control of feeding? There are 3 main hypothalamic nuclei critically involved in the control of feeding:

1. Paraventricular nucleus: involved in the release of ACTH and thyrotropin from the anterior pituitary (mostly involved in metabolic regulation)
2. Lateral hypothalamus: coordinates motor responses involved in feeding behaviors
3. Arcuate nucleus: receives peripheral signals (leptin and insulin) about the state of the energy stores in the body, and projects to paraventricular nucleus and lateral hypothalamus to increase or decrease feeding

What are the mechanisms involved in the short-term regulation of feeding? There are signals for satiety and for hunger:

I. Hunger signals:

- Sight of food and thinking about food: raises activity of autonomic nervous system, which activates pancreas to release insulin in blood circulation - produces a drop in blood glucose that initiates a response in the nucleus of the solitary tract (see below)
- Hypoglycemia: a drop in blood glucose levels that is sensed by specialized receptors onto neurons of the area postrema (no blood-brain-barrier), and peripherally in the liver, via the vagus nerve (neurons in the nucleus of the solitary tract in the medulla)
- Lipoprivation: a drop in fatty acid levels available to cells, detected in liver and other abdominal organs. Information provided to brain via vagus nerve

II. Satiety signals:

- Gastric distension: somatosensory receptors located in gastrointestinal tract and enteric nervous system sense stomach distension, and provide this information to nucleus of the solitary tract via the vagus nerve
- Cholecystokinin (CCK): peptide released from gastrointestinal tract and enteric nervous system - responds to both volume and caloric content of food being absorbed - acts on vagal somatosensory receptors and synergises with gastric distension signals from gastrointestinal tract
- High levels of Insulin (released from b-cells of pancreas) *and* glucose in blood serve as a satiety signal at the level of the hypothalamus (arcuate nucleus)

With regard to water balance, how much of the human body is water? Approximately 70%.

What are the two mechanisms responsible for water balance (homeostasis)?

1. Osmotic thirst (cellular dehydration): increase in concentration of dissolved substances in the blood (hypertonicity)

- specialized hypothalamic neurons in area called vascular organ of the lamina terminalis (OVLT) sense hypertonicity
- OVLT neurons send their axons to paraventricular nucleus neurons that produce vasopressin (antidiuretic hormone – ADH) that, when activated, release vasopressin in posterior pituitary

2. Hypovolemic thirst: decrease in overall blood volume

- increases water retention via two mechanisms:

a) reduced blood flow in renal system produces release of angiotensin II from kidneys which is sensed by hypothalamic subfornical organ.

- subfornical organ activates paraventricular ADH neurons to release vasopressin from posterior pituitary.

b) mechanoreceptors (baroreceptors) in wall of large blood vessels and heart signal loss of blood to the hypothalamus via vagus nerve and nucleus of the solitary tract (NTS).

- NTS also projects to paraventricular nucleus and synergizes with effects of angiotensin and activate sympathetic nervous system to help correct the reduction in blood pressure (produces vasoconstriction)

- NTS also projects to lateral hypothalamus to stimulate drinking behaviors (finding water, ingesting fluids).

Emotions

What are the early theories of emotions?

I. James-Lange theory (1884): a theory of emotion suggesting that behaviors and physiological responses are directly elicited by situations and that feelings of emotions are produced by feedback from these behaviors and responses.

Example: sight of a bear elicits increases in autonomic (heart rate, blood pressure, etc.), and behavioral responses (running), which in turn produce the conscious feeling of fear.

II. Cannon-Bard theory (1900's): a theory suggesting that emotional experiences and emotional expression (autonomic, hormonal, and behavioral responses) occur in parallel and have no direct causal relation to one another.

Example: sight of a bear elicits, at the same time, the feeling of fear and the autonomic, hormonal and behavioral responses.

What are the predictions of these two theories?

The James-Lange theory predicts that without autonomic, hormonal, and somatic feedback, a person would not feel emotions.

The Cannon-Bard theory predicts just the opposite, that person does not need feedback to feel emotions.

Studies of patients with various spinal cord injuries have lent support to both theories, while pointing to their limitations.

- patients with injuries which remove most feedback from autonomic and somatic origin still experience emotional “feelings”;

- however, these patients report much different emotional experiences, being weaker, of diminished intensity.

What is Damasio's somatic marker theory of emotions?

Suggestion that signals (markers) arising from internal and external environment (emotional stimuli) act to guide behavior and decision making, usually in an unconscious process

What is the brain system associated with emotions?

An early influential theory by Papez (1937) defined the “limbic system” as the brain circuit involved in the elicitation of emotional expression and feelings.

- The limbic system consists of several interconnected structures, the most important of which include the hippocampus, amygdala, cingulate cortex, fornix, septum, mammillary body, and some hypothalamic nuclei.

- Papez proposed that emotional expression was produced by limbic activity upon the hypothalamus, whereas emotional experience (feeling) was produced by limbic activity upon the cortex.

- Papez was right, to some extent, although the concept of the limbic system has greatly evolved since his first proposal; the role of the amygdala in emotions has particularly received a lot of attention.

What is the Kluver-Bucy syndrome?

It is a cluster of behaviors originally observed in monkeys sustaining bilateral anterior temporal lobectomies (also observed with amygdala lesions, and later observed in humans).

The behaviors included:

- flat affect (emotions);
- consumption of nearly everything edible;
- increased, but inappropriate, sexual activity (often towards inanimate objects);
- tendency to repeatedly investigate same objects;
- tendency to investigate objects with mouth;
- increased tameness, lack of fear.

What are fear reactions?

Fear reactions are characterized by a constellation of autonomic, hormonal, and behavioral responses preparing an organism for fighting or fleeing.

What is the brain area that regulates this constellation of reactions?

The central nucleus of the amygdala, which has connections to most brain areas controlling specific aspects of the fear reactions.

What has been learned about fear in humans?

Patients evaluated for neurosurgery and subjected to electrical brain stimulations show autonomic signs of fear when stimulated in the hypothalamus; however, they do not report any fearful “experiences”; however, amygdala stimulation elicits both autonomic and experiential fear reactions.

- patients with bilateral amygdala damage respond to fear provoking stimuli in a much blunted way; they also cannot use negatively charged emotions to remember details of a fearful situation.
- brain imaging experiments in human subjects shown frightening movies or slides show particularly high activity levels in the amygdala.

How was stress originally described?

Hans Selye (1940's) described a set of physiological effects related to a “generalized” alarm system in response to illness and surgery.

How is stress now defined?

A physiological reaction caused by the “perception” or “detection” of aversive or threatening situations that jeopardize some homeostatic function.

What are some examples of stressful situations?

Stressors normally fall into two classes:

1. Psychological stressors:
 - marriage, divorce, job loss, new job;
 - entering college;
 - death of a loved one;
 - public speech;
2. Systemic stressors:
 - limb fracture;
 - surgical procedures;
 - viral or bacterial infections;

- food poisoning;
- illnesses (cancer, heart conditions, etc.).

What are the physiological responses to stressful situations?

There are two different sets of responses; one produced by *acute* stressors (normally advantageous), and one produced by *chronic* stressors (normally disadvantageous):

1. Acute stress responses:

- activation of autonomic and endocrine responses;
- release of adrenaline and noradrenaline by the adrenal medulla;
- release of cortisol by the adrenal cortex;
- increases in heart rate and blood pressure to bring more blood to muscles;
- mobilization of energy resources (production and release of glucose for use by muscles);
- inhibition of inflammatory responses;
- resistance to infection;
- inhibits sexual functions and sex steroid production and secretion.

2. Chronic stress responses:

- hypertension (high blood pressure);
- gastrointestinal ulcers;
- diabetes;
- inhibition of growth (particularly important in young children –psychological dwarfism);
- infertility;
- suppression of the immune system;
- damage to the brain (hippocampus).

How does the brain control the autonomic and endocrine responses to stress?

Sympathetic neurons of the autonomic nervous system located in the brainstem innervate and activate the secretory cells of the adrenal medulla to secrete adrenaline and noradrenaline in the general circulation.

The hypothalamus (paraventricular nucleus) releases corticotropin-releasing hormone (CRH) in the median eminence, which is transported to the anterior pituitary and elicits the release of adrenocorticotropic hormone (ACTH) in the general circulation, which produces the release of glucocorticoids (cortisol) in the general circulation from the adrenal cortex.

What brain areas are involved in the perception of different stressful situations?

1. Limbic system: involved in the perception of “psychological stressors”;
2. Circumventricular organs: involved in the detection of “blood born pathogens” – poisons;
3. Nucleus of the solitary tract: involved in the detection of infections.

All these areas converge upon the paraventricular nucleus of the hypothalamus, which controls the anterior pituitary via the release of CRH and the brainstem autonomic nuclei by direct neural connections.

How can one control stress?

A lot of evidence suggests that the perception of control over stressful situations reduces several physiological reactions produced by these stressful situations. The perception of control produced by behavioral or mental responses is termed the *coping response*.