Klinika adiktologie
1. LF UK a VFN v Praze

Provided by:	Department of Addictology, 1st Faculty of Medicine, Charles University, and General University Hospital in Prague	Expert supervisor:	PharmDr. Magdalena Šustková
Faculty:	1st Faculty of Medicine	Teacher:	PharmDr. Magdalena Šustková
Valid from:	2014	Title:	**Introduction to Biomedical Addictology**
Semester:	n. a.		
Scope, examination:			
Points:			
e-Credits:			
Examination format:	oral or written		
Scope of instruction per academic year:	6 x 90 min + 45 min		
Number of places:	unlimited		
Minimum number of students:	unlimited		
Course status:	currently available		
Language of instruction:	Czech		
Format of instruction:	part-time		
Level:	Ph.D.		
Note:	Prof. PhDr. Michal Miovský, Ph.D.		

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Annotation

The course is aimed at familiarising the students with the basic concepts and principles of biomedical addictology. Although addictology is a non-medical field by definition, graduates in it are most likely to work closely with physicians and other health professionals of various specialisations in providing prevention and treatment interventions. Therefore, their knowledge of the basic biomedical terms and principles is essential for their effective communication with medical practitioners. A basic command of neuroscience, including the basics of the functioning of the nervous system, means by which information is transmitted in the body, an understanding of the main mechanisms of action of addictive drugs of abuse, and the mechanisms of addictive behaviour and the ways in which it can be influenced by means of both pharmacotherapeutic/pharmacological and non-pharmacological procedures, are vital for the understanding of the correlates, relationships, and implications with relevance to the majority (if not all) of domains and levels addictology involves.

The students will learn the basics of biomedical addictology in the following thematic units:

a) introduction to neuroscience (basic concepts and general principles, the nervous system, signal transmission, receptors and neurotransmitters and their functions; the effect and toxicity of substances, adverse effects, dosage, routes of administration, etc.)
b) neurobiological mechanisms of the effects of “drugs” I. (stimulants – e.g. cocaine, amphetamine, methamphetamine, entactogens – “ecstasy”, nicotine, cathinones. etc.)
c) neurobiological mechanisms of the effects of “drugs” II. (depressants – e.g. alcohol, opioids, benzodiazepines, anaesthetics – such as ketamine)
d) neurobiological mechanisms of the effects of “drugs” III. (hallucinogens – e.g. LSD, psilocybin, marijuana, new synthetic drugs, combination of “drugs”, etc.)
e) neurobiological mechanisms of addictive behaviour (outline of the state-of-the-art knowledge, neural systems, circuitry, and neurotransmitters with relevance to addiction, etc.)
f) possibilities of higher vulnerability/predisposition to addictive behaviour – external and internal factors (genetics, age, gender, illness, stress, combinations thereof, etc.)

The knowledge and understanding of the subject matter will be tested by the final written exam.

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Course objective
The objective of the course is to familiarise the students with the basics of biomedical addictology: the basic concepts of neuroscience, the neurobiological/neuropharmacological action of “drugs” and addictive behaviour and related (pharmaco-) therapeutic procedures. The purpose is to provide an insight into the state-of-the-art knowledge of the basic principles of the mechanisms behind the effects of drugs and addictive behaviour, including specific risks/liabilities that contribute to substance addiction, and a general understanding of major relevant (pharmaco-) therapeutic or preventive interventions. Given its predominantly neurobiological focus, the course should provide the students with more thorough and comprehensive expertise in relation to substance abuse and addiction. In addition, the course should improve prospective addictologists’ abilities to communicate and engage in active collaboration with medical/health professionals. The completion of the “Introduction to Biomedical Addictology” course is also a basic prerequisite for a follow-up biomedicine-specific course – “Biomedicine and Biomedical Addictology: Special Issues”.

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Descriptors

Course outcome descriptors:

Knowledge:

Students will be expected:

- to know the basic concepts used in biomedical addictology, i.e. the neurobiology of the effects of "drugs" and substance addiction
- to have a general understanding of the types of drugs of abuse, including the types and mechanisms of effects of the main categories of drugs
- to know/have a general understanding of the latest scientific knowledge of mechanisms (especially neurobiological) and possible predispositions involved in the development and maintenance of substance addiction
- to understand the basics of medical addictology and be able to use them in their wide-ranging addictological practice together with other addiction-specific knowledge and skills (see below)

Skills:

Using the knowledge acquired (see above), the students can orient themselves in the basic biomedical terminology, understand standard technical texts, and engage in efficient communication with medical professionals on a peer-to-peer footing as part of their addiction-specific research, prevention, and treatment activities.

Their knowledge makes the students able to make a better assessment/evaluation of a specific situation. Being able to match the effects described and observed with the type of drug (effect), they can also identify the risks related to the use of the drug (or overdose on the drug or its use in combination with other substances) and thus be more effective in responding to the situation.

Making particular use of their knowledge of risk/predisposition factors involved in addictive behaviour, in their future addictological practice (prevention and treatment activities) students can be more accurate in estimating the risks, consequences, and correlates of the phenomena under consideration, such as the different types of stress, behavioural characteristics, and family history, which may play a role in the individual's/client's relationship with addictive substances.

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Moreover, such knowledge can help the graduate contribute more effectively to work/activities/practice in the field of addictology-specific prevention, treatment, and research.

Competences:

As previously mentioned, thanks to their knowledge of biomedicine and general understanding of the neurobiological mechanisms of the effects of "drugs" and the neurobiological mechanisms of addictive behaviour, as well as their awareness of both internal (both innate and learnt) and external (social, etc.) major risks and predispositions for elevated vulnerability to the effects of certain drugs and addictive behaviour, the students possess a much more robust knowledge base and perception capacities which make them more effective in pursuing both their scientific and therapeutic practice in addictology.

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Literature

Textbooks and information sources:

Required reading:

* Druga R., Grim M., Dubovský P.: Anatomie centrálního nervového systému. Galén, Karolinum2011; především ss 11-19, 79-100, 109-152,vybrané části z 186-219

* Lincová, Farghali a kol: Základní a aplikovaná farmakologie Galén, 2007 (2. vydání) studium ss 207-216

* Kalina K.: Základy klinické adiktologie. Grada 2014 (nové přepracované vydání), kapitola „Neurobiologie závislostí“ a kapitola „Genetické dispozice k drogovým závislostem a epigenetika“

* Ganong WF: Přehled lékařské fyziologie. Galén 2005 (5. vydání) ss

* Barret E, Barman SM, Boitano S et al: Ganong's Review of Medical Physiology, 24th Edition (LANGE Basic Science) 2012

* Rang and Dale´s Pharmacology (6th ed. 2007 or 7th ed. 2011) …

*Katzung …Farmakologie toxikologie

Recommended further reading:

* Koukolík F.: Lidský mozek. Funkční systémy. Norma a poruchy. Galén 2012 (3. přepracované vydání)

* Cooper JR, Bloom FE, Roth RH: The biochemical basis of neuropharmacology. Oxford University Press 2003 (8. edition)

* Nestler EJ, Hyman SE, Malenka RC: Molecular Neuropharmacology. A foundation for clinical neuroscience. McGraw-Hill Companies,Inc. 2009 (2. edition)

* Clark DL and Boutros NN: The Brain and Behavior. An Introduction to behavioral neuroanatomy. Blackwell Science,Inc , USA 1999

* Koob GF: Drugs, Addiction and the Brain. Elsevier, 2014 (1. edition)

* Koob GF a Volkow ND Neurocircuitry of addiction: Neuropsychopharmacology Reviews (2010) 35, 217–238

* Volkow ND, Wang GJ, Fowler JS, Tomasi D, Telang F: Addiction: beyond dopamine reward circuity. PNAS, (2011) 108 (37):15037-15042

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* Hyman SE, Malenka RC, Nestler EJ: Neural mechnanisms od addiction: the role of reward-related learning and memory
* Everitt BJ, Belin D, Economidou D, Pelloux Y, Dalley JW, Robbins TW (2008). Review. Neural mechanisms underlying the vulnerability to develop compulsive drug-seeking habits and addiction. Phil Trans Royal Soc London B Biol Sci 363:3125–3135.
* Kalivas PW, O'Brien C (2008). Drug addiction as a pathology of staged neuroplasticity. Neuropsychopharmacology 33: 166–180.
* Kalivas, P.W., Volkow, N.D. (2005). The neural basis of addiction: a pathology of motivation and choice. American Journal of Psychiatry, 162, 1403-1413.
* Koob GF (2008). A role for brain stress systems in addiction. Neuron 59: 11–34.
* Koob GF (2009). Neurobiological substrates for the dark side of compulsivity in addiction. Neuropharmacology 56(Suppl 1): 18–31.
* Koob GF a Volkow ND Neurocircuitry of addiction. Neuropsychopharmacology Reviews (2010) 35, 217–238
* Nestler EJ (2005). Is there a common molecular pathway for addiction? Nat Neurosci 8: 1445–1449.
* Nestler EJ, Aghajanian GK. 1997. Molecular and cellular basis of addiction. Science 278:58–63
* Nielsen DA, Utrankar A, Reyes JA, Simons DD, Kosten TR Epigenetics of drug abuse: predisposition or response Pharmacogenomics (2012) 13(10), 1149–1160
* Ducci F, Goldman D (2012) The genetic basis of addictive disorders. Psychiatr Clin N Am 35:495-519
* Goldman D, Oroszi G, Ducci F. (2005) The genetics of addictions: uncovering the genes. Nat Rev Genet; 6 (7): 521-532.
* Maze I, Nestler EJ (2011) The epigenetic landscape of addiction. Ann NY acas Sci 1261:99-113
* Mayer P, Hollt V (2005) Genetic disposition to addictive disorders – current knowledge and future perspectives. Current Opinion in Pharmacol 5:4-8
* Nielsen DA, Untrankas A, Reyes JA, Simons DD, Kosten TR (2012) Epigenetics of drug abuse: predisposition or response. Pharmacogenomics 13(10):1149-1160
* Lowinson JH. Substance abuse: a comprehensive textbook. 4th ed. Philadelphia: Lippincott Williams &

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Wilkins; 2005

List of supporting study materials for the course (or internet links to supporting study materials, as applicable):

The students should be familiar with the following major websites containing relevant information about the drugs problem:

www.drogy-info.cz

www.emcdda.europa.eu

http://drugabuse.gov

www.erowid.org

www.mzcr.cz

http://www.lf3.cuni.cz/cs/pracoviste/farmakologie/Neuropsychofarmakologie
or http://www.lf3.cuni.cz/drogy – note the review articles available on this site.

See the particular subject areas for further links to specialised websites.

Methods of instruction
Organisation and structure of the course in the part-time format: **Lectures with discussion:** The course is organised as blocks of lessons taking place at times as agreed. Participation in the session is compulsory. Attendance is recorded and included in the final evaluation. Instruction will be provided in three blocks (three sessions comprising two thematic blocks), each lasting three hours (4 x 45-minute lessons). **Homework and extended supporting study materials:** The syllabus includes: a) additional recommended reading, b) additional e-learning support, c) homework assignments and recommendations for home-based studying. **Extended office hours:** In order to facilitate students' homework, the teacher is available for consultations via her e-mail and on-line chat for a two-hour period (in the form of consultation) at a time agreed with the students at the session. The date will fall within the credit week.

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Examination requirements/course completion
Course completion requirements: 80% attendance is required. Upon prior agreement with the teacher, illness or other reasons for authorised absence from the session can be compensated for by an individual home-prepared project addressing a relevant topic. **Course passing requirements:** a) 20% of evaluation: attendance (80%) b) 30% of evaluation: activity during lessons + success in test c) 50% of evaluation: final test in basic terms and concepts **Final evaluation:** a) 100-85%: Excellent b) 84-70%: Very good c) 69-55%: Good d) 54% or less: Failed

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Syllabus

Thematic Block I:

Title and content: **Introduction to Neuroscience**

The introductory lecture will provide the general technical background and basis for the understanding of neurobiological mechanisms and the key concepts that are necessary to gain an insight into neuroscience (and information to build upon in the subsequent lectures in the course). The students will become familiar with the basic functions and the structure of the nervous system (neuron, synapse, receptor, etc.), with a focus on the central nervous system (CNS).

The topics to be covered include the basic mechanisms of the transmission of information in the CNS, functions of selected (neuro-) mediators (including dopamine, noradrenaline/adrenaline, serotonin, glutamate, GABA, acetylcholine, endogenous opioids, and endocannabinoids), the principles of their synthesis, storage, and degradation, their involvement in the transmission of information in the nervous system (selected basic neural circuits that are involved in the action of drugs and addiction mechanisms, memory, decision-making processes, and stress responses), and the ways in which mediators may influence each other and in which such processes may be influenced externally – the mechanisms of the action of substances that are foreign to the body (xenobiotics), including drugs and medicinal products (effect selectivity, agonist, antagonist, direct and indirect effect, impact of such action – effects).

The basic terms, such as dose, interaction, primary effects and side effects, systemic/local/central/toxic effect, etc., and their meanings will be explained.

Key terms and concepts: essential concepts and principles of neuroscience (the basis for the understanding of the subsequent lectures in the course)

1) The nervous system – the general structure of the nervous system, CNS, neuron, synapse, receptor, transmission of information, neurotransmitters, dopamine, (nor-) adrenaline, serotonin, opioids, GABA, glutamate, cannabinoids, synthesis, metabolisation, storage and release of mediators, central neural systems relevant to addictology

2) Possibilities of exerting external influence on neural systems – mechanisms of the effects of

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xenobiotics/“drugs” – basic principles and concepts (types of effects of xenobiotics, dose, interaction, systemic and central effect, toxic effect, impact of action on individual mediators, etc.)

Required reading:

* Kalina K.: Základy klinické adiktologie. Grada 2014 (nové přepracované vydání), kapitola „Neurobiologie závislostí“

* Ganong WF: Přehled lékařské fyziologie. Galén 2005 (5. vydání).

* Druga R., Grim M., Dubovský P.: Anatomie centrálního nervového systému. Galén, Karolinum2011; především ss 11-19, 79-100, 109-152,vybrané části z 186-219

* Lincová, Farghali a kol: Základní a aplikovaná farmakologie Galén, 2007 (2. vydání) studium ss 207-216

Additional reading:

Berridge KC and Robinson TE. 2003. Parsing reward. Trends Neurosci. 26(9):507–13

Berridge KC, Robinson TE. 1998. What is the role of dopamine in reward: hedonic impact, reward learning, or incentive salience? *Brain Res. Brain Res. Rev.* 28:309–69

Clark L, Bechara A, Damasio H, Aitken MR, Sahakian BJ, Robbins TW (2008). Differential effects of insular and ventromedial prefrontal cortex lesions on risky decision-making. Brain 131: 1311–1322.

Kelley AE, Berridge KC. 2002. The neuroscience of natural rewards: relevance to addictive drugs. J. Neurosci. 22:3306–11

Koob GF (2008). A role for brain stress systems in addiction. Neuron 59: 11–34.

Koob GF (2009). Neurobiological substrates for the dark side of compulsivity in addiction. Neuropharmacology 56(Suppl 1): 18–31.

Koob GF a Volkow ND Neurocircuitry of addiction. Neuropsychopharmacology Reviews (2010) 35, 217–238

Kreek MJ a Koob GF (1998) Drug dependence: stress and dysregulation of brain reward pathways. Drug and alkohol dependence 51(1-2):23-47

Laviolette SR, Alexson TO, van der Kooy D (2002). Lesions of the tegmental pedunculopontine nucleus

block the rewarding effects and reveal the aversive effects of nicotine in the ventral tegmental area. J Neurosci 22: 8653–8660.

Montague PR, Hyman SE, Cohen JD. 2004. Computational roles for dopamine in behavioural control. Nature 431:760–67

Nestler EJ (2005). Is there a common molecular pathway for addiction? Nat Neurosci 8: 1445–1449.

Olds J, Milner P (1954). Positive reinforcement produced by electrical stimulation of septal area and other regions of rat brain. J Comp Physiol Psychol 47: 419–427.

Saal D, Dong Y, Bonci A, Malenka RC. 2003. Drugs of abuse and stress trigger a common synaptic adaptation in dopamine neurons. Neuron 37:577–82

Salamone JD, Correa M, Farrar A, Mingote SM (2007) Effort-related functions of nucleus accumbens dopamine and associated forebrain circuits. Psychopharmacology (Berl) 191:461–482.

Volkow ND, et al. (2006) Cocaine cues and dopamine in dorsal striatum: Mechanism of craving in cocaine addiction. J Neurosci 26:6583–6588.

Volkow ND, Fowler JS, Wang GJ (2003) The addicted human brain: Insights from imaging studies. J Clin Invest 111:1444–1451.

Volkow ND, Fowler JS, Wang GJ, Baler R, Telang F (2009) Imaging dopamine's role in drug abuse and addiction. Neuropharmacology 56(Suppl 1):3–8.

Volkow ND, Wang GJ, Fowler JS, Tomasi D, Telang F Addiction: beyond dopamine reward circuity. PNAS, (2011) 108 (37):15037-15042

Wolf ME (2002). Addiction: making the connection between behavioral changes and neuronal plasticity in specific pathways. Mol Intervent 2: 146–157.

Thematic Block I – Homework exercise assignment:

Complete the charts with the terms for/names of brain structures and areas.

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Thematic Block II:

Title and content: **Neurobiological Mechanisms of the Effects of "Drugs" I (stimulants – conventional stimulants – cocaine, amphetamine, methamphetamine, nicotine, "ecstasy", cathinones, new synthetic drugs)**

– The students will learn about the basic types of effects produced by this group of substances (including stimulating, entactogenic, and empathogenic ones) and the mechanisms of the effects of selected stimulants, the signs of such effects and major related risks (types and severity), and acute and chronic effects and toxicity (adaptation mechanism principle). The role of the dynamics of effect and general kinetic parameters (substance absorption – the influence of the route of administration, passage through biological membranes – availability to CNS, speed of onset of effect, duration of action, acute and chronic effects, toxicity, etc.) will also be covered.

The biomedical characteristics of selected substances/"drugs" that are generally categorised as stimulants (substances with stimulating effects) will be presented/summarised.

Cocaine – inhibits the reuptake of monoamines from the neural synapse, indirect effect, short-term effect, etc.

Methamphetamine – massive release of monoamines into the synapse, indirect effect, long-term effect, etc.

Amphetamine – massive release of monoamines into the synapse, indirect effect, mid-term effect, etc.

Nicotine – agonist of acetylcholine receptors, direct effect, mediated effect on dopamine/monoamines, short-term effect, etc.

"Ecstasy" (MDMA) – release of monoamines (especially serotonin) into the synapse, indirect effect, mid-term effect, "dance drugs", etc.

Cathinones – mephedrone – increase in the concentration of monoamines in the synapse, indirect effect, mid-term effect, etc.

Other new synthetic drugs (NSDs)/stimulants – general information – key aspects of the issue of NSDs on the black market, etc.

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Key terms and concepts:

1) Differentiation of effects – stimulating, entactogenic, empathogenic, presumed main mechanisms of these effects; dopamine, serotonin, monoamines, reuptake of neurotransmitters from the synapse

2) Influence of the dose and the route of administration of the "drug"/stimulant on its effect, general kinetic characteristics and parameters, etc.

3) Selected types of stimulants/substances – general characteristics and risks – cocaine, amphetamine, methamphetamine, nicotine, "ecstasy", cathinones – mephedrone, new synthetic drugs, etc.

Required reading:

* Volkow ND, Wang GJ, Fowler JS, Tomasi D, Telang F: Addiction: beyond dopamine reward circuity. PNAS, (2011) 108 (37):15037-15042

http://www.lf3.cuni.cz/cs/pracoviste/farmakologie/Neuropsychofarmakologie .... přehledový článek: MDMA (3,4-methylendioxymethamphetamine) "Ecstasy" - Fišerová M., Páleníček T.

http://www.lf3.cuni.cz/cs/pracoviste/farmakologie/Neuropsychofarmakologie .... přehledový články: Taneční drogy I. a Taneční drogy II.

Additional reading:

Volkow ND, et al. (2006) Cocaine cues and dopamine in dorsal striatum: Mechanism of craving in cocaine addiction. J Neurosci 26:6583–6588.

http://www.lf3.cuni.cz/cs/pracoviste/farmakologie/Neuropsychofarmakologie – další souhrnné články

http://www.extc.cz/

http://www.party-trend.cz/

www.slzt.cz

www.dokurte.cz

www.odvykani-koureni.cz

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Thematic Block III:

Title and content: **Neurobiological Mechanisms of the Effects of "Drugs" II – Depressants (alcohol, opioids, benzodiazepines, barbiturates, anaesthetics, sedatives, etc.).**

– This block focuses on substances that slow down the activity of the CNS. The basic types of mechanisms of the effects manifested by depression of the CNS/sedation/reduction of motor activities, analgesic effect (pain relief), myorelaxation (relaxation of the skeletal muscles), etc.

(Neuro-) mediators and receptors that are involved in these effects/mechanisms – gamma-aminobutyric acid (GABA) and GABAergic receptors, endogenous opioids and opioid receptors and their types, glutamate and ionotropic NMDA receptors, etc., effect specificity/selectivity, mediated effect, comprehensive effect, etc. The general risks associated with these groups of substances (their types and severity) and acute and chronic toxicity (adaptation mechanisms) as they relate to the mechanisms of effects will be covered.

Biomedical characteristics of selected substances/"drugs" that are generally categorised as depressants (substances with principally depressive/sedative effects) will be presented/summarised. Tolerance principle. Analgesic effect – practical use.

Alcohol – a GABA receptor agonist, an NMDA receptor antagonist, influence on other mechanisms, etc. – comprehensive effect, mediated effect, length and intensity/type of effect depending on the dose, tolerance, etc.

Benzodiazepines – diazepam – GABA-A receptor agonist, types/classification of benzodiazepines (BDZs), direct and mediated effect, general signs/types of effects of BZDs, diazepam – depressive/sedative, anxiety-relieving (anxiolytic), spasm-relieving, and myorelaxing (skeletal muscle relief) effects, long-term effect, etc.

(New) synthetic opioids on the black market – new risks – phentanyl and its derivatives, etc.

Central anaesthetics/sedatives – associative – such as barbiturates (GABA-A receptors), ether, nitrous oxide, etc – comprehensive effects, volatile liquids – see solvents (inhalants); dissociative anaesthetics (ketamine, "angel dust") rank among the hallucinogens.

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Key terms and concepts:

1) Differentiation of effects – sedative, psychotropic, analgesic, passively anxiolytic, myorelaxing, principle of tolerance and correlations, presumed main mechanisms of these effects – main neurotransmitters – GABA, glutamate, endogenous opioids, etc., receptors – selectivity of effects, etc.

2) Influence of the dose and the route of administration of the drug/depressant on its effect, general kinetic characteristics and parameters (specificity of alcohol), etc.

3) Selected main types of depressants – general characteristics and risks – alcohol, heroin, morphine, buprenorphine, phentanyl, barbiturates; new synthetic drugs, etc.

Required reading:

Koob GF a Volkow ND Neurocircuitry of addiction. Neuropsychopharmacology Reviews (2010) 35, 217–238

Additional reading:

Hnasko TS, Sotak BN, Palmiter RD. 2005. Morphine reward in dopamine-deficient mice. Nature 438:854–57

Shalev U, Grimm JW, Shaham Y (2002). Neurobiology of relapse to heroin and cocaine seeking: a review. Pharmacol Rev 54: 1–42.

www.alkoholismus.wz.cz

http://aacesko.sweb.cz

MIOVSKÝ, M., URBÁNEK, T. Tabák, alkohol a nelegální drogy mezi středoškoláky. Čs Psychologie, 2002, 46, s. 165-177 s.

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Thematic Block IV:

Title and content: **Neurobiological Mechanisms of the Effects of "Drugs" III – hallucinogens, cannabis, solvents, etc. Combination and interaction of drugs.**

The students will learn about the mechanisms of changes in the perception of reality and oneself – the role of the serotonergic system (serotonin, serotonergic receptors), cholinergic system (muscarine receptors), and neural circuitry. Hallucinations, ecstatic states, delusions, illusions, perception of time, colours, sound, and combinations thereof. Hallucinogens: derivatives of various chemical structures (ergolines, tryptamines, phenylethylamines, delirogens, dissociative anaesthetics, cannabinoids) – pure and mixed effects, effect-dose dependence, etc. The role of "set" and "setting" in the effects of hallucinogens; "good trip" and "bad trip"; toxic psychosis. Traditional use of selected substances.

Methods of hallucinogen use, dependence-related aspects (minor impact on dopamine, mostly outside the nucleus accumbens), toxicity, risks! Mechanisms behind the effect of conventional hallucinogens.

Cannabis – special attention will be paid to this, given its widespread use among the population – types of cannabis, types of products, mechanism of effect, endocannabinoids (such as anandamide) and cannabinoid receptors, important substances contained in cannabis (including THC and cannabidiol), metabolisation, kinetics, methods of use – principles, effects. Issue of synthetic cannabinoids – risks.

Categorisation of hallucinogens (according to their chemical structure):

Ergolines – LSD

Tryptamines – psilocin, dimethyltryptamine (DMT), harmine, 5-MeO-DIPT, etc.

Phenylethylamines – mescaline, DOB, DOI, etc.

Delirogens – atropine, scopolamine, etc.

Dissociative anaesthetics – ketamine, angel dust (PCP), etc.

Cannabinoids – THC

Examples and characteristics of selected hallucinogens – synthetic and natural products:

LSD – serotonergic receptors, methods of use, "trip", risks

Psilocin – liberty caps – hallucinogenic "magic" mushrooms, risks

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Other natural hallucinogens – examples – herbal (mescaline, atropine, scopolamine, muscarine, ibogaine, bulbocapnine, DMT, etc.), animal (bufotenine, etc.).

Other synthetic hallucinogens – examples – DOB, DOI, DOM (STP), TMA, ketamine, PCP, synthetic cannabinoids (see below), etc., new synthetic drugs

Cannabis – THC – methods of use, risks; synthetic cannabinoids – methods of use, risks

Inhalant use – specific aspects, types, effects, methods of use, risks – toxicity

Drug combination and interaction – interaction principle – mutual relationsips/influences – enhancement/potentiation of effect, reduction/antagonisation of effect, no mutual influence; pharmacodynamic and pharmacokinetic interaction; antidotes – practical use in toxicology

deliberate and accidental/inadvertent interaction/combination: drug + drug, drug + medication, drug + other substances (such as those contained in food); examples of risky combinations of selected drugs.

Key terms and concepts:

a) Hallucinogens – hallucinogenic, delirogenic, ecstatic, and other effects.; the role of "set" and "setting", good and bad "trip", illusions, delusions, hallucinations; mechanism of the effects of conventional hallucinogens, serotonergic system; methods of hallucinogen use; choice of hallucinogens – risks; cannabis
b) cannabis and cannabinoids, endocannabinoids, THC, cannabidiol, synthetic cannabinoids, methods of use, risks
c) inhalants (solvents) – a specific issue

Required reading:

Schultes R. E. a Hofman A.: Rostliny bohů. Volvox Globator a Maťa, Praha 1998

Additional reading:

MIOVSKÝ, M. Konopné drogy. In KALINA, K., et al. Drogy a drogové závislosti 1. Mezioborový přístup. Praha : Úřad vlády ČR, 2003, 174-179 s.

MIOVSKÝ, M., URBÁNEK, T. Tabák, alkohol a nelegální drogy mezi středoškoláky. Čs Psychologie, 2002, 46, s. 165-177 s.

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MIOVSKÝ, M. Halucinogenní drogy. In KALINA, K., et al. Drogy a drogové závislosti 1. Mezioborový přístup. Praha : Úřad vlády ČR, 2003, s. 169-173.

FELDMAN, RS., MEYER, JS., QUENZER, LF., et al. Principles of Neuropsychopharmacology. Massachusetts (USA), Sinauer Associates Inc., 1997, pp. 549-590, 731-780.

HOFFMANN, A. LSD - mé nezvedené dítě. Praha : M. Háša-Profes, 1996.

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Thematic Block V:

Title and content: **Neurobiological mechanisms of addictive behaviour**

– The students will become familiar with the basic principles – currently recognised knowledge of the neurobiological mechanisms behind addictive behaviour.

Dependence on addictive substances (or psychoactive/psychotropic substances/drugs, drug addiction) ranks among the multifactor chronic relapsing diseases of the central nervous system (CNS) (WHO ICD-10: F10-F19 Mental and behavioural disorders due to psychoactive substance use; in the Czech Republic since 1994; updated in 2013). It is therefore apparent that both the innate and modulated setup of the CNS and the central neurobiological mechanisms (including adaptation changes and neural and synaptic, even molecular, plasticity associated with recurrent drug use) play a key role in the process of drug addiction. The chronic use of alcohol, stimulants, opioids, and other drugs leads to progressive changes in the brain and behaviour. Drug addiction implies the continuous use of the drug despite its apparently harmful consequences, i.e. loss of control over drug use. The repeated use of a drug results (in addition to other central and peripheral effects) in the reconfiguration/disruption of a number of important brain circuits, which becomes manifested in the elevated motivational significance of the drug to the detriment of natural stimuli, a compulsive urge to seek the drug and increased negative emotionality (both with the involvement of extended limbic neural circuits), and impaired cognitive flexibility and control and decision-making processes (with the involvement of areas of the frontal cortex). Current research seeks to understand the genetic/epigenetic, cellular, and molecular mechanisms that are responsible for the transition/change from occasional, controlled drug use to drug addiction, i.e. the loss of behavioural control over drug seeking and taking and over chronic relapses following even very long periods of abstinence.

- The basic concepts will be explained and the main brain systems, neural circuits, and neurotransmitters and the basic principles of these processes will be covered: e.g. the brain reward system – a phylogenetically old system which serves to “distinguish”, remember, and prefer (when one has several options to choose from) elements of behaviour that lead to the preservation of the

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organism and the kind, the ventral tegmental area, the striatum (ventral, dorsal), the hippocampus, the prefrontal cortex – the system of a sense of reward and conditioning. The limbic system. Conditioning principle, control and decision-making principle. Adaptation mechanisms, withdrawal/withdrawal symptoms, craving.

Addictive behaviour (substance dependence) – recurrent stages of a cycle:

a) intoxication

b) withdrawal

c) craving

The neural circuitry and neurotransmitters involved in particular stages of the cycle will be covered. Reward – dopamine, endocannabinoids, endogenous opioids, serotonin, etc.; reward conditioning – glutamate, dopamine, GABA, endocannabinoids; conditioning principle, behaviour control principle; stress – corticotropin, corticoid-releasing factor, dynorphin, (nor-) adrenaline, craving – glutamate; adaptation mechanisms, relevant neurotransmitter systems and certain networks

Key terms and concepts:

Addictive behaviour – dependence on addictive substances – basic concepts, principles, and mechanisms.

Brain reward system. The limbic system. Neural systems involved in addiction mechanisms – neurotransmitters, correlations, general principles.

Basic concepts – reward, craving, conditioning principle, comparison, choice, decision-making principle, withdrawal/withdrawal symptoms, adaptation processes, tolerance, sensitisation, epigenetic changes, etc.

Substance addiction stage – a) intoxication, b) withdrawal, c) craving – the basic roles, mechanisms, etc.

Required reading:

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Thematic Block VI:

Title and content: **Possibilities of Higher Vulnerability/Predisposition to Addictive Behaviour – Risk Factors.**

The students will become familiar with the possibilities and mechanisms of certain kinds of elevated vulnerability to the effects of drugs/substances and the development of addictive behaviour – see below – with an emphasis on the potential use of such knowledge in addictological practice.

Drug addiction does not develop in every user; the general neurobiological mechanisms may work differently in terms of their manner and extent from individual to individual. The sensitivity and vulnerability of brain mechanisms and the organism as a whole to the action of a drug are determined by the combination of a range of both external and individual factors. A major external factor for drug addiction (in addition to other correlates such as the availability of the drug, environment, and social context) is the various high-risk types of stress. On the one hand, stress has a great influence on the intake of a drug of abuse and, on the other hand, the drug intake has a strong impact on the stress-related neural circuitry. Both the acute and chronic intake of an excessive quantity of the drug provoke changes in the gene expression with the signalling effects in molecules associated with reward and stress. This in turn influences the transmission within the stress and reward circuitry. A similar epigenetic influence of excessive acute and, especially, chronic cumulated stress with an impact on the intake of drugs, food, etc. can also be observed. Noteworthy individual factors include a) both drug-specific and non-drug- specific intrinsic/genetic liabilities that, in a predisposed individual exposed to a certain type of drug, may account for up to 50% of the risk of the development of drug addiction (as regards alcoholism, for example, 50-60% inheritance has been reported, depending on the type of disorder). Genetic and epigenetic research into drug addiction has seen rapid development in recent years. As substance addiction is a heterogeneous and comprehensive disorder, multiple and often interacting genes are responsible for the genotype of chemical dependence. Recent genetic studies of drug addicts suggest numerous correlations with other psychological/psychiatric disorders. It has been found that the role of both genetic and environmental influences that modulate the risk of the

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development/maintenance of drug addiction changes over the course of people's lives. In addition to congenital predispositions being modulated by intrinsic factors, e.g. during the maturing of an individual, genetic traits (phenotype) can also be shaped by the environment. Although the mechanisms of the interaction between genes and the environment have not been fully clarified yet, some studies show that a socially favourable environment can modulate or even dramatically reduce the influence of genetic predispositions to mental disorders, including risky drug use. Another risk factor in terms of the development of substance addiction is b) the immaturity of the organism. As a stage of neurodevelopment, the period of puberty and adolescence is marked by poor control over conduct and a strong urge to seek limbic reward, excitement, new sensations and experiences, and social interactions which are necessary for the maturation process but also work as alcohol/drug use predictors. While in early adolescence grey matter grows in volume and changes its structure significantly (overproduction of axons and synapses, etc.), in later adolescence the volume of grey matter decreases. In comparison to the adult brain, the immature brain with a surplus of synapses shows extensive but less effective frontal activation, slower reaction time, and poorer performance. Major neuronal remodelling takes place during adolescence: e.g. depletion of excitation glutamatergic input to the prefrontal cortex (PFC) and, conversely, an increase in the dopaminergic and serotonergic input to the PFC; cholinergic PFC innervation also intensifies and significant changes in the limbic system can be observed; there is marked hippocampal neurogenesis that has a positive bearing on learning, memory, and adaptation capacities. This remodelling development stage is highly sensitive to external interventions and psychiatric disorders. The sedative effect of alcohol, for example, is experienced by adolescents to a smaller degree than it is the case with adults. While this is conducive to their "binge" drinking, it also makes adolescents much more sensitive to alcohol neurotoxicity (e.g. the number of D1 and D2 dopaminergic receptors in the frontal cortex decreases, histone acetylation in the frontal cortex and in the limbic system intensifies, and the hippocampal neurogenesis sustains major neurodegeneration, etc.); adolescents with higher levels of alcohol use also show lower volumes of the prefrontal grey and white matter which correlates with bad mood and poorer decision making. A similarly elevated vulnerability can be observed in adolescents who use other drugs (such as tobacco,

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marijuana, and stimulants). It is therefore obvious that the heavy consumption of drugs/alcohol during puberty may cause some individuals long-term, even permanent, harm. Other risk factors include c) female sex (women are generally more sensitive, particularly to the toxic effects of drugs) and d) certain diseases and other disorders – e.g. mental disorders such as depression, anxiety, ADHD, etc. Correlations with the immune system are discussed. Like stress, all addictive drugs chronically raise basal glucocorticoid levels, which contributes, inter alia, to the activation of the brain nuclear transcription factor of activated B-monocytes (NF-κB) and the induction of expression of a series of intrinsic immunity genes and this correlates with bad mood, anxiety, depression, etc. Apparently, the mutual combination of various potential factors (e.g. cumulative stress experienced by an adolescent with an anxiety disorder combined with alcohol abuse, etc.) increases the risk of the development and severity of drug addiction.

Key terms and concepts:

Vulnerability/liability to the action of drugs and the development of addictive behaviour – significance for addictological practice.

1) External factors – drug availability, stress, and social influences, including the immediate environment, etc.
2) Internal factors –
    a) genetic/intrinsic dispositions (drug-specific, non-drug-specific, combinations thereof)
    b) immaturity of the organism
    c) female sex
    d) certain diseases and other disorders
    e) combinations of different influences

Required reading:

Kalina a kol – Základy klinické adiktologie (2014; druhé přepracované vydání) – kapitola Genetické dispozice k drogovým závislostem a epigenetika

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Final revision test: The students will have the opportunity to demonstrate their knowledge and understanding of the subject matter dealt with in this course during the final revision test.

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