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<tr>
<th><strong>Provided by:</strong></th>
<th>Department of Addictology, 1&lt;sup&gt;st&lt;/sup&gt; Faculty of Medicine, Charles University, and General University Hospital in Prague</th>
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<tr>
<td><strong>Faculty:</strong></td>
<td>1&lt;sup&gt;st&lt;/sup&gt; Faculty of Medicine</td>
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<td><strong>Valid from:</strong></td>
<td>2014</td>
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<td><strong>Semester:</strong></td>
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<td><strong>Scope, examination:</strong></td>
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<td><strong>e-Credits:</strong></td>
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<td><strong>Examination format:</strong></td>
<td>oral or written</td>
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<td><strong>Scope of instruction per academic year:</strong></td>
<td>6 x 90 min + 45 min</td>
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<td><strong>Number of places:</strong></td>
<td>unlimited</td>
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<td><strong>Minimum number of students:</strong></td>
<td>unlimited</td>
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<td><strong>Course status:</strong></td>
<td>currently available</td>
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<td><strong>Language of instruction:</strong></td>
<td>Czech</td>
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<td><strong>Format of instruction:</strong></td>
<td>part-time</td>
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<td><strong>Level:</strong></td>
<td>Ph.D.</td>
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<td><strong>Note:</strong></td>
<td>Prof. PhDr. Michal Miovský, Ph.D.</td>
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**Expert** Mgr. Roman Gabrhelík, Ph.D., PharmDr. Magdaléna Šustková, Ph.D.

**Teachers**: PharmDr. Magdaléna Šustková, Ph.D., Mgr. Roman Gabrhelík, Ph.D.

**Attributes**: Addictology

**Title**: Biomedical Addictology: Special Issues
Annotation

This course builds upon the Introduction to Biomedical Addictology course and extends it to include other areas, such as research methods used in addictology (a general overview is provided, with a focus on specific models of addiction), the basics of pharmacotherapy as an integral part of a comprehensive therapeutic/preventive approach, epidemiology, and clinical trials.

The knowledge, skills, and competences that the students are expected to acquire (see Section 2) should ensure their general theoretical background and resources for the practical use of biomedical research in addictology.

In summary, the students will learn:

a) general addictology-relevant research methods
b) general epidemiological principles
c) the basics of the (pharmacological) treatment of substance addiction
d) general principles of clinical trials

Course objective

The course is intended to familiarise the students with the current practice of biomedical addictology, including the element of research and theoretical and practical training needed for them to pursue their own research projects and gain a critical insight into work in the field.

The course features several areas of focus. One of them is a general overview of the research methods used in the field. Another is an introduction to the basic principles of the epidemiology of addiction. The core principles of clinical trials will follow up on the outline of the fundamental elements of addictology-specific pharmacotherapy.
2. Course outcome descriptors:

Knowledge:
The students will be expected to show thorough and wide-ranging knowledge of the characteristics of scientific and research approaches and methods specific to biomedicine, including their categorisation, and the basic theoretical framework reflecting the state-of-the-art knowledge in the field. Such expertise should encompass a general understanding of topical issues surrounding the practical use of these methods in modern biomedical addictology and in interdisciplinary and transdisciplinary research. They will know and understand the possibilities of combining various research designs and the sampling methods and the data collection, processing, analysis, interpretation, and publication methods such designs involve. They should demonstrate both their understanding of these methods and ability to apply them appropriately with respect to specific ethical aspects of qualitative approaches.

Skills:
Using the knowledge and understanding of the theoretical and practical framework of the biomedical approach and methods, the students should be able to address independently various scientific biomedicine-specific issues in both theoretical and practical terms. They should be able to choose and combine suitable research strategies and methods in such a way as to devise a unique research design that can respond appropriately to the research problem. They can correctly define and categorise the problem while proposing and laying down an appropriate procedure to be used to subject it to scientific enquiry or identify mistakes and/or the shortcomings of any previous procedures. They will be able to act independently in applying ethical principles to an actual research procedure and identifying its strengths and weaknesses. While doing so, they should be able to integrate the
knowledge from different disciplines and correctly interpret and evaluate the results of their work.

**Competences:**

At their level of expertise, the students are able to recognise on their own the basic types of epidemiological problems and devise procedures and methods to investigate such problems. They should be able to use and work with international literature and transpose modern knowledge across different models, as well as applying these to the context of a given research issue while adhering to ethical principles.
6. Textbooks and information sources:

6.1. Required reading:


   http://www.who.int/whosis/indicators/WHS10_IndicatorCompendium_20100513.pdf


12. Savitz DA. Interpreting Epidemiologic Evidence: Strategies for Study Design and

6.2. Recommended further reading:

4. Rothman KJ, Greenland S, Lash TL. Modern Epidemiology, 3rd Ed. Lippincott Williams & Wilkins:


23. Fišerová, M. (2000). Historie, příčiny a léčení drogových závislostí. Postgraduální medicína; ročník 2; číslo 3; 288 - 298,


like effects during long-term cocaine administration. Psychopharmacology (Berl). Feb;219(4):1141-52. (Maier et al., 2012)


58. Zaostřeno na drogy 8/2013. 1-2. Úřad vlády ČR
Methods of instruction

3. 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, 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 teachers are available for consultations via his/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.
**Examination requirements**

**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 (examination): 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
Syllabus

Thematic Block I:

Title and content: Research methods in addictology

The students will acquire a general background to the major research approaches, levels, and methods employed in addictology, with an emphasis on more specific methods, including common experimental models of addiction.

In recent years the study of addiction has been underpinned by the so-called bio-psycho-socio-spiritual model, which reflects, or highlights, the multifaceted nature of the issue. This is also one of the reasons why in the Czech Republic addictology has been defined as a standalone transdisciplinary field of study to integrate all these perspectives into a single domain. Accordingly, addictological research is also very comprehensive and multifaceted in its nature.

The scientific enquiry into the abuse of (psychotropic, narcotic, etc.) substances and addictive behaviour (including substance addiction) involves practically all levels of research, i.e. pre-clinical and clinical research featuring a wide range of investigational approaches, from preparatory phases taking place separately from the organism, such as syntheses of substances, including potential medicinal agents, and binding studies (the testing of substances in terms of their abilities to influence binding sites/receptors), i.e. the (sub-)molecular level (in vitro) and research into tissues/tissue cultures and entire organs (in situ methods) to methods involving the entire organism (in vivo) (in organisms that are either alert and freely moving or anaesthetised). State-of-the-art research at all levels has been using cutting-edge instrumentation and automated testing/computerised data collection and evaluation, which helps in standardising and objectivising the research techniques (making them more independent of the researcher=investigator). In addition, the correct statistical assessment of the data is crucial for any research.

Some general research rules will be mentioned. They include: standard/defined testing...
conditions (= providing for the reproducibility of results), use of control/standard (exposed to standard factors) individuals for the comparison of effects, and the rules ensuing from statistical data processing, which predicts the validity and utilisation of the results and relevant conclusions.

Pre-clinical experimental research methods generally involve the use of laboratory animals (the most commonly used species and the principles guiding the choice of experimental animals will be mentioned). Animal testing plays a significant role in the understanding of both the biological and environmental factors which are involved in the development of substance addiction. Animal experimentation makes it possible to create specific conditions and model situations where changes can be looked for with respect to selected elements only, which is hardly feasible in human studies. Recent addiction research has used a number of specific experimental animal models of drug addiction designed to examine various stages of the addiction process (including the initiation of substance use, recreational use, the loss of control over usage, drug withdrawal syndrome, and relapse) and factors which affect liability to the development of addiction. Besides the above-mentioned ethical principles, experimental research is governed by a number of additional general rules of major importance. Both experiments on animals and their husbandry when the experiments are not under way must take place in an accredited standard setting (an accredited menagerie and test rooms for experiments on the whole animal) and under standard conditions as defined by the law (in the Czech Republic Act No. 246/1992 Coll. on the protection of animals against cruelty is the relevant legal regulation in this respect). These include a standard room temperature and humidity, sufficient soundproofing, and the observance of a lighting regime (mostly set at 12-hour cycles). The persons who come into contact with laboratory animals (both attendants and researchers) must be properly qualified and trained for work with laboratory animals (staff accreditation). Furthermore, each experimental study must feature a control animal group (this also applies to molecular and other types of both pre-clinical and clinical research). In comparison to the “standard”
reference group (where a well-established agent, a “standard”, is applied instead of a new substance under investigation), “control” experimental subjects are exposed to testing conditions and procedures which are totally identical to those applied to “investigational” subjects, but a “placebo/vehicle” is administered instead of a study agent.

Experimental models of addictive behaviour to be covered include: a) drug-conditioned place preference, b) self-administration, c) drug discrimination, and d) low-intensity electrical self-stimulation of selected brain structures. As regards non-specific/general addiction research methods, behavioural methods and microdialysis will be addressed.

In the part dedicated to clinical research, a general outline of methods, including highly sensitive imaging techniques (often used at the preclinical stage), will be provided. Specific aspects of human research will be discussed: its strengths (verbal description, an account of both the current state and the history, including a description of how a person feels about their psychological and emotional state) and weaknesses (inevitable bias – the interplay of too many factors, study groups being too heterogeneous; self-report bias, concealing things, intentional manipulation, inability to express themselves, etc.).

Key terms and concepts:
Comprehensive approach to addiction research. Research – general rules for good research practice – both preclinical and clinical. Division/levels of research, interconnectedness, types of research, methods. Statistics.
Pre-clinical research – experimental animal research – strict rules must be observed, ethics, site and staff accreditation, standardisation, validity, etc.
Choice of pre-clinical methods: methods in general use (such as behavioural methods and microdialysis), (specific) experimental models of addiction – a) conditioned place preference, b) self-administration, c) drug discrimination, d) low-intensity electrical self-stimulation of selected brain structures.
Choice of clinical methods: including some highly sensitive imaging techniques

Required reading:

Additional reading:


effects of MDMA and the 5-HT(1A) receptor agonist 8-OH-DPAT. Pharmacol Biochem Behav. 2012 Apr;101(2):258-64
Thematic Block II:

Title and Content: Basics of the (Pharmacological) Treatment of Substance Addiction

The students will learn about the basic pharmacotherapeutic procedures, the general principles and mechanisms of pharmacological treatment as a way of influencing the individual stages of addiction and related complications, and the latest developments and promising tendencies in the treatment of addictive behaviour. An emphasis will be placed on the use of recent neurobiological evidence in the pharmacological treatment of drug addiction. The new objectives of pharmaceutical research will also be mentioned.

The findings presented as part of Introduction to Neuroscience, the neural and molecular correlations, imply a notion of a multi-level and comprehensive therapeutic approach to drug addiction (applicable to prevention in many respects) aimed at: a) lowering the reinforcing capacities of a drug (both positive and negative), b) increasing the rewarding capacities of natural sources of reward (enhancing the perception of the reward they involve), c) inhibiting learnt/conditioned associations (e.g. breaking the bond between the conditioned external reinforcement and the drug), d) enhancing motivation to activities not related to the drug, and (e) boosting inhibitory control.

The comprehensive therapeutic approach may also incorporate the pharmacological treatment of drug addiction, which is helpful in responding to intoxication (detoxification in cases of overdoses), managing severe, even life-threatening, withdrawal symptoms (as part of detoxification), reducing craving, and preventing relapse (anti-craving treatment; substitution).

The mechanisms of the effects of addiction therapies can be described as follows: the pharmaceuticals that are currently used in clinical practice a) influence the known specific mechanisms of the effects of drugs – they mostly act on (i) relevant binding receptors as agonists (nicotine, methadone, etc.), partial agonists (buprenorphine, varenicline), and antagonists (naloxone, naltrexone), or have a combined effect (acamprosate), but can also...
(ii) influence drug metabolism (disulphiram). Another possibility is to b) exert an effect on the more general mechanisms of drug addiction described above, which could be useful in treating certain types of addiction. An α2 agonist (clonidine), for example, reduces the stress-related noradrenergic activity during early abstinence. Recent research has explored the possibilities of treating drug addiction on the basis of the action on DA receptors (DA receptor partial agonists – D2 (aripiprazole) or D3, the action on GABAergic signalling (GABAergic neurotransmission modulators), and glutamatergic signalling (AMPA receptor antagonists, mGluR metabotropic receptor agonists, mGluR5 receptor antagonists), brain stress system modulators (CRF1 antagonists, dynorphin antagonists, neurokinin receptor-1 antagonists), and c) other mechanisms, such as vaccination (anti-cocaine vaccine). A chapter of its own in the pharmacotherapy of drug addiction belongs to epigenetic approaches, which are, indeed, still in their very infancy.

Key terms and concepts:
Pharmacotherapy, anti-craving treatment, inhibitory control increase

Required reading:


**Thematic Block III:**

**Title and content:** Epidemiology and General Principles I

**Key terms and concepts:**

The main areas of focus:

- Historical development of epidemiological thinking
- Causal models and disease models in epidemiology
- Population and time
- Nature of exposure and results
- Measurement of epidemiological risk
- Population health indicators

**Required reading:**


**Additional reading:**


Thematic Block IV:
Title and content: Epidemiology and Basic Principles II

Key terms and concepts:

The main areas of focus:

- Cohort studies
- Degrees of association
- Issues related to epidemiological monitoring and population health monitoring
- Screening and diagnostic accuracy
- Surveillance

Required reading:

Additional reading:


Thematic Block V:

Title and content: Clinical Trials I
Key terms and concepts:

The main areas of focus:

- History of clinical trials
- Definition and features of clinical trials
- Randomisation
- Types of clinical trial designs
- Masking treatment
- Outcome selection/surrogates
- Drug development process

Required reading:


Additional reading:


Thematic Block VI:

Title and content: Clinical Trials II
Key terms and concepts:

The main areas of focus:

- Generalisability and representativeness
- Ethical issues
- Analysis by treatment assignment
- Sample size for survival outcomes
- Data monitoring issues
- Reporting trials/CONSORT guidelines
- Publication of clinical trial results
- Using evidence from clinical trials in decision making

Required reading:


Additional reading:


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.
Evropský sociální fond
Praha a EU – Investujeme do vaší budoucnosti