



FACULTY OF MEDICINE

SCHOOL OF MEDICAL SCIENCES

DEPARTMENT OF PHARMACOLOGY

PHPH 3202

Neuropharmacology

COURSE OUTLINE

SESSION 2, 2009

Contents Page

Course Information	3
Assessment Procedures	4
Lecture Outlines	11
Timetable	14
Practical Class Notes	15
Marking Criteria	32

PHPH3202 Course Information

Neuropharmacology (PHPH3202) is a 3rd year Science Course worth Six Units of Credit (6 UOC). The course will build on the information you have gained in Pharmacology (PHPH2011) and Physiology (2101 & 2201) as well as Biochemistry (BIOC2101/2181)) and Molecular Biology (2201/2291) or Chemistry (2021/2041).

OBJECTIVES OF THE COURSE

Building on basic pharmacology skills learned in PHPH2011, the objectives of this course are to a) provide both knowledge and conceptual understanding of the use and action of various classes of drugs in the treatment of different human diseases affecting the brain and b) develop an appreciation of the need for further research to identify new drug targets for more effective therapies.

COURSE CO-ORDINATOR and LECTURERS:

Course Co-ordinators:

Dr Nicole Jones
Room M205
Wallace Wurth Building
Ph: 9385 2568
n.jones@unsw.edu.au

Professor Margaret Morris
Room M211
Wallace Wurth Building
Ph 9385 1560
m.morris@unsw.edu.au

Consultation time: Tuesday 3-4pm

Students wishing to see the course coordinator outside consultation times should make an appointment via email.

Lecturers in this course:

Dr. Trudie Binder	w.binder@unsw.edu.au
Dr. Jane Carland	j.carland@unsw.edu.au
Dr. Kay Double	k.double@powmri.edu.au
Dr. Gilles Guillemin	g.guillemin@cfi.unsw.edu.au
Dr. Ross Grant	r.grant@unsw.edu.au
Dr. Nicole Jones	n.jones@unsw.edu.au
Prof. Margaret Morris	m.morris@unsw.edu.au
Dr. Bryce Vissel	b.vissel@garvan.org.au
A Prof Laurence. Wakelin	l.wakelin@unsw.edu.au

COURSE STRUCTURE and TEACHING STRATEGIES

This is a 6 unit course and consists of:

- 2 lectures per week
- practical/tutorial sessions of up to 4 hours per week.

All learning activities occur on Tuesday (11am-12pm, 1-2pm, 2-3pm), and Friday (11am-2pm, 3-4pm). Students are expected to attend all scheduled activities for their full duration. Students are reminded that UNSW recommends that a 6 units-of-credit course should involve about 150-180 hrs of study and learning activities. The formal learning activities are approximately 76 hours throughout the semester and students are expected (and strongly recommended) to do at least the same number of hours of additional study.

Lectures will provide you with the concepts and theory essential for understanding the mechanism of action and clinical effects of drug classes which are used to treat CNS disorders. For each disease the pathological process will be outlined in the lecture and the relevant drug targets in the disease process

identified and current pharmacological treatments will be described. Lectures will focus on the mechanism of action and adverse effects of drugs currently in use, potential new therapies, drug targets and areas requiring further research for more effective therapies, will be identified and discussed.

To assist in the development of research and analytical skills practical classes and tutorials will be held. These classes and tutorials allow students to engage in a more interactive form of learning than is possible in the lectures. The skills you will learn in practical classes are relevant to your development as professional scientists.

APPROACH TO LEARNING AND TEACHING

The learning and teaching philosophy underpinning this course is centred on student learning and aims to create an environment, which interests, challenges, and enthuses students. The teaching is designed to be relevant and engaging in order to prepare students for future careers.

Although the primary source of information for this course is the lecture material, effective learning can be enhanced through self-directed use of other resources such as textbooks and Web based sources. Your practical classes will be directly related to the lectures and **it is essential to prepare for practical classes before attendance**. It is up to you to ensure you perform well in each part of the course; preparing for classes; completing assignments; studying for exams and seeking assistance to clarify your understanding.

STUDENT LEARNING OUTCOMES

PHPH3202 will develop those attributes that the Faculty of Science has identified as important for a Science Graduate to attain. These include; skills, qualities, understanding and attitudes that promote lifelong learning that students should acquire during their university experience.

Graduate Attributes

- A. Research, inquiry and analytical thinking abilities
- B. The capability and motivation for intellectual development
- C. Ethical, social and professional understanding
- D. Effective communication
- E. Teamwork, collaborative and management skills
- F. Information Literacy – the skills to locate, evaluate and use relevant information.

On completion of this subject students should:

1. Be able to describe the synthetic and metabolic pathways of the major CNS neurotransmitters
2. Be able to list examples of drugs used to treat major classes of brain and mind disorders.
3. Be able to outline the mechanism of action of specified drug classes used to treat the major types of brain and mind disorders.
4. Be able to communicate scientific information in a report.
5. Be able to demonstrate their ability to work in teams and communicate scientific information effectively.

ASSESSMENT PROCEDURES

• Progress exam (40 min duration – multiple choice + short answer questions)	10%
• Practical report	10%
• Practical quizzes	5%
• Assignment – “Controversial Research Topic in Neuropharmacology”	10%
• End of session examination (3 hours duration)	65%

The *practicals and tutorials* are provided to support lecture material and practise analytical skills. The practical classes and tutorials help you to develop graduate attributes A, C, D & E. During the practical course you will be required to submit a written report for one of the practical sessions. The report itself

should be in the form of a scientific communication comprising aims, results and discussion. Reports must be legible and as concise as possible, and are limited to a maximum of 4 pages of writing (excluding tables, figures and computer traces). The report will be due two weeks after the relevant practical class. Written assessment tasks must be accompanied by a signed plagiarism form and submitted to the student enquiry counter, located on the ground floor of the Wallace Wurth building (room MG14). The report also has to be submitted electronically *via* My eLearning VISTA, through Turnitin. A penalty will apply for late submissions. Material covered in the Practical Classes will also be examined in quizzes to be completed during practical sessions and also in the examinations.

Student assignment

Students will work in teams of 3-4 to research a “Controversial Research Topic in Neuropharmacology”. Each group member must participate in the development of an argument for or against the topic and groups will debate the topic in weeks 8 and 9. Topics will be assigned to groups in the first tutorial session. Individual group members will be required to submit a 500 word synopsis of their own debate. This assessment task will allow you to develop your research, information literacy, communication and time management skills, as well as allowing you to demonstrate your ability to work in a team and collaborate successfully (Graduate attributes A, D, E & F). Marking criteria will be distributed along with assignment topics at the first tutorial session. Written assessment tasks must be accompanied by a signed plagiarism form and submitted to the student enquiry counter, located on the ground floor of the Wallace Wurth building (room MG14). The report also has to be submitted electronically *via* My eLearning VISTA, through Turnitin. A penalty will apply for late submissions (10% per day).

The *progress examination* will be held during the lecture session (August 28th) in week 6. This exam will give you feed back on how you are succeeding in the course. The *progress examination* and *end of session examination* will test not only your knowledge of drugs used to treat major classes of brain and mind disorders but also your ability to apply the knowledge you have acquired from multiple lectures. The progress examination will be in the form of multiple choice and short answer questions. The questions will be based on the material covered in the lectures, practical classes and tutorials. Material covered prior to the progress exam may be again examined in the final exam. The exam will address graduate attributes A and B. The end of session examination will be held during the official examination period.

TEXTBOOK AND READING LIST

Recommended Primary Text:

- Nestler, Hyman and Malenka; Molecular Neuropharmacology: A Foundation for Clinical Neuroscience. 2nd Edition McGraw Hill, 2008. This book is available to purchase through the UNSW bookshop and there will be copies available in the UNSW library

Additional reading suitable as Secondary Resources:

- Rang, Dale, Ritter and Moore; Pharmacology 6th Edition. Churchill Livingstone, 2007
There are several copies available in the UNSW library
- Brunton, Lazo and Parker; Goodman and Gilman’s The Pharmacological basis of therapeutics. 11th Edition. McGraw Hill. There are several copies of this textbook and there is also an electronic resource – both are available through the UNSW library.

Other Resources:

- Additional articles of interest will be placed on the course pages on My eLearning Vista

COURSE EVALUATION AND DEVELOPMENT

Each year feedback is sought from students about the courses offered in the Department of Pharmacology and continual improvements are made based on this feedback. The Course and Teaching Evaluation and Improvement [CATEI] Process of UNSW is the way in which student feedback is evaluated and significant

changes to the course will be communicated to subsequent cohorts of students. Also a staff-student liaison group will be set up and students will be invited to become class representatives to seek feedback from their colleagues and meet with academic staff to discuss any issues that arise.

This course ran for the first time in 2008 and based on student feedback the course has been modified as follows:

- student assignment has changed (new assignment will allow better opportunity for groupwork).
- only one practical report will be assessed.
- students will do quizzes on practical work through the session.

GENERAL INFORMATION

The Department of Pharmacology is part of the School of Medical Sciences and is within the Faculty of Medicine. It is located on the lower ground, 2nd and 3rd floors of the Wallace Wurth building. General inquiries can be made at the School of Medical Sciences Student enquires counter, located on the Ground Floor of the Wallace Wurth (MG14). Office hours are 9.00 am - 5:00pm.

Professor Margaret Morris is Head of Department and appointments may be made through her Administrative Assistant in Room MG14.

There is an honours program conducted by the School. The Honours program is coordinated by Dr Angela Finch Room M207 (ph: 9385 1325). Any students considering an Honours year should discuss the requirements with the coordinator. Outstanding students may be considered for scholarships offered by the University and School and these are offered annually.

Postgraduate research degrees

The Department of Pharmacology offers students the opportunity to enter into the following graduate programs:

Doctorate (Ph.D): In Pharmacology. For further information contact the co-ordinator Dr Pascal Carrive (p.carrive@unsw.edu.au)

Departmental Vacation Scholarships: The Department of Pharmacology supports several summer vacation scholarships each year to enable good students to undertake short research projects within the department. For further details contact the Administrative Officer.

The School Teaching Administrator

Ms Carmen Robinson is able to provide additional information on any courses offered by the School. Student Enquires Counter MG14 Wallace Wurth, ph:9385 2464,
Email: Carmen.robinson@unsw.edu.au

OFFICIAL COMMUNICATION BY EMAIL

All students in the course PHPH3202 are advised that e-mail is now the official means by which the School of Medical Sciences at UNSW will communicate with you. All e-mail messages will be sent to your official UNSW e-mail address (e.g. z1234567@student.unsw.edu.au) and, if you do not wish to use the University e-mail system, you MUST arrange for your official mail to be forwarded to your chosen address. The University recommends that you check your mail at least every other day. Facilities for checking e-mail are available in the School of Medical Sciences and in the University library. Further information and assistance is available from DIS-Connect, ph. 9385 1777. Free e-mail courses are run by the UNSW Library.

Email etiquette: All email communications should be in formal business English; students should include their name, student number and course code in all email communications.

ATTENDANCE REQUIREMENTS

Attendance at practical classes is compulsory, and must be recorded in the class roll ON THE DAY OF THE CLASS. It is your responsibility to ensure that the demonstrator records your attendance and no discussions will be entered into after the completion of the class. Satisfactory completion of the work set for each class is essential. It should be noted that non-attendance for other than documented medical or other serious reasons, or unsatisfactory performance, **for more than 1 practical class during the session** may result in an additional practical assessment exam or ineligibility to pass the course.

BEHAVIOUR IN PRACTICAL CLASSES

The practical class is an opportunity for students to develop graduate attribute C by behaving in an ethical, socially responsible and professional manner within the practical class.

- Punctual arrival is expected.
- Turn off mobile phones before entering the class.
- A lab coat must be worn to all practical classes
- Enclosed shoes are compulsory.

Students must take due care with biological and hazardous material and make sure all equipment is left clean and functional. Those who don't adhere to these basic laboratory rules will be marked absent.

PRACTICAL CLASSES

The experimental procedure for each practical is given in this course outline. Students are required to familiarise themselves with the experimental procedure before attending each class.

In the interests of safety, special attention should be paid to any precautionary measures recommended in the notes. If any accidents or incidents occur they should be reported immediately to the demonstrator in charge of the class who will record the incident and recommend what further action is required.

Animal Experimentation

The procedures used in the laboratory classes involving *the use of animals* have been approved by Animal Care and Ethics Committee (registration number 07/54B and 07/46A). All experiments undertaken in the Department of Pharmacology adhere to the NHMRC code of conduct for animal experimentation.

NOTICEBOARDS

Noticeboards for this course can be found on the 2nd floor of the Wallace Wurth building. Current timetables and information relevant to you will be displayed here and on the course page on My eLearning Vista. It is your responsibility to check these regularly.

COMPUTING FACILITIES

Computer facilities may be available to students in Room G2/G4 and 106/108 of Wallace Wurth Building when the rooms are not used by classes. Access may be obtained by taking your student card to the Security Office on the ground floor (G009) of the Red Centre. Your student card will then allow you to operate the security lock on the door. Hours of access are 8:30am - 6:00pm. However, priority is given to scheduled classes and meetings. NB: The School would like to advise you that a record is kept of students entering the computer facility. Students will be held responsible for any damage.

Teaching Resources on the Department of Pharmacology's WWW Site

The Department of Pharmacology has chosen to use the University's central My eLearning Vista service to provide teaching material for all of its courses.

- To access these materials, either point your browser to: <http://vista.elearning.unsw.edu.au/> or go to the School's home page at: <http://medicalsciences.med.unsw.edu.au/> then select "Current Students" from the menu bar and click on My eLearning Vista, under "Quicklinks" in the left column.
- You will need to click through the "UNSW" at the left, then click the "Log on" button and enter your Unipass credentials (zStudentNo. and password).
- After logging on to My eLearning Vista, look for the course PPH3202. You should have access to it if you are properly enrolled.

Browser Settings that are needed for My eLearning Vista:

My eLearning Vista makes extensive use of "pop-up" windows. Most browsers now block such pop-ups so you will need to allow pop-ups on this site for it to work properly for you.

The My eLearning Vista service recommends the use of the "Firefox" browser when accessing My eLearning Vista. This will probably not be necessary in order to make use of the site for courses provided by the Dept. of Pharmacology.

You can make use of Lectopia (formerly ilectures) recordings taken of the lectures that are available on My eLearning Vista. Lecture notes will also be made available on My eLearning Vista.

HANDWRITING

Students whose writing is difficult to understand will disadvantage themselves in their written assessment. Make every effort to write clearly and legibly. Do not use your own abbreviations.

SPECIAL CONSIDERATION

Please note the following Statement regarding Special Consideration.

*If you believe that your performance in a course, either during session or in an examination, has been adversely affected by sickness or for any other reason, you should notify the Registrar and ask for special consideration in the determination of your results. Such requests should be made as soon as practicable after the problem occurs. **Applications made more than three days after an examination in a course will only be considered in exceptional circumstances.***

*When submitting a request for special consideration you should provide all possible supporting evidence (eg medical certificates) together with your registration number and enrolment details. Consideration request forms are available from the Student Centre in the Chancellery and from Course Offices. In exceptional circumstances further assessment may be given. **If you believe you might be eligible for further assessment on these grounds, you should contact the Course Authority or the relevant Course Office as soon as possible.***

Please refer to UNSW Student Central for further details regarding special consideration.

(<https://my.unsw.edu.au/student/academiclife/StudentCentralKensington.html>)

MISSED ASSESSMENT ITEMS

If in any circumstances you unavoidably miss an examination, progress exam or cannot hand in an assessment task on time, **you must inform the course coordinator and you must lodge a special consideration request**, supported by a medical certificate or other documentation to Student Central (<https://my.unsw.edu.au/student/academiclife/StudentCentralKensington.html>) within **3 DAYS**.

Your request for consideration will be assessed and a deferred exam may be granted. You cannot assume

you will be granted supplementary assessment. **The deferred exam may include a significant oral element.** If necessary, a supplementary final examination will be held in the week starting 30th November 2009.

Normally, if you miss an exam (without valid reasons) you will be given an absent fail. If you arrive late for an exam no time extension will be granted. It is your responsibility to check timetables and ensure that you arrive with sufficient time.

MISSED PRACTICAL CLASSES

Students who miss practical classes due to illness or for other reasons must submit a copy of medical certificates or other acceptable documentation to the course co-ordinator in Room M205. **Certificates should be lodged no more than 3 days after an absence. Certificates lodged after 3 days will not be accepted.** The following details must be attached: Name, Subject number, Group number, Date of the class, Name of class/es missed.

REPEATING STUDENTS

Practical class exemptions may be granted to repeat students but students **must** check with the course co-ordinator whether they have exemption **prior** to their first practical class. All students must be familiar with the material covered in the practical classes.

STUDENT SUPPORT SERVICES

Those students who have a disability that requires some adjustment in their teaching or learning environment are encouraged to discuss their study needs with the course coordinator prior to, or at the commencement of, their course, or with the Equity Officer (Disability) in the EADU 9385 4734. Issues to be discussed may include access to materials, signers or note-takers, the provision of services and additional exam and assessment arrangements. Early notification is essential to enable any necessary adjustments to be made.

STUDENT RIGHTS AND RESPONSIBILITIES

Refer to Student Central @:

<https://my.unsw.edu.au/student/academiclife/StudentCentralKensington.html>

PLAGIARISM

The School of Medical Sciences will not tolerate plagiarism in submitted written work. The University regards this as academic misconduct. Evidence of plagiarism in submitted assignments, etc. will be thoroughly investigated and may be penalised by the award of a score of zero for the assessable work. Evidence of plagiarism may result in a record being made in the Central Plagiarism Register and the Faculty Students Ethics Officer being notified.

What is Plagiarism?

Plagiarism is the presentation of the thoughts or work of another as one's own.* Examples include:

- direct duplication of the thoughts or work of another, including by copying material, ideas or concepts from a book, article, report or other written document (whether published or unpublished), composition, artwork, design, drawing, circuitry, computer program or software, web site, Internet, other electronic resource, or another person's assignment without appropriate acknowledgement;
- paraphrasing another person's work with very minor changes keeping the meaning, form and/or progression of ideas of the original;
- piecing together sections of the work of others into a new whole;

- presenting an assessment item as independent work when it has been produced in whole or part in collusion with other people, for example, another student or a tutor; and
- claiming credit for a proportion a work contributed to a group assessment item that is greater than that actually contributed.†
- For the purposes of this policy, submitting an assessment item that has already been submitted for academic credit elsewhere may be considered plagiarism.
- Knowingly permitting your work to be copied by another student may also be considered to be plagiarism.
- Note that an assessment item produced in oral, not written, form, or involving live presentation, may similarly contain plagiarised material.
- The inclusion of the thoughts or work of another with attribution appropriate to the academic discipline does *not* amount to plagiarism.
- The Learning Centre website is the main repository for resources for staff and students on plagiarism and academic honesty. These resources can be located via: www.lc.unsw.edu.au/plagiarism

The Learning Centre also provides substantial educational written materials, workshops, and tutorials to aid students, for example, in:

- correct referencing practices;
- paraphrasing, summarising, essay writing, and time management;
- appropriate use of, and attribution for, a range of materials including text, images, formulae and concepts.

Individual assistance is available on request from The Learning Centre.

Students are also reminded that careful time management is an important part of study and one of the identified causes of plagiarism is poor time management. Students should allow sufficient time for research, drafting, and the proper referencing of sources in preparing all assessment items.

* Based on that proposed to the University of Newcastle by the St James Ethics Centre. Used with kind permission from the University of Newcastle

† Adapted with kind permission from the University of Melbourne.

* Based on that proposed to the University of Newcastle by the St James Ethics Centre. Used with kind permission from the University of Newcastle

† Adapted with kind permission from the University of Melbourne.

APPEAL PROCEDURES

Refer to Student Central @:

<https://my.unsw.edu.au/student/academiclife/StudentCentralKensington.html>

GRIEVANCE RESOLUTION OFFICER

In case you have any problems or grievance about the course, you should try to resolve it with the Course Coordinator (Dr Nicole Jones ph: 9385 2568) or the Head of Department (Prof Margaret Morris ph: 9385 1560). If the grievance cannot be resolved in this way, you should contact the School of Medical Sciences Grievance Officer, Dr P.Pandey (9385 2483, P.Pandey@unsw.edu.au).

Neuropharmacology

LECTURE OUTLINES

The course timetable is appended at the end of these notes and can also be found on My eLearning VISTA.

The course is divided into 5 main themes covering Neuropharmacology

1. Introduction to Neuropharmacology
2. Neurotransmitter and Receptor systems in the brain
3. Brain Disorders – and drugs used to treat them
4. Analgesics and Anaesthetics
5. Neurodevelopment and Neuroimmunology

1. Introduction to Neuropharmacology

This lecture will provide an introduction to neuropharmacology - the study of drugs that affect the brain. It will briefly review the way that nerve cells communicate to each other via chemicals and receptors and provide an overview of the variety of different chemicals and receptors utilized and the nerve pathways and neuronal functions associated with different neurotransmitter systems.

2. Neurotransmitter and Receptor systems in the brain

Serotonin / Noradrenaline

This lecture will cover the mechanisms involved in synthesis and metabolism of serotonin and noradrenaline. Principle serotonergic and noradrenergic pathways in the CNS. Agonists and antagonists at receptors. Provide a general overview of therapeutic uses of drugs affecting 5HT, NA systems in the CNS.

Acetylcholine / Dopamine

This lecture will cover basic aspects of acetylcholine synthesis, storage and release. Nicotinic and muscarinic receptors in the brain and drugs which mediate cholinergic transmission in the CNS. An overview of cholinergic drugs used to treat CNS conditions. This lecture will cover pathways involved in dopamine synthesis and metabolism. Provide an overview of functional aspects of dopaminergic pathways in the brain (including motor control and behaviour). Pharmacology of drugs affecting dopamine; important adverse reactions to dopamine antagonists including the underlying mechanisms; selectivity of dopamine antagonists; types of dopamine receptors in the brain. Provide a brief summary of dopaminergic drugs used to treat brain disorders.

Neuropeptides

This lecture will cover the general characteristics of neuropeptides; how they act as neurotransmitters and neuromodulators; possible roles in modulating CNS functions; specific receptors; agonists and antagonists. Examples: substance P, neuropeptide Y and neurotensin

Co-Transmission

This lecture will introduce the concept of co-transmission, which occurs when more than one neurotransmitter is synthesised and released from the same cell. General information about synthesis, processing, co-localisation of transmitters, and co-ordinated central functions; history, receptor subtypes and clinical implications of co-transmission.

ATP as a neurotransmitter

ATP as a neurotransmitter; adenosine as a modulator; P1 and P2 classes of purinergic receptors; functional aspects of the receptors; drugs acting on the receptors. Nitric oxide, the only neurotransmitter not stored in vesicles; effects of nitric oxide; clinical conditions in which nitric oxide may play a role.

Amino Acids

Glutamate and GABA are amino acids that are key neurotransmitters within the mammalian CNS. This lecture will cover their synthesis and storage, the structure and function of glutamate and GABA receptors *in vivo* and look at some selective glutamatergic and GABAergic drugs.

3. Brain disorders – and drugs used to treat them**Depression**

Monoamine theory of depression; pharmacology of antidepressant drugs (tricyclic antidepressants; monoamine oxidase inhibitors; "atypical" antidepressants); important adverse reactions to these drugs including the underlying mechanisms; mode of action of lithium

Schizophrenia / Neuroleptic Drugs

Neuroleptic drugs are drugs that are used to treat psychosis such as schizophrenia. This lecture will briefly describe what schizophrenia is and the neuroleptic drugs which are used to treat this disorder. This lecture will also cover the brain and peripheral neurotransmitter receptors which neuroleptic drugs interact with, the proposed mechanism of clinical action and the side effects associated with neuroleptic drug use.

CNS control of Feeding / Obesity

Obesity is a growing health problem and a major contributor to burden of disease in our society. This lecture will review the physiology of appetite control and the major potential therapeutic targets: fat absorption, food intake and thermogenesis. The mechanism of action of current anti-obesity drugs, their adverse effects, and central signals that are potential new therapies for obesity will be considered.

Drug Addiction / Dependence

This lecture provides an overview of the effects of chronic drug use on the CNS and the adaptive responses that underlay withdrawal and dependence. Key concepts include drug withdrawal and dependence, synapses and cell signalling and the modulation of neurotransmitters and biochemical pathways contributing to drug addiction. Signalling pathways modulated by drugs of abuse can provide new targets for treating drug addiction.

Motor coordination: Parkinsons disease

This lecture is an introduction to pharmacological treatments for Parkinson's diseases. Mechanisms of action, efficacy and side-effects of commonly used pharmacological treatments will be considered. Choice of treatment and other treatment issues will also be discussed.

Epilepsy, anticonvulsants and anxiolytics

This lecture will provide an overview of the different types of epilepsy. Anticonvulsant drugs and how they work: (clonazepam, valproate, vigabatrin, phenobarbitone, primidone, phenytoin, carbamazepine, ethosuximide, trimethadione); adverse effects on CNS, blood and other tissues. There will also be a brief introduction to anxiety and a list of the desirable properties of anxiolytic drugs. Mechanism of action of benzodiazepines and barbiturates.

Stroke and Neuroprotection

This lecture will cover the incidence of stroke and the mechanisms involved in brain injury. It will provide an overview of the current therapies used to treat or prevent stroke in humans. There will be a mention of current clinical trials for stroke treatment and models used to identify neuroprotective drug candidates.

Neurodegeneration

These lectures will provide an overview of a number of neurodegenerative diseases (e.g. Alzheimer's disease, Amyotrophic lateral sclerosis, Huntingtons disease, Parkinson's disease); their pathophysiology, possible novel areas for therapeutic intervention and efficacy of current therapies.

4. Analgesics / Anaesthetics**Pain and Analgesia in the CNS**

This lecture provides an overview of central nervous system mechanisms of pain and analgesia. It encompasses modulatory mechanisms in nociceptive pathways, neurotransmitters involved in nociception, chemical signalling and the pharmacology of drugs such as opioids which modulate pain.

Local and General Anaesthetics

This lecture will provide an overview of the different types of local and general anaesthetic agents. Mechanisms of action of a number of different commonly used anaesthetics. The central nervous system effects; sites of action; adverse effects; effects on axonal and synaptic transmission.

5. Neurodevelopment and Neuroimmunology**Neuroimmunology**

This lecture will cover the immune response within the central nervous system including the description of cells involved, inflammatory mediators and examples of pathologies.

Neurodevelopment

This lecture will provide an overview of the role of neurotrophic factors in development. Neurotrophic factors, receptors and signaling pathways. Importance of neurotrophic factors as possible therapeutics in degenerative disorders.

CNS drugs and blood brain barrier

This lecture will discuss the blood brain barrier and its importance in protecting the brain and regulating the exchange of factors between the blood and brain. One problem facing the design of drugs for CNS disorders is blood brain barrier permeability, in particular large molecules are not able to get into the brain. Novel approaches to deliver agents to the brain will be discussed.

Wk	Wk beginning (Mon)	Lecture 1 Tuesday 11-12 Biomed B	Tutorial Tuesday 1-2pm, 2-3pm Goodsell LG21	Lecture 2 Friday 3-4pm Biomed B	Practical Class Friday 11am-2pm WW 106/108 or M210
1	20/7	Introduction: Neurochemical transmission and neuromodulation M.Morris	Assignment Information Research Topics distributed	Serotonin / Noradrenaline N.Jones	
2	27/7	Depression M. Morris	Group Work – Research Topics	Acetylcholine / Dopamine N.Jones	Behavioural Pharmacology N.Jones / L.Liu
3	3/8	Neuropeptides as transmitters L.Liu	Group Work – Research Topics	Neuroleptic Drugs and Schizophrenia N. Jones	
4	10/8	Motor coordination: Parkinsons disease K. Double	Treatments for Mood / Psychiatric Disorders	CNS control of Feeding/Obesity M.Morris	Animal Handling N.Jones / T. Binder
5	17/8	ATP as a neurotransmitter L.Liu	Group Work – Research Topics	Amino Acids – Glutamate N.Jones	Barbiturates N.Jones / T.Binder
6	24/8	Amino Acids –GABA and Glycine J.Carland	Neurodegeneration: Parkinsons patient N. Jones / K.Double	Mid Session TEST	
7	31/8	Co-Transmission N.Jones		Epilepsy, anticonvulsants and anxiolytics N. Jones	Narcotic analgesics * N.Jones / T.Binder
Mid Semester Break (September 5th-13th)					
8	14/9	Pain and Analgesia in CNS T.Binder	Mid Session TEST Feedback	Stroke and Neuroprotection N.Jones	Research Topics Group Discussion
9	21/9	Neurodegeneration R.Grant	CNS Neurotransmitters	Neurodegeneration / Regeneration B.Vissel	Research Topics Group Discussion
10	28/9	General and Local Anaesthetics L.Wakelin		Neuroimmunology G.Guillemain	Tissue Culture – neuronal toxicity (Group 1) N.Jones
11	5/10	Drug Addiction / Dependence T.Binder	Treatments for Neurological Disorders	Neurodevelopment N.Jones	Tissue Culture – neuronal toxicity (Group 2) N.Jones
12	12/10	CNS drugs and blood brain barrier N.Jones	Exam Revision	New Approaches to Neuropharmacology	Tissue Culture – neuronal toxicity (Group 1 & 2) N.Jones

Practical Class Notes

BEHAVIOURAL SCREENING OF CNS DRUGS

You will need to submit the answers to quiz questions prior to leaving the prac class. The quiz will be distributed at the beginning of the prac class.

(i) Behavioural screening of drugs - Completed quiz

(ii) Elevated plus maze – Answer the questions in space provided.

Aim

To observe and evaluate behavioural responses of animals to various pharmacological agents.

Introduction

A behavioural screening test is usually applied to new compounds to determine preliminary information on their activity and toxicity, and provide clues for their classification. Most screening tests are performed on animals, usually mice and rats, since it would be unethical to test drugs with potentially adverse side-effects on human beings. After drug administration, the animals are carefully monitored for various parameters, such as awareness, mood, motor activity, central nervous system excitation, muscle tone, reflexes etc., and scored on a numerical scale. From the scores given to the observations, tentative conclusions can be made about the pharmacology of the compound.

Behavioural screening studies are important in ensuring that pharmacologists are aware of the distinctive effects, efficacies and toxicities of the drugs. However, such studies require large quantities of animals, which cause financial and animal ethical concerns. Hence, the development of alternative approaches for teaching and researching behavioural pharmacology has become a worldwide issue.

In this practical you will be introduced to an alternative approach to teaching behavioural pharmacology, involving the use of pre-recorded video to demonstrate drug screening procedures in live animals. With the use of video sequences within the program, together with tutorial style questions, you will have a store of visual information available regarding the appropriate behavioural effects of some drugs, such as CNS stimulants, sedatives and narcotic analgesics.

Methods

PART 1. Observation of behaviour responses to pharmacological agents

Students will observe computer-based demonstrations and recordings of the actions of various CNS active agents and the responses of animals to these agents, and will be asked to comment upon and evaluate these during the class.

Make sure you read the **definitions** of various behaviours that may be observed in the tests before the class starts. Also make sure that you attempt the **questions** listed below at the end of each section.

Using the video presentation to observe the behavioural effects of the following agents:

- a) **Hypnotics/Sedatives:** Barbiturates//Benzodiazepines
- b) **Opioids:** Morphine

c) **Stimulants:** Amphetamine/Cocaine/Picrotoxin

Definitions of behaviours

Ataxia - loss of the ability to coordinate muscular movement.

Clonic convulsion - uncontrollable contractions of muscles marked by alternating contraction and relaxation of the muscles.

Corneal reflex - reaction of the eye to changes in light (change in the size of the pupil)

Dyspnoea - difficult or laboured breathing.

Hypertonia - excessive tone of the skeletal muscle.

Hypotonia -diminished tone of skeletal muscle.

Miosis - contraction of the pupil.

Mydriasis - dilation of the pupil.

Opisthotonus - a form of spasm consisting of extreme hypertension of the body.

Piloerection - erection of hair.

Ptosis - drooping or closure of the eyelids.

Salivation - secretion of clear alkaline from mouth.

Sedation - defined as the act or process of calm.

Spasms - sudden violent involuntary contraction of muscle.

Stereotypies – persistent repetition of stereotyped behavior, eg, preening and sniffing the floor.

Straub tail - raising the tail in the air.

Wet-dog shakes - twisting & shaking of the head and neck.

Use the following table to indicate the type(s) of behaviours you observe for each of the agents tested.

Behaviour	Hexobarbital	Morphine	Amphetamine	Picrotoxin
Ataxia				
Corneal reflex				
Clonic convulsion				
Dyspnoea				
Hypertonia				
Hypotonia				
Miosis				
Opisthotonus				
Piloerection				
Ptosis				
Respiratory depression				
Salivation				
Sedation				
Spasms				
Stereotypies				
Straub tail				
Wet dog shaking				

PART 2. ELEVATED PLUS MAZE

The elevated plus maze is a common behavioural test used to assess fear and anxiety in rats and mice. The equipment used for this test is an elevated 4 armed maze, 2 of the arms are completely open, while the other 2 arms have enclosed / raised sides. This test is used to determine whether drugs / treatments have potential anxiolytic (reduce anxiety) or anxiogenic (increase anxiety) actions.

Students will observe the behaviour of two rats on the elevated plus maze. Each rat has been injected with a drug and has been placed in the centre of the elevated plus maze. Each CD will contain 10 min video recordings from 2 individual rats. You will receive a short demonstration of how to measure the behaviour using the elevated plus maze.

For each rat your group will need to note down and measure:

- a) Rat ID
- b) Total time spent in the open arms (using timer)
- c) The number of entries into the open or the closed arm of the maze.

Note: each entry is counted as when the whole of the rat's body has entered an arm of the maze.

You should express your results according to the table below. Once you have filled in the table provided – add your results to the class data

Rat ID	# entries Open	# entries Closed	# entries Total	% Open entries / Total	Time spent in open arms (sec)

When all of the class data has been collected and the codes for the treatment groups have been revealed:

- Calculate the mean and standard deviation (% open entries) for both control and diazepam treated groups:
 1. Open GraphPad Prism via the following path: Class programs \ Physiology and Pharmacology \ Utilities and Office applications \ Graph Pad Prism
 2. Select “start with an empty data table”, Choose Graph “Column bar graph, vertical”, choose to plot “mean with SD”
 3. Enter control values (% open entries) in column “A” and diazepam values (% open entries) in column “B”
 4. Click on the “analyse” button, Under “column analyses, select t-test (and non-parametric tests)
 5. Select “paired test”, two-tailed, and use 95% confidence intervals
 6. Click “OK” and your Prism will perform the t-test

7. Click on "Graph" to view your bar graph
8. Label each axis. "X" = Treatment, "Y" = % open entries
9. Calculate the mean and standard deviation (Time spent in open arms) for both control and diazepam treated groups.
10. Repeat steps 1-8 (above), but use class data for Time Spent in open arms and label your "Y" axis on the graph accordingly.

BARBITURATES / TOLERANCE

INTRODUCTION

The barbiturates produce all degrees of depression of the CNS, from mild sedation to coma. The degree of depression obtained depends not only on the particular barbiturate, the dose, and the route of administration but also on the degree of excitability of the CNS at the time of administration and the extent to which previous experience with drugs has induced tolerance.

OBJECTIVE

To observe the effects of various drugs on the duration of pentobarbitone induced hypnosis in Balb-C mice.

METHOD

Pentobarbitone sleeping time in mice is measured by the difference in time between the injection and recovery of the righting reflex.

Following administration of pentobarbitone (45 mg/kg i.p) each group of mice is placed in a thermally regulated sleeping chamber maintained at 31°C or on hot water bottles (see demonstrator). Start timing from injection.

Carefully observe each mouse and notice the onset of motor inco-ordination and sedation. As these effects occur, turn each mouse on its back and note whether it has lost its ability to right itself.

Following the period of hypnosis, mice will begin exhibiting signs of recovery. This is usually manifested by twitching of the body and shortly afterwards each mouse will right itself and resume its normal upright posture. (Occasionally it may continually roll over without staying upright. To test this place it on its back again). Note its time of recovery and calculate its sleeping time as the difference between injection and recovery of the righting reflex.

Groups of 10 mice should be treated according to the following schedules: Each group of students will do a control group of mice (pentobarbitone treated) plus one of procedures 2 or 3.

1. **Control:**
Each of 10 mice should receive sodium pentobarbitone in normal saline (45 mg/kg, intraperitoneally). Record the times at which the righting reflex is regained i.e. the sleeping time.
2. **Pretreatment with Phenobarbitone**

10 mice have been pretreated with sodium phenobarbitone (80 mg/kg) daily for 3 Days. Dose each mouse with sodium pentobarbitone as described above. Note the length of the sleeping time, or if the animals do indeed lose their righting reflex.

3. Pretreatment with Ethanol

Administer ethanol 1.5 g/kg to each of 10 mice. Fifteen minutes later, dose each mouse with sodium pentobarbitone as described above. Record the sleeping time as described earlier.

DRUG LIST:

Pentobarbitone Sodium	4.5 mg/ml
Ethanol	150 mg/ml
Phenobarbitone Sodium	8 mg/ml

CALCULATIONS:

- i) Compute the mean, standard deviation and standard error of the sleeping times of the mice in each group.
- ii) Calculate the significance of the differences between pretreated mice and control mice by unpaired t-tests.
- iii) If some animals in any group do not lose their righting reflex, the significance of differences between treatments can be determined by chi-squared test.

EXPERIMENTAL DESIGN:

How could the experimental design be improved? Could the study have been controlled better?

NARCOTIC ANALGESICS

You will need to write a report on this practical. In your report, you will also need include: Mean, SD and SEM data, graphs and t-test results and answers to the questions provided.

- Aim**
- i) To observe the effects of morphine on the response to pain in QS mice.
 - ii) To conduct appropriate statistical examination of the experimental data.

Background

The analgesic activity of narcotic analgesics can be assessed in experimental animals by a variety of techniques including:

- i) application of heat
- ii) application of mechanical pressure
- iii) electrical stimulation
- iv) chemical irritation

In this experiment, the application of mechanical pressure is used to measure the analgesic effect of morphine. Analgesia is indicated by a prolonged time before a characteristic reaction occurs.

Methods

Each group will select five mice. The test for analgesia is the tail clip test. This involves applying a metal clip that has its jaws sheathed with rubber tubing to the base of the animal's tail. The response that is measured is an attempt by the animal to dislodge the clip. The animals must be kept under observation at all times while the tail clip is on. If a response is not observed in 60 seconds the clip is removed.

Procedure

1. Label the mice.
2. Weigh the mice.
3. Allocate a member of the group to monitor the animals as per the monitoring sheet.
4. Place the tail clip on the base of the tail of each of the mice and note their response times. Any mouse that takes longer than 15 seconds to respond should not be used in the study.
5. Each mouse is given 0.1 ml/10 grams by intraperitoneal injection of an unknown solution which contains one of the following:

Control	saline		
Morphine	0.15	mg/ml	(1.5 mg/kg)
Morphine	0.25	mg/ml	(2.5 mg/kg)

Morphine	0.5	mg/ml	(5 mg/kg)
Morphine	0.75	mg/ml	(7.5 mg/kg)

These solutions are labelled **A to E** and the injections are given "**blind**" in order to prevent bias in the measurement of the reaction time.

Injections. To inject a mouse, place a mouse on the bench and cover the top half of the mouse with a cloth. Gently holding the mouse, lift the tail and make the injection into the peritoneum. This procedure will be demonstrated.

Note the time of injection for each mouse.

6. To test for analgesia apply the tail clip to the base of the tail of each mouse 30 minutes after injection. Note the time for each mouse to respond. To remove the clip it is easier to pick up the mouse by the tail and place it on the grid of the cage and then remove the clip.
7. Choose the mouse that showed the longest response time and inject that mouse with 0.1ml/10g of solution X.
8. Wait 15 minutes and repeat the application of the tail clip on that mouse noting the time for it to respond.
9. Record your responses in the table provided.

Male Mice

Response time (sec)

Soln	A	B	C	D	E
Concentration of morphine					
	mouse 1	mouse 2	mouse 3	mouse 4	mouse 5
Group 1					
Group 2					
Group 3					
Group 4					
Group 5					
Mean					
SD					
SEM					
P value					

Male Mice

	mouse no.	morphine solution injected	response time after injection of solution X
Group 1			
Group 2			
Group 3			
Group 4			
Group 5			
Mean			
SD			
SEM			

Female Mice
Response time (sec)

Soln	A	B	C	D	E
Concentration of morphine					
	mouse 1	mouse 2	mouse 3	mouse 4	mouse 5
Group 6					
Group 7					
Group 8					
Group 9					
Group 10					
Mean					
SD					
SEM					
P value					

Female Mice

	mouse no.	morphine solution injected	response time after injection of solution X
Group 6			
Group 7			
Group 8			
Group 9			
Group 10			
Mean			
SD			
SEM			

Calculations

- 1) Compute the mean, standard deviation (SD) and standard error (SEM) of the reaction time of the animals for each solution administered. This is done on an excel spreadsheet. Enter the data in a column then select tools→data analysis→descriptive statistics. Enter the input range by selecting the data in the column and check the box labelled summary statistics then click OK. Your data will be displayed in a new worksheet.
- 2) Calculate the significance of any differences between treatment and saline control using unpaired t-tests. Compare each morphine solution administered with the saline control. Enter your data in an excel spreadsheet then select tools→data analysis→t-test: two sample equal variances. Select the 2 input ranges click OK and your data will be displayed in a new worksheet. Record the value for P ($T \leq t$) two tailed.
- 3) Plot reaction time against the logarithm of the dose on the graph paper provided. Is there any significant correlation between reaction time and log dose?
- 4) Is there any difference in the analgesic effect of morphine between male and female mice?
- 5) What might solution X be and what is its mechanism of action?

Animal Monitoring Sheet

Species: QS mice

Dose of Morphine (soln: A, B, C, D or E)

Observe the animal from the time of injection, placing a tick (4) if the animal is showing **no signs** of distress and a cross (6) if the animal is showing **any sign** of distress. Distress is indicated by difficulty in breathing or restlessness.

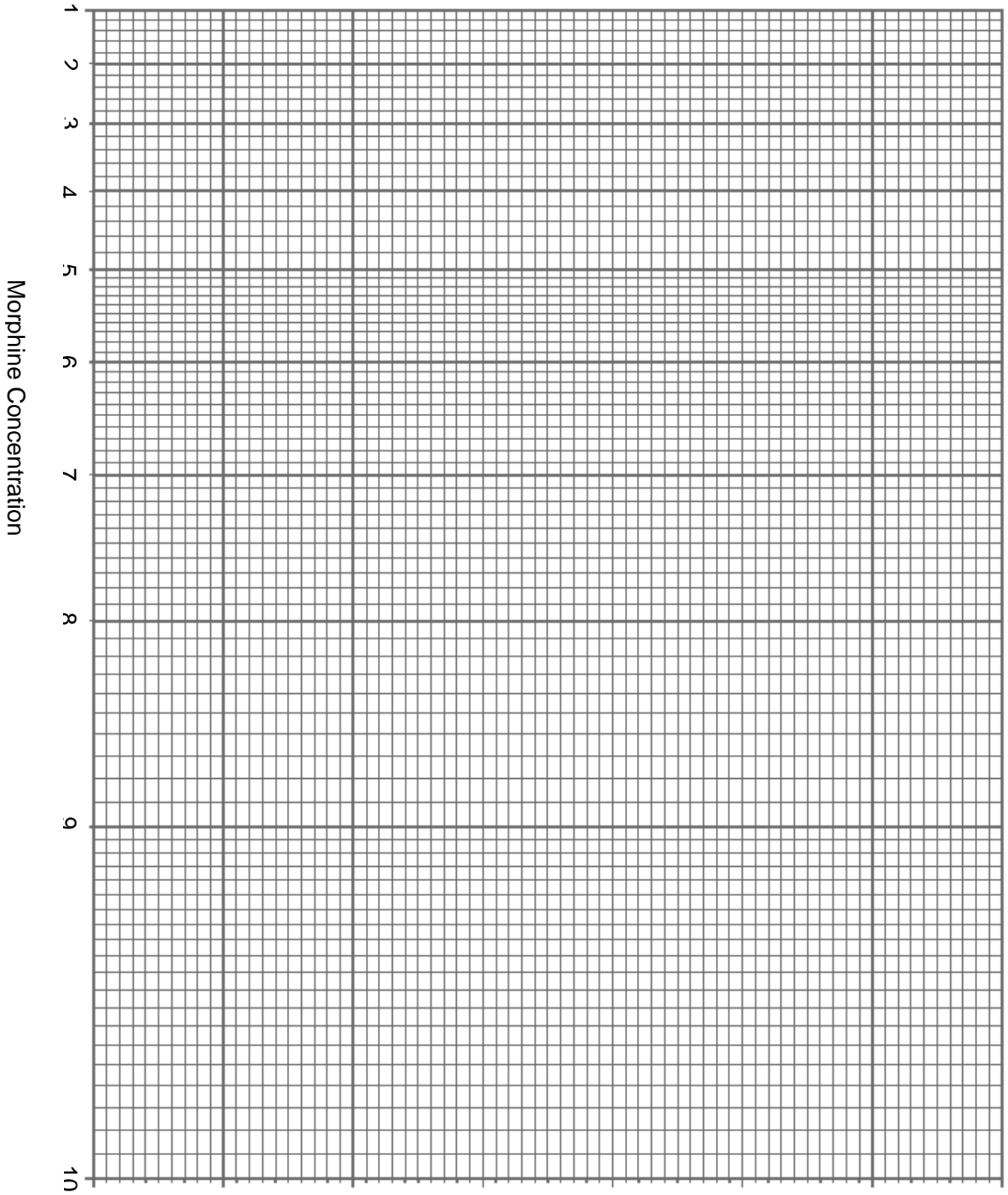
	Morphine Soln	Time after Morphine injection (min)					
		1	10	20	30	40	50
Mouse 1							
Mouse 2							
Mouse 3							
Mouse 4							
Mouse 5							

Dose of Solution X

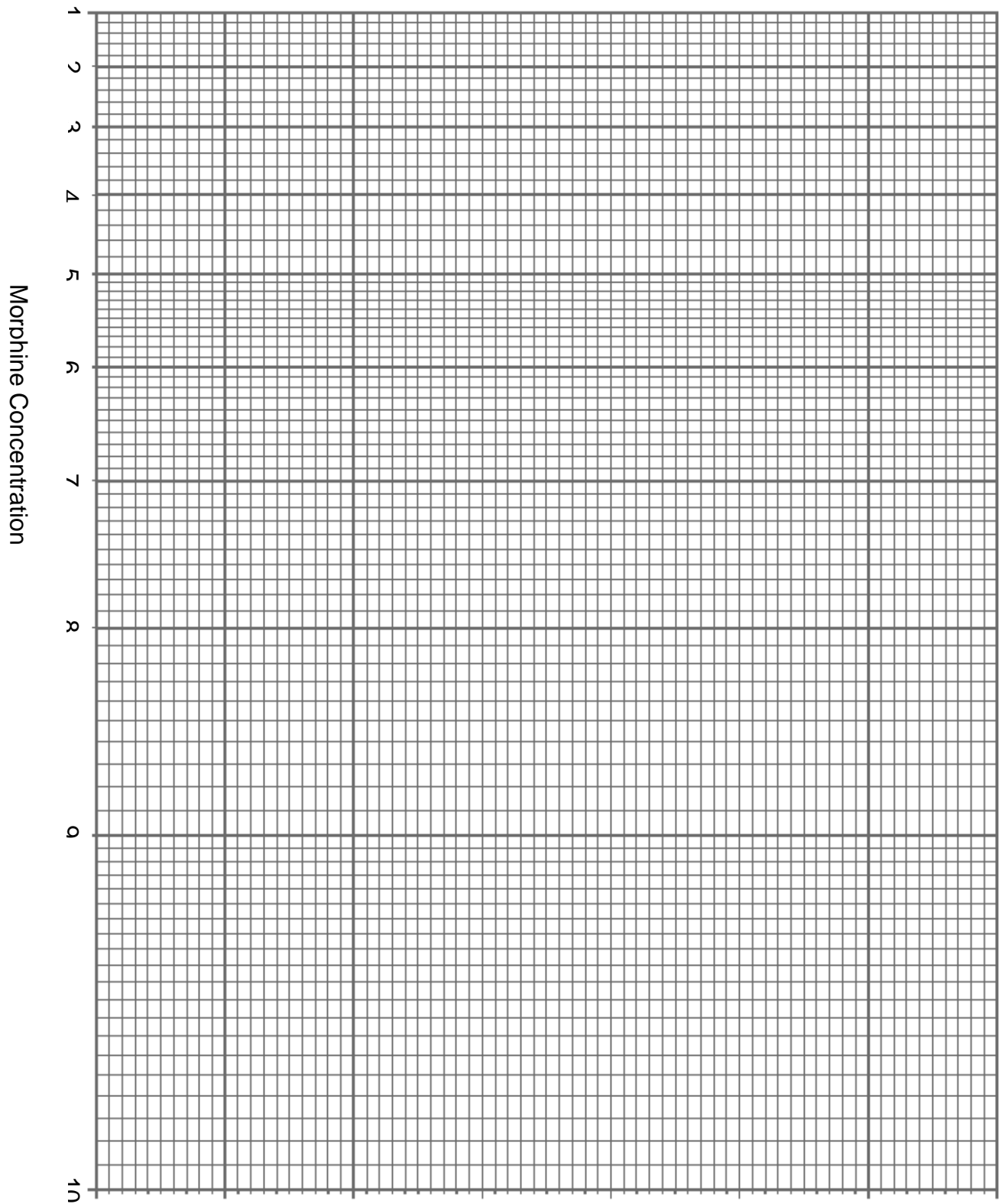
Observe the animal from the time of injection, placing a tick (4) if the animal is showing **no signs** of distress and a cross (6) if the animal is showing **any sign** of distress. Distress is indicated by difficulty in breathing or restlessness.

	Morphine Soln	Time after Solution X injection (min)					
		1	10	20	30	40	50
Mouse							

If an animal is showing any signs of distress alert a demonstrator immediately.



Response (sec)



TISSUE CULTURE – NEURONAL TOXICITY PRACTICAL

Notes for this session will be provided in class

Marking Criteria

NEUROPHARMACOLOGY Practical Report
Marking Criteria PPH3202 S2, 2009

Section	Component Parts	Comments
Title		
	Title less than 150 characters and clearly indicates subject matter of the paper. Name, student number and course information of the author is provided	/1
Introduction		
	Concise and clear account of the scientific background and the rationale of the experiment.	/10
	Final sentence summarises the broad conclusions of the paper.	/5
Methods		
	Appropriate detail and referencing of methods used.	/3
Results		
	Concise description of experimental results. Repetition of data in the text, tables and figures avoided.	/10
	No conclusions or interpretation of results presented.	/2
	Appropriate analysis of data performed. Data analysis was performed correctly.	/10
Discussion & Conclusion		
	Discussion is clear and succinct. Interpretation of the results with reference to previous scientific studies.	/10
	Re statement of the results avoided.	/4
	Main conclusions conveyed in a final paragraph with a clear statement of how the study advances knowledge and understanding in the field.	/5
Tables		
	Each table has a short title. Each column has a heading and the units of measurement in parentheses. Tables are self explanatory.	/5
Figures and Legends		
	Axes labelled and units of measurement given in parentheses. Legends explain the figures in sufficient detail that they can be understood without reference to the text.	/5
	Figures are provided when visual	/5

	representation of the data is helpful.	
Referencing		
	In-text citations follow British Journal of Pharmacology (BJP) conventions. Relevant information selected.	/5
	Reference list follows BJP conventions.	/5
Writing conventions		
	Overall readability (Sentence structure, correct grammar and word usage). Sentences and paragraphs well connected.	/5
	Clearly connected and coherent paragraphs. Topic sentences, supporting and concluding sentences	/4
	Appropriate written expression. Discipline specific: appropriate vocabulary and use of formal, not oral language. Has been proof read	/4
Formatting		
	Times New Roman, 12 font, 1.5 line spacing, margins 2 cm	/1
	Page limit – 3 pages of text maximum (not including figures, tables, references, question/quiz sheet answers)	/1

Content and structure: /85
Writing and formatting conventions: /15
Total: /100
FINAL MARK: /10%

Additional Comments:

Neuropharmacology PPH3202 S2, 2009
Group Debate
Academic Assessment Form

Group:

Topic:

	Mark (/10)
Presentation	
Brief introduction to topic. Why is the topic controversial?	/10
Critical evaluation of the literature	/10
Concluding statement to summarise the group's argument	/10
Questions	
Students understand the questions and answers are appropriate	/10
Overall impression – <u>were you persuaded?</u>	/10
Total (Mark / 50)	/50

Comments:

Strengths:

Improvement:

Points for clarification (if necessary)

Assessor: (sign) Date:

Neuropharmacology PPHP3202 S2, 2009
Group Debate
Peer Assessment Form

Group:

Topic:

Peer Group members:

Name:

Name:

Name:

Name:

	Mark (/10)
Presentation	
Brief introduction to topic. Why is the topic controversial?	/10
Critical evaluation of the literature	/10
Concluding statement to summarise the argument	/10
Questions	
Students understand the questions and answers are appropriate	/10
Overall impression – <u>were you persuaded?</u>	/10
Total (Mark / 50)	/50

Comments:

Strengths:

Improvement:

Points for clarification (if necessary)