Physiology 4650A  
Neurophysiology of homeostasis and stress  
Fall term 2019

The hypothalamus and limbic system contribute to the neural integration of autonomic, endocrine and skeletomotor responses which contribute to homeostasis and adaptive behaviors. Topics include the regulation of neuroendocrine function, blood pressure, energy and water balance, circadian rhythms and reproductive function, and how different system works together to promote the survival.

Course will consist of lectures followed by student presentations of selective research papers and paper discussions.

Lectures: Wednesday/ 9:30-11:20 am/Room MSB 282

Requisites: Prerequisite(s): Physiology 3120 and Physiology 3140A or equivalent, or by special permission from Course Manager.

Senate regulation regarding the student’s responsibility regarding requisites:  
Unless you have either the requisites for this course or written special permission from your Dean to enroll in it, you may be removed from this course and it will be deleted from your record. This decision may not be appealed. You will receive no adjustment to your fees in the event that you are dropped from a course for failing to have the necessary prerequisites.

Accessibility Statement
Please contact the course instructor if you require material in an alternate format or if any other arrangements can make this course more accessible to you. You may also wish to contact Services for Students with Disabilities (SSD) at 661-2111 x 82147 for any specific question regarding an accommodation.

Instructor Information

Physiology 4650A is a team taught course by Dr. W. Inoue and Dr. J. Ciriello

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**Dr. Wataru Inoue is also the Course Manager for Physiology 4650A.** His office is located on the seventh floor of the Robarts Research Institute (RRI 7241).

Feel free to make an appointment (winoue@robarts.ca and/or john.ciriello@schulich.uwo.ca) to discuss any aspect of the course. Your input is essential to making this an enjoyable learning experience.

**OWL:** [https://owl.uwo.ca/portal](https://owl.uwo.ca/portal)

*Students with OWL issues should see:* [https://owlhelp.uwo.ca](https://owlhelp.uwo.ca)

All announcements of importance, such as changes in exam room numbers or exam times and dates, exam results and all lecture notes will be posted on OWL under **Announcements**. Bookmark the website and access it on a regular basis to stay up-to-date as to periodic announcements.

OWL is **NOT** a forum in which professors will answer student questions concerning the lecture material. You must contact the Professor in question directly with any questions concerning the course or course material.

**Course Syllabus**

**General Objectives of the Course:**

*By the end of the semester, successful students will be able to:*

1) explain the definition of homeostasis in physiology, and describe examples of physiological homeostasis regulations and their underlying neurophysiology, through in class discussions as well as written exams.

2) deliver key findings and critique limitations of primary research papers through in class discussion and independent written summary reports.

3) explain some in depth examples of physiological regulations relevant to homeostasis (e.g. hypertension, obesity, stress and sleep apnea), and to assess research publications in these fields by student-driven presentations and discussions.

4) evaluate scientific literature and synthesize concepts to create a literature review about the neural regulation of homeostasis and stress response.
Lecture: 1 September 11/19 - Dr. W. Inoue - 9:30 - 10:20 am

COURSE INTRODUCTION

Lecture: 2 September 11/19 - Dr. W. Inoue - 10:30 - 11:20 am

HOMEOSTASIS AND STRESS RESPONSE: AN OVERVIEW

In biology, stress describes a state of threatened homeostasis. In order to defend homeostasis, an organism mounts a coordinated process (ie, stress response) against the threatening forces (ie, stressors). So, what is homeostasis? Homeostasis is a condition in which body’s internal environments are kept relatively stable (despite changes in external environment). In this lecture, we will first learn about homeostasis and the neurobiology that underlies homeostasis regulation. This will lead us to understand how stress response works to defend, or in some case fails to defend, homeostasis in the face of stressors.

References:

Lecture: 3. September 18/19 - Dr. W. Inoue - 9:30 - 10:20 am

INTRODUCTION TO AUTONOMIC NERVOUS SYSTEM AND CIRCULATORY CONTROL:

Body functions, which normally proceed independently of volitional activity, are regulated in part by reflex mechanisms that are served by afferent, efferent, and central integrating structures. Collectively, these structures form what was first described in by Reil 1857 as the "vegetative" or "autonomic" nervous system. Neurons of the autonomic nervous system innervate cardiac muscle, smooth muscle and glands. Anatomical and physiological differences within the autonomic nervous system are the basis for its further subdivision into sympathetic and parasympathetic components. The heart, blood vessels and glands are mostly innervated by both components and because these organs and tissues participate as effectors in almost all bodily functions, it follows that the autonomic nervous system has an extremely important role in the homeostatic control of the internal environment. Although this system is essentially autonomous, it is not entirely free from voluntary control, as autonomic reflexes and glandular secretions can be learned and modified and are thus also under cerebral cortical control.

In today's lecture, we will begin by reviewing the anatomical components of the autonomic nervous system. We will also examine some of the functional properties of these components. Finally, some of the anatomical and physiological properties of the sympathetic and parasympathetic pre-ganglionic neuron, the final common pathway from central structures controlling autonomic function will be reviewed.
We will also review both the anatomical and functional properties of the baroreceptor and chemoreceptor reflexes by examining the afferent neuronal system that relays information regarding cardiovascular variables (arterial pressure and blood O₂ and CO₂ tension) to the central nervous system.

References:


- Lecture: 4. September 18/19 - Dr. W. Inoue - 10:30 - 11:20 am

SEX DIFFERENCES IN BLOOD PRESSURE CONTROL

In humans, premenopausal women have been shown to have lower blood pressure as compared to age matched men. However, between the ages of 50-60, women tend to have a significantly higher prevalence of hypertension as compared to men. The mechanisms for these influences of sex and age remain incompletely understood. In the second part of today’s lecture we will examine sex differences in central mechanisms in circulatory control, with a focus on the role of the steroid hormone estrogen.

References:


STRESS RESPONSE: AUTONOMIC AND ENDOCRINE RESPONSE I & II
Stressors can take various forms, for example psychological (i.e. exam) or physiological (i.e. injury). These different modalities of sensory information are processed in different brain areas, yet eventually drive the common physiological responses; the activation of the autonomic (sympathetic) nervous system and the hypothalamic-pituitary-adrenal (HPA) axis. The paraventricular nucleus of the hypothalamus (PVN) regulates both of the common stress responses following a wide range of stressor, thereby serving as a key integrator of stress information. In this lecture, we will review the anatomical components and functional properties of neural circuits that feed into the PVN for this stress information integration. This is an area of active research, and there are still much more to be clarified. We will start our discussion from some of the classic researches and then move onto the latest advances using a new technology optogenetics.

References:


  Student presentations: TBA

- **Lectures: 9-10. October 9/19** - Dr. W. Inoue - 9:30 - 11:20

**STRESS RESPONSE: THE LIMBIC AND CORTICAL CONTROL I & II**

The hypothalamus and the brain stem regions regulate the physiologic expression of stress response. Multiple limbic forebrain regions, including the amygdala, the hippocampus and the prefrontal cortex, provide higher-order processing of stress information and modulate the activity of downstream activity of hypothalamus and the brainstem. In this lecture, we will learn the neuroanatomical and neurophysiological basis through which these limbic regions influence the hypothalamus and the brainstem.

- **References:**


NEUROBIOLOGY OF STRESS ADAPTATION I & II

Stress response is versatile and dynamic, and prior stressful experiences constantly reshape subsequent stress responses. In other words, organisms learn and remember stress. At mechanistic levels, this ‘learning’ involves neurochemical, synaptic and structural changes in neural circuits underlying the stress response. Indeed, the actions of the mediators of stress (e.g. glucocorticoids) strongly modulate the cellular and molecular mechanisms of neuroplasticity such as neurogenesis, structural remodeling and synaptic plasticity. In this lecture, we will discuss how the actions of stress mediators mediate/modulate neuroplasticity, and as a consequence change future stress responses.

Reference:


- Lectures: 13-14. October 23/19 – Dr. J. Ciriello -

FOREBRAIN CIRCUMVENTRICULAR ORGANS AND THEIR ROLE IN BODY FLUID AND CARDIOVASCULAR HOMEOESTATIS I & II

The renin-angiotensin system is known to play an important regulatory function with the within the peripheral circulation by controlling both water and salt balance. However, all components of the renin-angiotensin system have been identified within the brain. Central angiotensin exerts its effects predominantly within the hypothalamus on neuronal groups controlling body fluid balance, blood volume and blood pressure. Angiotensin within the systemic circulation can also exert effects on the hypothalamus by activating specialized brain structures called circumventricular organs (CVO’s). Normally, the capillaries of the brain form a unique barrier that permits only specific molecules or ions to be transported across the endothelial cells, thus creating a blood-brain barrier. This barrier is present throughout the brain except in a few specialized midline structures along the third and fourth ventricle of the brain. These structures, the CVO’s, lack a functional blood-brain barrier. They allow a variety of small molecules to pass through fenestrated capillaries to gain direct access to the nervous tissue. These central CVO structures include the
subfornical organ (SFO), the organum vasculosum of the laminae terminalis, area postrema, median eminence and pineal gland. The first three structures have neurons that project to and make synaptic connections with other areas in the central nervous system. Thus, these CVO’s can exert profound effects on the neuronal circuits controlling endocrine and autonomic function, and behaviour. We will examine some of the evidence indicating the role of the CVO’s, in particular the SFO in fluid balance and blood pressure regulation. In addition, we will examine some of the evidence indicating that activation of these systems may lead to the development of hypertension but altering the activity of other brainstem or forebrain structures.

References:


  
  Student presentations: TBA

- Fall Break November 6/19 –
  
  – No lecture


BODY ENERGY BALANCE I

The regulation of “Body Energy Balance” is not well understood. A 1% error in the balance between intake of body energy and energy expenditure would result in an approximate doubling of our body weight each year. We now face an obesity "epidemic" in the Western world. In recent years, no other hormone has drawn more attention than LEPTIN on the control of appetite, body weight and obesity. This hormone, produced by adipose tissue, enters the brain via a saturable specific transport mechanism. Leptin acts at the hypothalamus to modulate food intake, heat production, hormonal release and the autonomic nervous system.
In this session we will examine the overall control of energy balance together with elements which are involved in this regulation, including physical, biochemical, physiological and behavioural mechanisms.

Reference:

BODY ENERGY BALANCE II.

In addition to leptin, the newly discovered peptide orexin, has been shown to be involved in ingestive behaviours. This peptide is selectively found only within hypothalamic neurons. In today’s lecture we will examine its function in both ingestive behaviour and autonomic regulation.

Reference:

• Lectures: 19-20. November 13/19 – Dr. J. Ciriello - 10:30 - 11:20

SLEEP APNEA AND AUTONOMIC CONSEQUENCES I & II.
Obstructive Sleep Apnea (OSA) is the most common form of breathing sleep disorder. OSA is characterized by the repetitive cessation of respiratory airflow resulting from upper pharyngeal airway collapse and obstruction. The resulting apnea primarily induces intermittent hypoxia and hypercapnia, and the decreased haemoglobin oxygen saturation results in myocardial and systemic hypoxemia. OSA has been shown to occur in a considerable percentage of the population. It is estimated that 24% and 9% of middle age men and women, respectively, suffer from OSA, although the number of women that suffer from OSA increases considerably after menopause. There are now considerable data indicating that a significant number of adolescents also suffer from OSA. Untreated, the initial consequences of OSA are sleepiness and an associated decrease in the quality of life as a result of the sleep fragmentation. However, there are now clinical data suggesting that OSA may have direct and long term deleterious effects on cardiovascular function and structure through several mechanisms, including sympathetic activation due to activation of chemoreceptors, oxidative stress, inflammation, and endothelial dysfunction. OSA has been shown to be associated with atherosclerosis and coronary heart disease, cardiac arrhythmias, diabetes mellitus, and stroke and transient ischemic attacks. In this series of lectures we will examine the effects of OSA on neuronal circuits involved in regulating blood pressure and body weight.

Reference:


  
  Student presentations: TBA

  
  Student presentations: TBA
Course Materials

Textbook: No textbook required for the course. Selected papers for review can be obtained through library services.

You may also want to download the Power Point Notes from the course web site and bring them to the lectures. Ideally, if you print the Power Point Notes in a 3 panels per page format, this will leave room for your hand-written notes on one side of the page in class. Power Point Notes for a lecture will be placed on web-ct normally a week ahead of the scheduled class.

Evaluation:

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<thead>
<tr>
<th>Component</th>
<th>Date</th>
<th>% of Final Mark</th>
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<tbody>
<tr>
<td>Midterm assignment</td>
<td>Due October 23, 2019</td>
<td>15</td>
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<tr>
<td>-November 11 - Last day to drop a first-term half course (without academic penalty)-</td>
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<tr>
<td>Research Paper Presentation</td>
<td>Through-out Term</td>
<td>15</td>
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<td>Discussion Leader Grade</td>
<td>Through-out Term</td>
<td>5</td>
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<tr>
<td>Short Lay Summaries</td>
<td>3 summaries/ Through-out Term</td>
<td>15</td>
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<tr>
<td>Final exam</td>
<td>TBA</td>
<td>25</td>
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<tr>
<td>Assignment (Review Paper)</td>
<td>Due December 4, 2019</td>
<td>25</td>
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For Short Lay Summaries, you can pick two papers among the papers for student presentation. Due dates for the summaries are on the next Wednesday (1 week after) the presentation of the paper you choose.

For all assignment, send an electronic copy (word file) by email to Dr. Inoue (winoue@robarts.ca) by 5 pm of the due date.

A detailed and comprehensive set of regulations concerning the scheduling of tests, assignments, etc. is available at:
http://www.westerncalendar.uwo.ca/PolicyPages.cfm?PolicyCategoryID=5&command=showCategory&SelectedCalendar=Live&ArchiveID=

Policy on the Rounding and Bumping of Marks:

Across the Basic Medical Sciences Undergraduate Education programs and within the department of Physiology and Pharmacology we strive to maintain high standards that reflect the effort that both students and faculty put into the teaching and learning
experience during this course. All students will be treated equally and evaluated based only on their actual achievement. **Final grades** on this course, irrespective of the number of decimal places used in marking individual assignments and tests, will be calculated to one decimal place and rounded to the nearest integer, e.g., 74.4 becomes 74, and 74.5 becomes 75. Marks WILL NOT be bumped to the next grade or GPA, e.g. a 79 will NOT be bumped up to an 80, an 84 WILL NOT be bumped up to an 85, etc. The mark attained is the mark you achieved and the mark assigned; requests for mark “bumping” will be denied.

**Additional Information/Statements**

**Statement on Academic Offences**

“Scholastic offences are taken seriously and students are directed to read the appropriate policy, specifically, the definition of what constitutes a Scholastic Offence, at the following website: [http://www.uwo.ca/univsec/handbook/appeals/scholastic_disipline_undergrad.pdf](http://www.uwo.ca/univsec/handbook/appeals/scholastic_disipline_undergrad.pdf)

With regards to major course assignment, please NOTE:

“All required papers may be subject to submission for textual similarity review to the commercial plagiarism detection software under license to the University for the detection of plagiarism. All papers submitted for such checking will be included as source documents in the reference database for the purpose of detecting plagiarism of papers subsequently submitted to the system. Use of the service is subject to the licensing agreement, currently between The University of Western Ontario and Turnitin.com (http://www.turnitin.com ).”

**Statement on the use of Cell Phone and Electronic Devices**

The Schulich School of Medicine and Dentistry is committed to ensuring that testing and evaluation are undertaken fairly across all our departments and programs. For all tests and exams, it is the policy of the School and the Department of Physiology and Pharmacology that any electronic devices (e.g. cell phone, tablet, camera, watch, smart watch, ipod, ear buds, headphones) are strictly prohibited. These devices **MUST** be left either at home or with the students bag/jacket at the front of the room and **MUST NOT** be at the test/exam desk or in the individuals pocket. Any student found with one of these prohibited devices will receive a grade of zero on the test or exam. Non-programmable calculators are only allowed when indicated by the instructor. The Department of Physiology and Pharmacology is not responsible for stolen/lost or broken devices.

**Statement on Discussion of Grades**

The Department of Physiology and Pharmacology is committed to fair assessment of student work and encourages students to discuss course content and graded work with their peers in an effort to improve learning.
**For Students:** While all students have the right to question their grade should they feel it’s inaccurate, this exercise should be undertaken in a respectful manner. Professionalism and respect should be demonstrated in all interactions with instructors and peers. When discussing a grade or exam question with a professor or teaching assistant, the discussion should focus on your individual concern. Students should remember that some forms of assessment or specific questions are designed to be more challenging than others. In this situation, there may be several students that don’t receive the correct answer and this does not necessarily mean that there is a problem with the question or assessment. Concerns from one student that indicate that they are communicating on behalf of a larger group of peers (mob/crowd mentality) will not be considered. Concerns with an assessment should be communicated to the instructor and should reflect your individual concern. Threats of any sort will not be tolerated and will be considered a violation of the student code of conduct. It is a requirement that you treat your instructors with respect and you should expect the same respect returned to you by your instructor.

**For Professors and Teaching Assistants:** All professors and teaching assistants should keep an open mind when discussing graded work with students. Make an effort to listen to students and try and see their point of view. If there was ambiguity in a question or multiple correct answers that a student brings to your attention, you should revise the grade. If the student concern is not adequately justified, explain your reasoning. Students that have concerns regarding an exam question or graded assignment deserve to be treated with respect. Treat with them with the same respect that you expect from them. That being said, concerns from one student that indicate that they are communicating on behalf of a larger group of peers (mob/crowd mentality) should not be considered.

**Statement on Appeals**

The Department of Physiology and Pharmacology follows the Western University student academic appeals policy (http://www.westerncalendar.uwo.ca/PolicyPages.cfm?Command=showCategory&PolicyCategoryID=1&SelectedCalendar=Live&ArchiveID=#SubHeading_181). All appeals to individual graded course components must be submitted to the course instructor within 3 weeks of the grade being released. All final course grade appeals must be received by January 31 (1st term classes) or June 30 (2nd term half classes and full year classes). You must first appeal to the course manager. If this appeal is rejected, then you can appeal to the Undergraduate Chair of the Department of Physiology and Pharmacology. If this appeal is rejected, you may then appeal to the Associate Dean of the Bachelor of Medical Sciences Undergraduate Education Committee.

You must have suitable grounds for appeal which may include: 1) appeal on medical or compassionate grounds; 2) appeal based on extenuating circumstances beyond your control; 3) appeal based on bias, inaccuracy or unfairness. All appeals must be accompanied by a detailed explanation along with supporting documentation. You should
submit your appeal as an e-mail with a single attachment. If you have multiple supporting documents, you should merge them into a single document.

Absence from course commitments

Medical/Compassionate Relief Program Policy

A. Absence for medical illness or non-medical absence:

Students must familiarize themselves with the Policy on Accommodation for Medical Illness for Undergraduate Students, located at:
http://www.westerncalendar.uwo.ca/PolicyPages.cfm?PolicyCategoryID=1&Command=
showCategory&Keywords=medical&SubHeadingID=323&SelectedCalendar=Live&Ar
chiveID=#SubHeading_323

If you are unable to meet a course requirement due to illness or other serious circumstances, you must seek approval for the absence as soon as possible. Students should familiarize themselves with the procedures for academic consideration and note the process for self-reporting.
http://www.westerncalendar.uwo.ca/PolicyPages.cfm?PolicyCategoryID=1&Command=
showCategory&Keywords=absence&SubHeadingID=323&SelectedCalendar=Live&Ar
chiveID=#SubHeading_323

Approval can be granted either through a self-reporting of absence or via the Academic Counselling unit. The Academic Counselling is located in NCB 280, and can be contacted at scibmsac@uwo.ca.

B. Accommodation for Religious Holidays

The policy for accommodation for Religious Holidays can be found at:
http://www.westerncalendar.uwo.ca/PolicyPages.cfm?PolicyCategoryID=1&Command=
showCategory&Keywords=absence&SubHeadingID=323&SelectedCalendar=Live&Ar
chiveID=#SubHeading_323

Documentation is required for all missed tests, research paper presentations or assignments regardless of the mark value. Such documentation must be submitted by the student directly to the appropriate Faculty Dean’s Office and NOT to the instructor. It will subsequently be the Dean’s Office that will determine if accommodation is warranted. For missed tests and presentations, the major assignment paper will be re-weighted accordingly when appropriate documentation is provided for the missing tests or presentations. With regards to the major assignment, a late submission will result in the final grade achieved reduced by one grade level lower.
For **non-medical absences** from tests, research paper presentations, late assignments, documentation is still required, and such documentation must be submitted by the student directly to the appropriate Faculty Dean’s Office and **NOT** to the instructor. It will subsequently be the Dean’s Office that will determine if accommodation is warranted.

### C. Special Examinations

http://www.westerncalendar.uwo.ca/PolicyPages.cfm?PolicyCategoryID=5&Command=showCategory&Keywords=special%20examination&SubHeadingID=70&SelectedCalendar=Live&ArchiveID=#SubHeading_70

A Special Examination is any examination other than the regular final examination, and it may be offered only with the permission of the Dean/Academic Counselling Office of the Faculty in which the student is registered, in consultation with the instructor and Department Chair. Permission to write a Special Examination may be given on the basis of compassionate or medical grounds with appropriate supporting documents.

A Special Examination must be written at the University or an Affiliated University College no later than 30 days after the end of the examination period involved. To accommodate unusual circumstances, a date later than this may be arranged at the time permission is first given by the Dean/Academic Counselling Office of the Faculty. The Dean/Academic Counselling Office will consult with the instructor and Department Chair and, if a later date is arranged, will communicate this to the Office of the Registrar.

If a student fails to write a scheduled Special Examination, permission to write another Special Examination will be granted only with the permission of the Dean/Academic Counselling Office in exceptional circumstances and with appropriate supporting documents. In such a case, the date of this Special Examination normally will be the scheduled date for the final exam the next time the course is offered.

When a grade of Special (SPC) or Incomplete (INC) appears on a student's record, the notations will be removed and replaced by a substantive grade as soon as the grade is available.

### Support Services:

Registrarial Services: [http://www.registrar.uwo.ca](http://www.registrar.uwo.ca)

Academic Counselling (Science and Basic Medical Sciences): [http://www.uwo.ca/sci/counselling](http://www.uwo.ca/sci/counselling)

USC Student Support Services: [http://westernusc.ca/services/](http://westernusc.ca/services/)

Student Development Services: [http://www.sdc.uwo.ca](http://www.sdc.uwo.ca)
Student Health Services: [http://www.shs.uwo.ca/](http://www.shs.uwo.ca/)

Students who are in emotional/mental distress should refer to Mental Health@Western [https://www.uwo.ca/health/mental_wellbeing/self/student.html](https://www.uwo.ca/health/mental_wellbeing/self/student.html) for a complete list of options about how to obtain help.