Physiology 4560A
Neurophysiology of homeostasis and stress
Fall term 2017

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 the integration of reproductive function.

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

Lectures: Wednesday/ 9:30-11:20 am/Room TBA

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.

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

Dr. Waturu Inoue
winoue@uwo.ca
Office: Robarts Research Institute 7241
Telephone: 519.931.5777, Ext. 24373

Dr. John Ciriello
john.ciriello@schulich.uwo.ca
Office: Medical Science Building M260
Telephone: 519-661-3484
Dr. Wataru Inoue is also the Course Manager for Physiology 4650A. His office is located on the seventh floor of the Robarts Research Institute (RRI7241).

Feel free to make an appointment (winoue@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
Once on the site, Log onto OWL using your UWO username and password. Select Human Physiology 4650A to get to the course website.

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 Web-CT 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.

If you have any questions or experience any OWL issues, please email owl@uwo.ca.

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 five 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) organize existing knowledge and develop a general understanding of contemporary neurophysiology underlying the regulation of homeostasis and stress response, through an independent written report.
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:
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:


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:


**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:**


- Lectures: 9-10. October 11/17
  - No lecture (Fall Break/work on assignments)

  - Student presentations: TBA


  **NEUROBIOLOGY OF STRESS ADAPTATION 1**

  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:


  **NEUROBIOLOGY OF STRESS ADAPTATION 2**

  In this lecture, we continue to learn about the mechanisms of neuroplasticity that are caused by stress, and in turn modulate stress response. We will also discuss the implications of these mechanisms in the detrimental consequences of stress, such as memory impairment and the development of mood disorders.

  Reference:

  
  Student presentations: TBA


THE HYPOTHALAMUS: CIRCULATORY REGULATION AND HYPERTENSION.

During this session we will examine the contribution of hypothalamic and other forebrain structures in the control of the circulation. Although virtually the whole brain is involved in maintaining the internal environment constant, neurons involved in homeostasis are concentrated within the hypothalamus. Because of this, the hypothalamus has often been called the "head ganglion" of the autonomic nervous system.

The limbic structures, in association with the hypothalamus, contributes to higher order integration of autonomic, endocrine and behavioural responses for homeostatic regulation of the internal environment for the adaptation of the animal to the continuously changing external environment. The neural integrative activities of these structures ensure that the "house-keeping chores" occur routinely in relation to the varying demands of the behaving animal.

We will examine some of the evidence that indicates that a malfunction in the neuronal circuits within the hypothalamus and limbic system that control the circulation is involved in the hypertensive process. We will examine the connectivity of the hypothalamus, the physiological functions generally controlled by the hypothalamus and the direct role of some hypothalamic nuclei in controlling sympathetic nervous system activity

Reference:


BODY ENERGY BALANCE.
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:

- Lectures: 19-20. November 15/17 –
  No lecture / work on assignments


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:


  
  Student presentations: TBA

- **Lecture 25-26: December 6/17.** - Dr. J. Ciriello - 9:30 - 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:*


Note that December 6/17 is the LAST DAY of class for this semester.

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:

<table>
<thead>
<tr>
<th>Component</th>
<th>Date</th>
<th>% of Final Mark</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midterm assignment</td>
<td>Due October 18, 2017</td>
<td>15</td>
</tr>
<tr>
<td>-November 12 - Last day to drop a first-term half course (without academic penalty)-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Research Paper Presentation</td>
<td>Through-out Term</td>
<td>15</td>
</tr>
<tr>
<td>Discussion Leader Grade</td>
<td>Through-out Term</td>
<td>5</td>
</tr>
<tr>
<td>Short Lay Summaries</td>
<td>2 summaries/ Through-out Term</td>
<td>10</td>
</tr>
<tr>
<td>Class Participation</td>
<td>Through-out Term</td>
<td>10</td>
</tr>
<tr>
<td>Final exam</td>
<td>TBA</td>
<td>20</td>
</tr>
<tr>
<td>Assignment (Review Paper)</td>
<td>Due December 6, 2017</td>
<td>25</td>
</tr>
</tbody>
</table>
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@uwo.ca) by 5 pm of the due date.

Note: it is the policy of the Department of Physiology and Pharmacology and the BMSc program in the Schulich School of Medicine and Dentistry to report the grade you earned in the course. Grades will not be “bumped”. For example, if your final grade is 78.45%, it will be entered as 79% and will not be “bumped” to 80%.

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_discipline_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 ).”

Absence from course commitments

A. Absence for medical illness:

Information about “Accommodation for Medical Illness – Undergraduates: POLICY ON ACCOMMODATION FOR MEDICAL ILLNESS - UNDERGRADUATE STUDENTS” can be found in the Academic Handbook at
http://www.uwo.ca/univsec/handbook/appeals/accommodation_medical.pdf

Students must familiarize themselves with the Policy on Accommodation for Medical Illness:
https://studentservices.uwo.ca/secure/index.cfm
Statement from the Dean's Office, Faculty of Science

If you are unable to meet a course requirement due to illness or other serious circumstances, you must provide valid medical or other supporting documentation to the Dean's office as soon as possible and contact your instructor immediately. It is the student's responsibility to make alternative arrangements with their instructor once the accommodation has been approved and the instructor has been informed. In the event of a missed final exam, a "Recommendation of Special Examination" form must be obtained from the Dean's Office immediately. For further information please see:

A student requiring academic accommodation due to illness, should use the Student Medical Certificate when visiting an off-campus medical facility or request a Record's Release Form (located in the Dean's Office) for visits to Student Health Services. The form can be found at:
https://studentservices.uwo.ca/secure/medical_document.pdf

The Policy on Accommodation for Medical Illness is also available on the BMSUE secure site:  http://www.uwo.ca/bmsc/

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.

B. Absence for non-medical reasons:

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

A Special Examination is any examination other than the regular examination, and it may be offered only with the permission of the Dean 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 of the Faculty. The Dean will consult with the instructor and Department Chair and, if a later date is arranged, will communicate this to Registrarial Services.

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 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.

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.sds.uwo.ca](http://www.sds.uwo.ca)

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

Students that are in emotion/mental distress should refer to Mental Health@Western [http://www.uwo.ca/uwocom/mentalhealth/](http://www.uwo.ca/uwocom/mentalhealth/) for a complete list of option about how to obtain help.

**D. Policy on Rounding and Bumping of Grades**

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 in 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.

**E. Policy on Plagiarism**

The Department of Physiology and Pharmacology strongly condemns plagiarism. Plagiarism is the “act or instance of copying or stealing another’s words or ideas and attributing them as ones own.” (Excerpted from Black’s Law Dictionary, West Group, 1999, 7th ed. Pg 1170 and
the definition used by Western’s Scholastic Discipline document). Plagiarism can be intentional or unintentional and regardless of intent, is a scholastic offence. It should be noted that self-plagiarism, plagiarizing one’s own words for multiple assignments is subject to the same penalty as plagiarizing another. Courses in Physiology and Pharmacology use turnitin, a similarity checking software embedded within OWL. We encourage all students to run their assignments through turnitin prior to submitting their reports for grading. Any report flagged as yellow (25-49% matching text), orange (50-74% matching text) or red (75-100% matching text) will be considered plagiarism (pending investigation by the instructor). It should be noted that a document could be plagiarized yet still pass the similarity check on turnitin. The minimum penalty for a first-time plagiarism offence of any kind is a grade of zero on the assignment. In addition, details of the offence will be forwarded to Dean’s office and stored. A second offence will carry a much stricter penalty in line with Western’s Scholastic Discipline policies (https://www.uwo.ca/univsec/pdf/academic_policies/appeals/scholastic_discipline_undergrad.pdf).