AUTONOMIC FUNCTION & DISEASES

Three (3) credits

Pre-requisites: By permission only
Place: BC 126
Time: Monday 5:00 pm - 7:45 pm

Office hours: Tuesday 5:00 pm – 7:45 pm at BC 327, bldg 71
Course Offered: by Dr. Rui Tao

Course Description

The course covers both the physiological and clinical study of autonomic nervous system (ANS), emphasizing the neural circuitry aspects of systemic regulation. Topics are introduced in lectures and followed up by discussions of recent journal articles.

Course Objectives:

Students will be expected to demonstrate following

1. They will learn the major neural circuitry of autonomic regulation in response to sensory stimuli and be able to compare similarities and differences with the somatic nervous system.
2. Students will demonstrate and explain important characteristics of the sympathetic and parasympathetic regulation
3. They will be able to interpret autonomic failure in some diseases when sufficient clinical information provided, and will draw conclusions

Week 1: *Introduction to homeostatic regulation*

Objectives
1. Describe neurons 2. Compare and contrast sensory, autonomic and somatic nervous systems 3. List sympathetic and parasympathetic nervous systems 4. Describe homeostasis and thermoregulation
Required readings
1. Ruby NF. (2003) Hibernation: when good clocks go cold. J Biol Rhythms. 18(4):275-86.

Week 2: *Happy Labor Day*

Objectives
1. Describe your best scheduled for Orlando 2. Miami 3. Boca
Required readings
Consumer Reports

Week 3: *Thermal physiology*

Objectives
1. Describe the ascending thermosensory pathway from dorsal root ganglian to spinal cord lamina I to brain insular cortex (Nomoto et al., 2004) 2. List the transit receptor potential (TRP) family members (Nomoto et al., 2004; Caterina, 2007; Romanovsky, 2007) 3. Compare the obligatory and facultory thermogenesis with respect to their energy expenditures 4. Describe these organs with functional structures involving thermoregulations: BAT, muscles, sweat glands, counter-current exchanges 5. Explain the role of anteroventral third ventricular (AV3V) in thermogenesis 6. Describe the circumventricular organs (CVO), and explain the their functions in the development of fever
Required Readings
2. Silvestri E, Schiavo L, Lombardi A, Goglia F. (2005) Thyroid hormones as molecular determinants of thermogenesis. Acta Physiol Scand. 184(4):265-83.

Week 4: Literature discussion

Presented by	**Literature**
1.	Bratincsak A, Palkovits M. (2005**)** Evidence that peripheral rather than intracranial thermal signals induce thermoregulation. Neuroscience.135(2):525-32
2.	Endo Y, Yamauchi K, Fueta Y, Irie M. (2001) Changes of body temperature and plasma corticosterone level in rats during psychological stress induced by the communication box. Med Sci Monit. 7(6):1161-5.
3.	Chen GF, Sun Z. (2006) Effects of chronic cold exposure on the endothelin system. J Appl Physiol. 100(5):1719-26
4.	Seebacher F, Franklin CE. (2005) Physiological mechanisms of thermoregulation in reptiles. J Comp Physiol 175(8):533-41.
5.	Hiranandani N, Varian KD, Monasky MM, Janssen PM. (2006) Frequency-dependent contractile response of isolated cardiac trabeculae under hypo-, normo-, and hyperthermic conditions. J Appl Physiol. 100(5):1727-32.
6.	Wu X, Drabek T, Kochanek PM, Henchir J, Stezoski SW, Stezoski J, Cochran K, Garman R, Tisherman SA. Induction of profound hypothermia for emergency preservation and resuscitation allows intact survival after cardiac arrest resulting from prolonged lethal hemorrhage and trauma in dogs. Circulation.113(16):1974-82.

Week 5: *Biorhythms*

Objectives
1. Describe the role of vagus nerve in thermoregulation (Szekely, 2000) 2. Place the role of raphe pallidus in thermoregulation (Morrison, 2004)

3. Identify the thermal related hormones from HPA and HPT axis (Silvestri et al., 2005) 4. Understand the role of T3/T4 in the obligatory thermoregulation and NA in the facultory regulation 5. Compare the circadian rhythms of core temperature and sleep-wake cycle (Krauchi, 2007) 6. Define the approaches for free-run experiments (Benstaali et al., 2001); 7. Describe how melatonin controls the body clock, and explain neural pathways of circadian timing system (Hofman, 2000; Waterhouse et al., 2005) 8. Explain the integrative role of hypothalamus in circadian rhythms (Saper et al., 2005)
Required Readings
3. Kräuchi K. (2007) The human sleep-wake cycle reconsidered from a thermoregulatory point of view. Physiol Behav. 90(2-3):236-45.

Week 6: Literature discussion & **Exam 1**

Presented by	Literature
7.	Silva JE (2003) The thermogenic effect of thyroid hormone and its clinical implications. Ann Intern Med. 139(3):205-13.
8.	Catalina F, Milewich L, Frawley W, Kumar V, Bennett M. (2002) Decrease of core body temperature in mice by dehydroepiandrosterone. Exp Biol Med. 227(6):382-8
9.	Gómez F, Graugés P, Martín M, Armario A (1998) The effect of chronic administration of antidepressants on the circadian pattern of corticosterone in the rat. Psychopharmacology (Berl). 140(2):127-34

Week 7: *Thermoregulation in heat stress*

Objectives
1. Describe the temperature rhythms in hibernation (Ruby, 2003) 2. Define the term *thermoneutral zone* and *minimal lethal* T_{cor} (Leon et al., 2005) 3. Describe a biphasic thermoregulatory response to the heat stress followed by recovery at low ambient temperatures (Leon et al., 2005) 4. Describe heat stroke and explain how the hormonal response to endotoxin and GI permeability 5. Describe the heat acclimation (Horowitz 2002) 6. Describe the functional relationship of hsp70 with denatured proteins (Sherman and Gabal 2006) 7. Role of sweating in heat loss (Shibasaki et al., 2006)
Required Readings
4. Hampl R, Starka L, Jansky L. (2006) Steroids and thermogenesis. Physiol Res. 55(2):123-31.

Week 8: *Thermoregulation in cold stress*

Objectives

1. Autonomic and hormonal response to cold exposures (Leppaluoto et al., 2005) 2. BAT: subscapular area, around vessels in the surroundings of the kidney, aorta and neck (Leppaluoto et al., 2005) 3. Thyroid hormone (Silvestri et al., 2005) 4. UCP and brown adipose tissue (Morrison, 2004; Mozo et al., 2005)
Required Readings
5. Leppaluoto J, Paakkonen T, Korhonen I, Hassi J. (2005) Pituitary and autonomic responses to cold exposures in man. Acta Physiol Scand. 184(4):255-64.

Week 9: Literature discussion

Presented by	Literature
10.	Leon LR, DuBose DA, Mason CW. (2005) Heat stress induces a biphasic thermoregulatory response in mice. Am J Physiol Regul Integr Comp Physiol. 288(1):R197-204.
11.	Lambert GP, Gisolfi CV, Berg DJ, Moseley PL, Oberley LW, Kregel KC. (2002) Selected contribution: Hyperthermia-induced intestinal permeability and the role of oxidative and nitrosative stress. J Appl Physiol. 92(4):1750-61;
12.	Palinkas LA, Makinen TM, Paakkonen T, Rintamaki H, Leppaluoto J, Hassi J. (2005) Influence of seasonally adjusted exposure to cold and darkness on cognitive performance in circumpolar residents. Scand J Psychol. 46(3):239-46
13.	van der Zee J. (2002) Heating the patient: a promising approach? Ann Oncol. 13(8):1173-84.
14.	Morrison SF. (2004) Central pathways controlling brown adipose tissue thermogenesis. News Physiol Sci. 19:67-74.
15.	Wu X, Drabek T, Tisherman SA, Henchir J, Stezoski SW, Culver S, Stezoski J, Jackson EK, Garman R, Kochanek PM. (2007) Emergency preservation and resuscitation with profound hypothermia, oxygen, and glucose allows reliable neurological recovery after 3 h of cardiac arrest from rapid exsanguination in dogs. J Cereb Blood Flow Metab. 2007

Week 10: *Thermoregulation in psychological stress*

1. Describe the neural circuitry from limbic system to hypothalamus for psychological stress-induced hyperthermia and tachycardia (DiMicco et al., 2006) 2. Describe thermoregulational changes in social defeat (Keeney et al., 2001; Bhatnagar et al., 2006), (Endo 2001) 3. The role of AV3V in social stress (Whyte and Johnson, 2007)
Required Readings

6. Olivier B, Zethof T, Pattij T, van Boogaert M, van Oorschot R, Leahy C, Oosting R, Bouwknecht A, Veening J, van der Gugten J, Groenink L. (2003) Stress-induced hyperthermia and anxiety: pharmacological validation. Eur J Pharmacol. 463(1-3):117-32.

Week 11: literature discussion and **Exam 2**

Presented by	Literature
16.	Bhatnagar S, Vining C, Iyer V, Kinni V. (2006) Changes in hypothalamic-pituitary-adrenal function, body temperature, body weight and food intake with repeated social stress exposure in rats. J Neuroendocrinol. 18(1):13-24
17.	Keeney A, Jessop DS, Harbuz MS, Marsden CA, Hogg S, Blackburn-Munro RE. (2006) Differential effects of acute and chronic social defeat stress on hypothalamic-pituitary-adrenal axis function and hippocampal serotonin release in mice. J Neuroendocrinol. 18(5):330-8
18.	Ruby NF, Dark J, Burns DE, Heller HC, Zucker I (2002) The suprachiasmatic nucleus is essential for circadian body temperature rhythms in hibernating ground squirrels. J Neurosci. 22(1):357-64

Week 12: *Fever*

Objectives
1. Describe the humeral hypothesis of fever induction 2. Explain biphasic and polyphasic response induced by LPS (Roth, 2006) (Romanovsky1998) 3. Describe Toll-like receptors and IL-1 formation (Simon and van der Meer, 2007) 4. Describe inflammatory molecules: IL1, IL6 5. Explain the relationship of OVLT on POAH 6. Describe PGE2 formation and explain its role in fever induction 7. Describe the endogenous antipyretics (Roth, 2006) 8. Describe the neural pathway for fever induction
Required Readings
7. Roth J. (2006) Endogenous antipyretics. Clin Chim Acta. 371(1-2):13-24.

Week 13: *Temperature-related diseases*

Objectives
1. Describe the functions of classic neurotransmission (e.g., 5HT, DA, NA, GABA, glutamate) in thermoregulation (Hedlund et al., 2003), 2. Describe the effect of alcohol on body temperature (Wasielewski and Holloway, 2001) 3. Describe the effect of NMMA (Rusyniak and Sprague, 2005) 4. Define the role of dopamine in neuroleptic maglinant syndrome (Gurrera and Romero, 1992) 5. Understand periodic fever syndrome (hereditary autoinflammatory syndrome)

(Simon and van der Meer, 2007) 6. Understand hyperthermia in cancer treatment
Required readings
8. Simon A, van der Meer JW. (2007) Pathogenesis of familial periodic fever syndromes or hereditary autoinflammatory syndromes. Am J Physiol Regul Integr Comp Physiol. 292(1):R86-98.

Week 14: Literature discussion

Presented by	Literature
19.	Kiyatkin EA (2005) Brain hyperthermia as physiological and pathological phenomena. Brain Res Rev. 50(1):27-56 (part 1: pg 1-15)
20.	Kiyatkin EA (2005) Brain hyperthermia as physiological and pathological phenomena. Brain Res Rev. 50(1):27-56 (part 2: pg 16-end)
21.	Nicholas AC, Seiden LS. (2003) Ambient temperature influences core body temperature response in rat lines bred for differences in sensitivity to 8-hydroxy-dipropylaminotetralin. J Pharmacol Exp Ther. 305(1):368-74
22.	Bautista DM, Siemens J, Glazer JM, Tsuruda PR, Basbaum AI, Stucky CL, Jordt SE, Julius D. (2007) The menthol receptor TRPM8 is the principal detector of environmental cold. Nature. 448(7150):204-8.
23.	Conti B, Sanchez-Alavez M, Winsky-Sommerer R, Morale MC, Lucero J, Brownell S, Fabre V, Huitron-Resendiz S, Henriksen S, Zorrilla EP, de Lecea L, Bartfai T. (2006) Transgenic mice with a reduced core body temperature have an increased life span. Science. 314(5800):825-8
24.	Nakamura K, Morrison SF.(2007) Central efferent pathways mediating skin cooling-evoked sympathetic thermogenesis in brown adipose tissue. Am J Physiol Regul Integr Comp Physiol. 292(1):R127-36.

Week 15: *Age-related changes in thermoregulation*

Objectives
1. Describe hot flushes 2. Compare of circadian rhythms of core temperature between ages (Weinert and Waterhouse, 2007) 3. Describe the relationship between body temperature and life span (Conti et al., 2006) 4. Describe the effect of hyperthermia on aging (Zhang et al., 2002; Wilson and Morley, 2003), (Wachulec1997) 5. Describe relationship between leptin and aging (Zimmermann-Belsing et al., 2003)

Required Readings
9. Stearns V, Ullmer L, Lopez JF, Smith Y, Isaacs C, Hayes D. (2002) Hot flushes. Lancet. 360(9348):1851-61.

Week 16: **Exam 3**

Textbook & References:

No textbook is required. The handouts and objectives will be posted on the university's blackboard system, available at http://blackboard.fau.edu/

Attendance Policy

You are required to attend all classes. However, if you cannot attend class for understandable reason, you should inform me before a class (preferably). Notification after-the-fact will only be accepted as an excuse if you have proof to show you were physically unable to inform me in advance

Examinations and Grades:

The final grade for this class will be derived from averaging the total points as earned by taking the three required exams that will be given throughout the semester (including the final exam, which will not be cumulative). Each literature discussion will be worth 30 pts and exam 70 points. Final grades will be determined by using the following scale.

A:
90 -100%
B:
80 – 89%
C:
70 – 79%
D:
60 – 69%
F:
59% or lower

References

Benstaali C, Mailloux A, Bogdan A, Auzeby A, Touitou Y (2001) Circadian rhythms of body temperature and motor activity in rodents their relationships with the light-dark cycle. Life Sci 68:2645-2656.

Bhatnagar S, Vining C, Iyer V, Kinni V (2006) Changes in hypothalamic-pituitary-adrenal function, body temperature, body weight and food intake with repeated social stress exposure in rats. J Neuroendocrinol 18:13-24.

Caterina MJ (2007) Transient receptor potential ion channels as participants in thermosensation and thermoregulation. Am J Physiol Regul Integr Comp Physiol 292:R64-76.

Conti B, Sanchez-Alavez M, Winsky-Sommerer R, Morale MC, Lucero J, Brownell S, Fabre V, Huitron-Resendiz S, Henriksen S, Zorrilla EP, de Lecea L, Bartfai T (2006) Transgenic mice with a reduced core body temperature have an increased life span. Science 314:825-828.

Gurrera RJ, Romero JA (1992) Sympathoadrenomedullary activity in the neuroleptic malignant syndrome. Biol Psychiatry 32:334-343.

Hedlund PB, Danielson PE, Thomas EA, Slanina K, Carson MJ, Sutcliffe JG (2003) No hypothermic response to serotonin in 5-HT7 receptor knockout mice. Proc Natl Acad Sci U S A 100:1375-1380.

Hofman MA (2000) The human circadian clock and aging. Chronobiol Int 17:245-259.

Keeney AJ, Hogg S, Marsden CA (2001) Alterations in core body temperature, locomotor activity, and corticosterone following acute and repeated social defeat of male NMRI mice. Physiol Behav 74:177-184.

Krauchi K (2007) The human sleep-wake cycle reconsidered from a thermoregulatory point of view. Physiol Behav 90:236-245.

Leppaluoto J, Paakkonen T, Korhonen I, Hassi J (2005) Pituitary and autonomic responses to cold exposures in man. Acta Physiol Scand 184:255-264.

Morrison SF (2004) Central pathways controlling brown adipose tissue thermogenesis. News Physiol Sci 19:67-74.

Mozo J, Emre Y, Bouillaud F, Ricquier D, Criscuolo F (2005) Thermoregulation: what role for UCPs in mammals and birds? Biosci Rep 25:227-249.

Nomoto S, Shibata M, Iriki M, Riedel W (2004) Role of afferent pathways of heat and cold in body temperature regulation. Int J Biometeorol 49:67-85.

Romanovsky AA (2007) Thermoregulation: some concepts have changed. Functional architecture of the thermoregulatory system. Am J Physiol Regul Integr Comp Physiol 292:R37-46.

Roth J (2006) Endogenous antipyretics. Clin Chim Acta 371:13-24.

Ruby NF (2003) Hibernation: when good clocks go cold. J Biol Rhythms 18:275-286.

Rusyniak DE, Sprague JE (2005) Toxin-induced hyperthermic syndromes. Med Clin North Am 89:1277-1296.

Saper CB, Lu J, Chou TC, Gooley J (2005) The hypothalamic integrator for circadian rhythms. Trends Neurosci 28:152-157.

Shibasaki M, Wilson TE, Crandall CG (2006) Neural control and mechanisms of eccrine sweating during heat stress and exercise. J Appl Physiol 100:1692-1701.

Silvestri E, Schiavo L, Lombardi A, Goglia F (2005) Thyroid hormones as molecular determinants of thermogenesis. Acta Physiol Scand 184:265-283.
Simon A, van der Meer JW (2007) Pathogenesis of familial periodic fever syndromes or hereditary autoinflammatory syndromes. Am J Physiol Regul Integr Comp Physiol 292:R86-98.
Szekely M (2000) The vagus nerve in thermoregulation and energy metabolism. Auton Neurosci 85:26-38.
Wasielewski JA, Holloway FA (2001) Alcohol's interactions with circadian rhythms. A focus on body temperature. Alcohol Res Health 25:94-100.
Waterhouse J, Drust B, Weinert D, Edwards B, Gregson W, Atkinson G, Kao S, Aizawa S, Reilly T (2005) The circadian rhythm of core temperature: origin and some implications for exercise performance. Chronobiol Int 22:207-225.
Weinert D, Waterhouse J (2007) The circadian rhythm of core temperature: effects of physical activity and aging. Physiol Behav 90:246-256.
Wilson MM, Morley JE (2003) Invited review: Aging and energy balance. J Appl Physiol 95:1728-1736.
Zhang HJ, Drake VJ, Morrison JP, Oberley LW, Kregel KC (2002) Selected contribution: Differential expression of stress-related genes with aging and hyperthermia. J Appl Physiol 92:1762-1769; discussion 1749.
Zimmermann-Belsing T, Brabant G, Holst JJ, Feldt-Rasmussen U (2003) Circulating leptin and thyroid dysfunction. Eur J Endocrinol 149:257-271.