Syllabus

MEETING TIME and PLACE: Wednesdays 4 to 6:30, Meyer 815

INSTRUCTOR: Chiye Aoki, Professor of Neural Science and Biology ca3@nyu.edu, 1056 Meyer, office hour by appointment

MAXIMUM NUMBER OF STUDENTS: 15

PRE-REQUISITES: BINS, CMNeurobio

DESCRIPTION:

Is your brain still growing? Are events more memorable to you now than they will be later in life? Why do so many mental illnesses emerge for the first time during adolescence? We will ask and try to answer these questions, as we read and discuss papers on adolescent brain development and behavior.

Brain function is exquisitely dependent on childhood experience. Starting from the foundational works of Torsten Wiesel and David Hubel, much has been learned about the molecular mechanisms underlying developmental plasticity of the juvenile brain. In contrast, relatively less is known about the developmental events during the succeeding, final developmental stage – adolescence. Adolescence is characterized by great bursts in creativity and energy, but is also the stage when many mental illnesses emerge for the first time. What is the neurobiological basis for the vulnerability of teens to addiction, depression, anxiety, risky behaviors, schizophrenia or eating disorders? Might some of the vulnerabilities be tied to developmental changes that occur during adolescence? How is the teen brain different from a juvenile's brain or an adult's brain, molecularly and structurally? These are some of the questions that will be addressed through critical readings and discussions.

General structure. A different topic for discussion has been chosen for every week, usually revolving one or two key authors in the field. Students will take turns presenting assigned papers, usually on research that has used an animal model (30 min per student/paper). Every week, except for week 1, everyone will be tested on preparedness to discuss the papers by taking a 5 min quiz at the beginning of class. Each student will have a minimum of two opportunities to present papers and lead discussions.

Course grade will be based on the 5-min quiz scores + class participation (20%), class presentations (10% for the first + 20% for the second = 30%), and a term paper (50%).

The term paper. The topic for the term paper will be mutually agreed upon by the student and Professor Aoki. The tentative title of the term paper will be due on Feb 17. The first version of the bibliography will be due on March 2. A rough draft may be submitted for evaluation and feedback on March 30. A more polished draft may be submitted on April 13. Students will receive an un-graded evaluation of the March 30 version and a tentative grade with written critique for the version submitted on April 13. On April 27 and May 4, students will take turn describing the content of the term paper as an oral presentation, so as to receive helpful criticisms and suggestion from classmates. The final draft is due anytime during Week 15 but no later than May 17.

An essential component for the term paper is the quality (originality, substantiation) of the student's **working hypothesis** revolving one of the questions addressed during the semester OR **delineation of an unanswered question**, with a convincing explanation as to why it is important to test the hypothesis or get

an answer to the question. Other essential components are: the **description of the subject matter**, description of the **background literature** leading up to the question/hypothesis, **suggestions of experiments** that can address the question or test the hypothesis and why that approach would be useful, an explanation of what the **expected outcome** would be, if your hypothesis were to be correct or wrong, and a **bibliography**.

Here are some of the questions I will be using to assess the quality of the paper, adapted from educators at Northern Illinois University and Barbara Walvoord, Winthrop University, Virginia Community College System, Univ. of Washington, NYU and Hunter College).

Clarity…Is the working hypothesis or unanswered question presented clearly? Is the demarcation between what is known and what remains unknown clear?

Organization…Is the sequence of ideas and transitions logical, smooth and effective? Are sub-headers or opening sentences being used effectively to bind together related information?

Support/reasoning…Are ideas substantiated by published works and clearly segregated from ideas that are yours? Have you presented your opinion as to whether the findings that you've reviewed are well-grounded or are speculative? If so, have you provided an explanation for your opinion? How thorough is the citation of relevant work, without being redundant or out-dated? Is the importance of the question explained convincingly?

Completeness…Is the writing free of grammatical errors, typos, or redundancies? Is each sentence written clearly and simply? Will the completed paper be submitted on time?

LEARNING OBJECTIVES:

Familiarization with current literature on adolescent brain development and behavior.

Development of skills in critical reading of scientific literature, scientific writing, oral presentation, discussions and debates.

SCHEDULE:

Week 1. January 27. Adolescent Brains: Is anything still growing? Retracting? Pruning?

One of the problems with surveying the literature of this field is that the term, 'adolescence' has been used differently among investigators. What are the key developmental events that define the beginning and the end of adolescence? How different is adolescent behavior? How different are their brains?

References cited on Jan 27:

- L.P. Spear (2000) The adolescent brain and age-related behavioral manifestations, Sections 1 and 2. *Neuroscience and Biobehavioral Reviews* 24: 417-424
- Jay N. Giedd et al. (1999) Brain development during childhood and adolescence: a longitudinal MRI study. Nature Neurosci 2: 861-863
- Kathryn Mills et al. (2014) The developmental mismatch in structural brain maturation during adolescence. Dev Neurosci 35:147-60.
- Goddings et al (2014) The influence of puberty on subcortical brain development. *Neuroimage* 88: 242-51.
- ER Sowell, PM Thompson, CJ Holmes, TL Jernigan, AW Toga. 1999. In vivo evidence for post-adolescent brain maturation in frontal and striatal regions. Nature Neurosci 2(10) 859-861.

Homework: Required reading for the upcoming week's topic on "Vulnerability of Adolescents to Alcoholism

Week 2. February 3. Vulnerability of Adolescents to Alcoholism

Required Reading:

- L.P. Spear (2000) Sections 1 - 3. (p. 417-28).
- Varlinskaya and Spear (2002) Acute effects of ethanol on social behavior of adolescent and adult rats: Role of familiarity of the test situation. *Alcoholism: Clinical and Experimental Research* 26: 1502-11.
- Varlinskaya and Spear (2006) Differences in the social consequences of ethanol emerge during the course of adolescence in rats: Social facilitation, social inhibition, and anxiolysis. Dev. Psychobiology 48: 146-61.
- Pautassi et al (2008) Adolescent but not adult rats exhibit ethanol-mediated appetitive second-order conditioning. 32(11): 2016-27.
- Varlinskaya et al (2014) Chronic intermittent ethanol exposure during adolescence: Effects on social behavior and ethanol sensitivity in adulthood. *Alcohol* 48:433-44.

Suggested reading to review the topic on Feb 3:

- L.P. Spear (2014) Adolescents and alcohol: Acute sensitivities, enhanced intake, and later consequences. *Neurotoxicology and Teratology* 41: 51-59.

Homework: Required reading for the upcoming week's topic on "GABA receptors: A molecular substrate for alcoholism"

Week 3. February 10. GABA Receptor: A Molecular Substrate for Alcoholism

Required Reading:

- J. Liang, Y. Shen, XM Shao, MB Scott, E Ly, S. Wong, Al. Nguyen, K. Tan, B. Kwon, RW Olsen, I Spigelman (2014) Dihydromyricetin prevents fetal alcohol exposure-induced behavioral and physiological deficits: The roles of GABAA receptors in adolescence. Neurochem Res 39(6) 1147-61.
- Homework question: What is zolpidem, picrotoxin, PTZ, FAE, THIP, DGC, DHM; What is meant by 'extrasynaptic'?

Suggested reading, to help digest this paper:

- RW Olsen and I Spigelman (2012) GABAA receptor plasticity in alcohol withdrawal. In: J.L. Noebels, M. Avoli, M.A. Rogawski, RW Olsen and AV Delgado-Escueta, eds., Jasper's Basic Mechanisms of the Epilepsies [Internet], 4th Ed, Bethesda (MD): National Center for Biotechnology Information (US)
- M. Wallner (2014) In honor of Professor Richard Olsen. Neurochem Res 39(6): 989-991.

Homework: Required reading for upcoming week's topic on "The Impact of Gonadal Hormones on Hippocampal Physiology and Learning"

Week 4. February 17. The impact of gonadal hormones on hippocampal physiology and learning

Required Reading: Papers by Sheryl Smith

- Shen, H., et al., 2007. Reversal of neurosteroid effects at alpha4-beta2-delta GABA-A receptors triggers anxiety at puberty. Nat Neurosci. 10**,** 469-477.
- Shen, H., et al., 2010. A critical role for alpha4-beta-delta GABA-A receptors in shaping learning deficits at puberty in mice. Science (Supp.Online Material). 327**,** 1515-1518.
- JD Cushman MD Moore RW Olsen MS Fanselow (2014) The role of the delta GABA(A) receptor in ovarian cycle-linked changes in hippocampus-dependent learning and memory. Neurochem Res 39: 1140-46.

Homework: Submit a tentative topic for the term paper.

Week 5. February 24. Literature Search Training at Bobst Library, Avery Fisher Center West Room, Floor 2 With Kelly Johnson

Homework: Required reading for the upcoming week's topic on "Vulnerability of Adolescents to Nicotine Addiction" plus a bibliography of the term paper, due March 2.

Week 6. March 2. Vulnerability of Adolescents to Nicotine Addiction

Required Reading:

- ED Levin, A Rezvani, D. Montoya, J Rose, H. Swartzwelder (2003) Adolescent-onset nicotine self-administration modeled in female rats. Psychopharmacology 169: 141-149.
- ED Levin, SS Lawrence, A Petro K Horton, AH Rezvani, FJ Seidler, TA Slotkin. (2007) Adolescent vs. adult-onset nicotine self-administration in male rats: Duration of effect and differential nicotinic receptor correlates. Neurotoxicology and Teratology 29: 458-465.
- JD Belluzzi, AG Lee, HS Oliff, FM Leslie (2004) Age-dependent effects of nicotine on locomotor activity and conditioned place preference in rats. Psychopharmacology 174: 389-395.
- OV Torres, HA Tejeda, LA Natividad, LE O'Dell (2008) Enhanced vulnerability to the rewarding effects of nicotine during the adolescent period of development. Pharmacology, Biochemistry and Behavior 90: 658-663
- M. Lenoir, AK Starosciak, J Ledon, C. Booth, E. Zakharova, D. Wade, B. Fignoli, S. Izenwasser. (2015) Sex differences in conditioned nicotine reward are age-specific. Pharmacology, Biochemistry and Behavior 132: 56-62.

Homework: Required reading for the upcoming week's topic on "Progression from Licit Drug Use During Adolescence to Illicit Drug Use in Adulthood"

Week 7. March 9. Progression from Adolescent Licit Drug to Illicit Drug Use in Adulthood

Required Reading:

- SL Collins, R Montano, S Izenwasser (2004) Nicotine treatment produces persistent increases in amphetamine-stimulated locomotor activity in periadolescent male but not female or adult male rats. Developmental Brain Research 153: 175-187.
- SL Collins and S Izenwasser (2004) Chronic nicotine differentially alters cocaine-induced locomotor activity in adolescent vs. adult male and female rats. Neuropharmacology 46: 349-362.
- PE Dickson, MM Miller, TD Rogers, CD Blaha, G Mittleman (2014) Effects of adolescent nicotine exposure and withdrawal on intravenous cocaine self-administration during adulthood in male C57BL/6J mice. Addict Biol 19: 37-48.
- BM Kelley and LD Middaugh (1999) Periadolescent nicotine exposure reduces cocaine reward in adult mice. Journal of Addictive Diseases. 18: 27-39.
- SC McQuown, JD Belluzzi, FM Leslie (2007) Low dose nicotine treatment during early adolescence increases subsequent cocaine reward. Neurotoxicol Teratol 29: 66-73.
- BA McMillen, BJ Davis, HL Williams, K Soderstrom (2005) Periadolescent nicotine exposure causes heterologous sensitization to cocaine reinforcement. European Journal of Pharmacology 509: 161-164.

- JJ. Anker and ME Carroll (2011) Adolescent nicotine exposure sensitizes cue-induced reinstatement of cocaine seeking in rats bred for high and low saccharin intake. Drug Alcohol Depend 118: 68-72.

Homework: Required reading on the upcoming week's topic on "Developmental Changes of the Dopamine System and Striatum During Adolescence"

Optional homework: First draft of the term paper, due March 30

SPRING BREAK

Week 8. March 23. Developmental Changes of the Dopamine System and Striatum During Adolescence

Required Reading:

- A Galvan, TA Hare, CE Parra, J Penn, H Voss, G Glover, BJ Casey (2006) Earlier development of the accumbens relative to orbitofrontal cortex might underlie risk-taking behavior in adolescents. J Neurosci 26: 6885-92.
- JN Porter, AK Roy, B Benson, C Carlisi, PF Collins, E Leibenluft, DS Pine, M Luciana, M Ernst (2015) Age-related changes in the intrinsic functional connectivity of the human ventral vs dorsal striatum from childhood to middle age. Dev Cogn Neurosci 11: 83-95.
- A Galvan, TS Peris (2014) Neural correlates of risky decision making in anxious youth and healthy controls. Depress Anxiety 31: 591-8.
- SL Andersen, M Rutstein JM Benzo JC Hostetter, MH Teicher. (1997) Sex differences in dopamine receptor overproduction and elimination. Neuroreport 8(6): 1495-8.
- SL Andersen, AT Thompson, M Rutstein, JC Hostetter, MH Teicher (2000) Dopamine receptor pruning in prefrontal cortex during the periadolescent period in rats. Synapse 37(2) 167-9.

Suggested Review Articles

- A Galvan. (2010) Adolescent development of the reward system. Frontiers in Human Neuroscience 4: 1-9.
- Nelson et al 2005. The social re-orientation of adolescence: A neuroscience perspective on the process and its relation to psychopathology. Psychol med 35: 163-74.
- Ernst M, Romeo R, Andersen S. 2009. Neurobiology of the development of motivated behaviors in adolescence: a window into a neural systems model. Pharmacol Biochem Behav 93: 199-211.
- Ernst M, Daniele T, Frantz, K 2011. New perspectives on adolescent motivated behavior: attention and conditioning. Dev Cogn Neurosci 1: 377-89.

Homework: Required reading for the upcoming week on "Eating Disorders".

Optional homework: A rough draft of the term paper, due March 30

Week 9. March 30. Eating disorders – a mental illness with its first onset dominated by adolescent females.

Required Readings: Papers by Aoki

- C Aoki, G Wable TG Chowdhury, NA Sabaliauskas, K Laurino and NC Barbarich-Marsteller (2014). Neuroscience 265: 108-123.
- TG Chowdhury, MB Rios, TE Chan, DS Cassataro, NC Barbarich-Marsteller, C Aoki (2014) Activity-based anorexia during adolescence disrupts normal development of the CA1 pyramidal cells in the ventral hippocampus of female rats. Hippocampus 24: 1421-29.

Homework: Required reading for the upcoming week's discussion on "Neurogenesis During Adolescence"

Week 10. April 6. Hippocampal Neurogenesis During Adolescence.

Required Reading: Papers by Tracy Shors

- N Toni and S Sultan (2011) Synapse formation on adult-born hippocampal neurons. European Journal of Neuroscience 33: 1062-68. (Review Article)
- DM Curlik, G DiFeo, TJ Shors (2014) Preparing for adulthood: thousands upon thousands of new cells are born in the hippocampus during puberty, and most survive with effortful learning. Frontiers in Neuroscience 8:70.

Homework: Required reading for the upcoming week's topic on "The Impact of Stress On The structure of Adolescent Brain".

Optional but strongly recommended homework: Improved draft of the term paper, due April 13.

Week 11. April 13. The Perfect Storm: The Impact of Stress On the Structure of Adolescent Brain

Required Reading:

- L Eiland, J Ramroop, MN Hill, J Manley, BS McEwen (2012) Chronic juvenile stress produces corticolimbic dendritic architectural remodeling and modulates emotional behavior in male and female rats. Psychoneuroendocrinology 37: 39-47.
- RD Romeo, SJ Lee, N Chhua, CR McPherson, BS McEwen (2004) Testosterone cannot activate an adult-like stress response in prepubertal male rats. Neuroendocrinology 79: 125-32.
- RD Romeo, SJ Lee, BS McEwen. (2004) Differential stress reactivity in intact and ovariectomized prepubertal and adult female rats. Neuroendocrinology 80: 387-393.
- MP Leussis and SL Andersen (2008) Is adolescence a sensitive period for depression? Behavioral and neuroanatomical findings from a social stress model. Synapse 62: 22-30.

Suggested Reviews:

- R Romeo (2010) Pubertal maturation and programming of hypothalamic-pituitary-adrenal reactivity. Frontiers in Neuroendocrinology 31: 232-240 (Review).

- RD Romeo and BS McEwen (2006) Stress and the adolescent brain. Annals of the New York Academy of Sciences 1094: 202-214. (Review)

Homework: Required reading for the upcoming week's discussion on "The Influence of Adolescence on Fear Memories"

Week 12. April 20 The Influence of Adolescence on Fear Memories and Anxiety

Required reading: Papers by Francis Lee

- SS Pattwell, KG Bath, BJ Casey, I Ninan, FS Lee (2011) Selective early-acquired fear memories undergo temporary suppression during adolescence. Proceedings of the National Academy of Sciences 108: 1182-87.
- SS Pattwell, S Duhoux, CA Hartley, DC Johnson, D Jing, MD Elliott, EJ Ruberry, A Powers, N Mehta, RR Yang, F Soliman, CE Glatt, BJ Casey I. Ninan, FS Lee (2012) Altered fear learning across development in both mouse and human. Proceedings of the National Academy of Sciences. 109: 16318-323.
- J McCallum, J H Kim, R Richardson (2010) Impaired extinction retention in adolescent rats: effects of D-cycloserine. Neuropsychopharmacology 35: 2134-42.

Recommended reading:

- BJ Casey and FS Lee (2015) Optimizing treatments for anxiety by age and genetics. Annals of the New York Academy of Sciences. 1345: 16-24.

Week 13. April 27. Student Presentations of Term Paper Topics (12 minutes + 3 min for discussion maximum per student)

Week 14. May 4. Student Presentations of Term Paper Topics (12 minutes + 3 min for discussion maximum perstudent)

Week 15. Term Paper Due May 17.