BIOGRAPHICAL SKETCH

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NAME: Yetnikoff, Leora

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Assistant Professor of Psychology, Doctoral faculty member in the PhD Program in Biology

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Concordia University	B.A.	05/2005	Psychology (Honors)
McGill University	M.Sc.	08/2007	Psychiatry
McGill University	Ph.D.	10/2011	Neuroscience
Saint Louis University School of Medicine	N/A	11/2011 – 11/2014	Neuroscience
Columbia University	N/A	11/2014 – 08/2016	Neuroscience

A. Personal Statement

My research goals are motivated by my interest in identifying the mechanisms underlying age-dependent emergence of dopamine-related psychopathology. These goals stem from the work I conducted as a graduate student with Dr. Cecilia Flores at McGill University, in which I examined whether netrin-1 guidance cues, proteins traditionally known for their involvement in the wiring of the dopamine system during development, play a role in the *reorganization* of this system by drugs of abuse. Using a combination of behavioral, molecular and pharmacological techniques, I investigated the role of the netrin-1 receptors in the enduring behavioral effects of stimulant drugs of abuse administered during adolescence and adulthood. These studies not only implicated netrin-1 receptor signaling in dopamine cell body regions as a critical mechanism in the cascade of glutamate-dependent cellular processes that lead to stimulant drug-induced plasticity, but also as a key factor in determining age-dependent individual differences in vulnerability to the behavioral effects of stimulant drugs. My graduate work resulted in several first-authored publications, each telling a unique and complete story. As a postdoctoral fellow in the lab of Dr. Daniel Scott Zahm at Saint Louis University School of Medicine, I examined whether the complement of inputs to midbrain dopamine neurons changes across the lifespan. Employing the use of retrograde tracers, I compared patterns of input to midbrain dopamine neurons in adolescent and adult rats and found that there is a delayed maturation of forebrain inputs to these neurons, with a particularly striking age effect in the nucleus accumbens. While fewer accumbens neurons project to dopamine neurons during adolescence, as compared to adulthood, anterograde-tracing studies revealed that accumbens neurons that *do* innervate dopamine neurons during adolescence have more varicosities (inferred synaptic connections) than in the adult. These findings suggest that dopamine neurons are influenced differently by accumbens neurons during adolescence and adulthood, wherein there is a less fine-grained capacity for accumbens modulation of dopamine neuron activity in adolescence. This work resulted in several publications, including two first-authored publications and a first-authored comprehensive review of dopamine circuitry organization. During my second postdoctoral fellowship, working with Dr. Stephen Rayport at Columbia University, I optimized and applied proximity ligation assay technology to visualize the morphological basis for dopamine neuron glutamate cotransmission, and how it correlates with optogenetic measures of functional connectivity. This work is nearing completion and will soon be prepared for publication(s). I am currently initiating my independent line of research investigating the development and plasticity of dopamine circuitry and function that builds logically on all my prior work and expertise.

B. Positions and Honors

Positions and Employment

2015-2016 Adjunct Assistant Professor, Department of Biology, Barnard College, New York, NY
2016- Assistant Professor, Department of Psychology, College of Staten Island, New York, NY
2017- Doctoral faculty, PhD Program in Biology, CUNY Graduate School, New York, NY

Other Experience and Professional Memberships

2006 - Member, Society for Neuroscience

2010 - *Ad hoc* reviews of original research for publication in the peer-review journals *Journal of Comparative Neurology, Journal of Neuroscience, Neuropsychopharmacology, Neuroscience,* and *Pharmacology, Biochemistry and Behavior.*

Honors and Graduate Research Support

2004 Canadian Psychological Association Award of Excellence for Best Undergraduate Thesis.

2004 Undergraduate Student Research Award, awarded by the Natural Science and Engineering Research Council of Canada (NSERC – competitive, federal award).

2005 J.W. Bridges Medal for Psychology, awarded by Concordia University.

2005 Recruitment Excellence Fellowship, awarded by the Psychiatry Department, McGill University

2005-2006 Masters Canada Graduate Scholarship, awarded by NSERC (competitive, federal award).

2005-2007 Masters fellowship, awarded by the Fonds de recherche du Québec – Nature et Technologies (FQRNT – competitive, provincial award).

2007 Recruitment Excellence Fellowship, awarded by McGill University

2007-2010 Doctoral fellowship, awarded by FQRNT (competitive, provincial award).

2008-2011 The Alexander Graham Bell Doctoral Canada Graduate Scholarship, awarded by NSERC (competitive, federal award).

2008 Nominated the most outstanding candidate at the Doctoral level by the Life Sciences and Psychology Scholarships and Fellowships Selection Committee (NSERC).

2008 Nominated for the Andre Hamer (D) Postgraduate Prize (NSERC).

2008 McGill Principals Award, awarded by McGill University.

2010 Leyton Addiction Research Prize, awarded for the best addiction-related research paper by McGill University (Yetnikoff et al., 2010. Netrin-1 receptor in the ventral tegmental area is required for sensitization to amphetamine. *European Journal of Neuroscience*, 31, 1292-1302).

2010 Canada Graduate Scholarship Michael Smith Foreign Study Supplement, awarded by NSERC to pursue a research experience at a research institution abroad. The award was held at Université Pierre et Marie Curie in Paris, France, with the group of Dr. Bruno Giros (competitive, federal award).

2012 Leyton Addiction Research Prize, awarded for the best addiction-related research paper by McGill University (Yetnikoff et al., 2011. Abolition of the behavioral phenotype of adult netrin-1 receptor deficient mice by exposure to amphetamine during the juvenile period. *Psychopharmacology*, 217, 505-514).

2013 Leyton Addiction Research Prize, awarded for the best addiction-related research paper (Yetnikoff et al., 2014. Adolescence: a time of transition for the phenotype of *dcc* heterozygous mice. *Psychopharmacology*, 231: 1705-1714).

C. Contributions to Science

1. Should adolescents be held criminally responsible for illegal behavior? In attending to this question loaded with practical, societal and moral ramifications, the judicial system has increasingly come to rely on developmental neuroscience research (Steinberg 2013, *Nat Neurosci Rev*, 14: 513 - 518). That adolescents are prone to impulsive and risky behaviors has long been recognized. However, only recently has it begun to be understood that the adolescent brain is structurally and functionally different from the adult brain, with changes in connectivity and myelination occurring throughout early adulthood. While precise mechanisms that underlie the uniquely vulnerable nature of adolescence are not known, the responsible maturational processes are thought to reside, at least in part, in specific neural circuits that affect dopamine system function. By providing novel perspectives on the development and plasticity of the dopamine system, my research contributes to the influence of neuroscience research on social policy and decision-making. In one line of work, I have shown there is a protracted maturation of inputs to midbrain dopamine neurons. These findings suggest that dopamine neurons are influenced differently by inputs during adolescence and adulthood and have important implications for understanding age-related variability in the function of the dopamine system. In a related project, I examined the long-lasting consequences of exposing the developing brain to stimulant drugs such as amphetamine and methylphenidate.

    a. **Yetnikoff L**, & Arvanitogiannis A (2013). Differential sensitivity to the acute and sensitizing behavioral effects of methylphenidate as a function of strain in adolescent and young adult rats. *Behavioral and Brain Functions*, 9: 38 (cited by 6, as of 01/15/2017).
    b. **Yetnikoff L**, Reichard RA, Schwartz ZM, Parsely KP, & Zahm DS (2014). Protracted maturation of forebrain afferent connections of the ventral tegmental area in the rat. *Journal of Comparative Neurology*, 522: 1031-1047 (cited by 15, as of 01/15/2017).
    c. **Yetnikoff L**, Lavezzi HN, Reichard RA, & Zahm DS (2014). An update on the connections of the ventral mesencephalic dopaminergic complex. Invited Review for a Special Issue of Neuroscience: The ventral tegmentum and dopamine systems: a new wave of diversity. *Neuroscience*, 282C: 23-48 (cited by 55, as of 01/15/2017).
    d. **Yetnikoff L**, Parsely KP, & Zahm DS (November 2014). Reorganization of the axon terminations of accumbens neurons projecting to the ventral tegmental area between adolescence and adulthood. *Society for Neuroscience Abstracts*, Washington, DC (manuscript currently in preparation).

2. In a second line of work, I investigated whether netrin-1 guidance cues, proteins typically known for their involvement in the wiring of the dopamine system during development, play a role in the plasticity of this system. Not only did my research identify netrin-1 receptor signaling in the dopamine cell body region as a novel mechanism in the series of cellular processes that lead to enduring plasticity by stimulant drugs, but also as a key factor in determining age-dependent individual differences in vulnerability to the behavioral effects of stimulant drugs. Because netrin-1 receptor heterozygosity exists in the human population, these findings hold important ramifications for the sanctioned or unsanctioned use of stimulant drugs by adolescents.

    a. **Yetnikoff L**, Labelle-Dumais C, & Flores C (2007). Regulation of netrin-1 receptors by amphetamine in the adult brain. *Neuroscience*, 150, 764-773 (cited by 29, as of 01/15/2017).
    b. **Yetnikoff L**, Eng C, Benning S, & Flores C (2010). Netrin-1 receptor in the ventral tegmental area is required for sensitization to amphetamine. *European Journal of Neuroscience*, 31, 1292-1302 (cited by 20, as of 01/15/2017).
    c. **Yetnikoff L**, Almey A, Arvanitogiannis A, & Flores, C (2011). Abolition of the behavioral phenotype of adult netrin-1 receptor deficient mice by exposure to amphetamine during the juvenile period. *Psychopharmacology*, 217, 505-514 (cited by 11, as of 01/15/2017).
    d. **Yetnikoff L**, Pokinko M, Arvanitogiannis A, & Flores C (2014). Adolescence: a time of transition for the phenotype of dcc heterozygous mice. *Psychopharmacology*, 231: 1705-1714 (cited by 5, as of 01/15/2017).

3. Other significant contributions I have made include identifying patterns of basal forebrain neuroanatomical organization and conceptualizing them into a neural systems context, with the aim of evaluating whether and how such forebrain systems may contribute to behavioral synthesis. In one key project, I directly compared inputs to the inhibitory rostromedial tegmental nucleus (RMTg), which strongly innervates midbrain dopamine neurons in the ventral midbrain, with the inputs the ventral tegmental area (VTA), a cell body region of midbrain dopamine neurons, as well as to inputs to the lateral habenula, a forebrain region that exerts profound inhibitory control on midbrain dopamine neurons via its excitatory inputs to the RMTg. Early reports indicated that inputs to the RMTg, excepting its very strong inputs from the lateral habenula, do not differ appreciably from those of the VTA. Presumably, however, the RMTg contributes more to behavioral synthesis than to simply invert the valence of the excitatory signal coming from the lateral habenula. Contrary to early reports, my work indicated that, while the inputs to the RMTg, VTA, and lateral habenula do originate within the same large pool of central nervous system structures, each is also related to structures that project more strongly to it than to the others. This work provides important insights into the organization of the circuitry of this important triad of structures (RMTg-VTA-lateral habenula), with one of the many functional implications of the study – the modulation of activity in the dopamine pathway – being of utmost importance to adaptive and addictive behavior. Additional contributions included the examination of the underlying mechanisms for the roles of the preoptic area and ventral pallidum in the generation of ambulatory activity, as well as a review article on the heterogeneity of dopamine synaptic connections in the striatum, just published in *Biological Psychiatry*.

    a. Zahm DS, Schwartz ZM, Lavezzi HN, **Yetnikoff L**, & Parsley KP (2014). Comparison of the locomotor-activating effects of bicuculline infusions into the preoptic area and ventral pallidum. *Brain Structure and Function*, 219: 511-526 (cited by 8, as of 01/15/2017).
    b. **Yetnikoff L**, Cheng A, Lavezzi HN, Parsely KP, & Zahm DS (2015). Sources of input to the rostromedial tegmental nucleus, ventral tegmental area and lateral habenula compared: a study in rat. *Journal of Comparative Neurology*, 523: 2426-2456 (cited by 10, as of 01/15/2017).
    c. Chuhma N, Mingote S, Kalmbach A, **Yetnikoff L**, & Rayport S (2017). Heterogeneity in dopamine neuron synaptic connections across the striatum and its relevance for schizophrenia. *Biological Psychiatry* 81: 43-51 (cited by 1, as of 01/15/2017).

D. Additional Information: Research Support and/or Scholastic Performance

<u>Completed Postdoctoral Research Support</u>

2011-2013 Postdoctoral fellowship, awarded by FQRNT (competitive, provincial award).

2013-2016 Postdoctoral fellowship, awarded by Fonds de recherche du Québec – Santé (FRSQ; competitive, provincial award).