

Aug. 9, 2016

Paul Sands

The Behavioral Pharmacology of Cocaine Self-Administration

For eight weeks this summer I lived in upper Manhattan and worked as a research assistant to post-doctoral fellow Dr. Erin Calipari. Dr. Calipari is a research fellow in the lab of Dr. Eric Nestler, whose lab focuses on researching the Neurobiology of Molecular Psychiatry within the Fishberg Department of Neuroscience at Mount Sinai School of Medicine. Dr. Nestler's lab consists of nine post-doctoral fellows, five graduate students, two lab managers/assistants, and a bioinformatics team that work on projects ranging from the neuroepigenetics of depressive behaviors in mice and rat models, to the bioanalytic chemical analyses of neurotransmitter release and kinetics in response to drug self-administration (SA) in rats, to the expression and regulation of microRNA fragments in various psychiatric disorders. I worked with Dr. Calipari on one major project regarding the neurobiology and psychopharmacology of cocaine SA in animals, in addition to collaborating with other lab members and faculty of the neuroscience department on many separate projects.

My project with Dr. Calipari was focused on discerning the differential behavioral pharmacologic effects of cocaine SA in male animals and female animals in estrus (high ovarian hormone circulation) or diestrus (low circulation). Dr. Calipari had collected behavioral economic data of the animals in which she ran the SA paradigm, and my project was to correlate the preliminary behavioral data with immunocytochemical images of cortical sections of each animal studied. In addition to staining cortical slices, I aided in the daily tasks of the lab, whether that be surgerizing rats or mice for viral injections, cannula implantations, and tissue

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dissection for collaborative projects within the lab team; attending seminar series, laboratory meetings, bioinformatic meetings, and job talks by various students and faculty of the neuroscience department; or helping to perform biochemical experiments for fellow lab members.

To speak more on the main project on which I worked, I performed immunocytochemical staining of cortical slices from animals that completed a cocaine SA paradigm in order to visualize and quantify the differential expression of the immediate early gene c-FOS. I focused on imaging the Medial Dorsal and Medial Lateral Striatum, Nucleus Accumbens (NAc) shell and core, and the Pre- and Infralimbic cortices. The images I collected offered a visual of the differential expression of c-FOS in the various brain regions as well as supplied a template on which quantitative data could be collected: using imaging software, I quantified the differential expression of c-FOS in the selected cortical areas and correlated the data to images for each animal. Dr. Calipari and I hypothesized that female animals in estrus, which demonstrate increased responses to cocaine in the SA procedure, would demonstrate a correlated increase in c-FOS expression compared to other groups. The results of the imaging and data analysis showed an increased expression of c-FOS in the NAc and Striatum regions, but not prefrontal regions, of female animals in estrus compared to females in diestrus and males, which was in line with our hypothesis.

After this data was collected, I was tasked with correlating the c-FOS images and graphs with behavioral economic data collected from the animals during the cocaine SA paradigm. Behavioral economics is an analytical science that describes the allocation of effort in drug SA experiments; this informs on behavioral aspects such as drug craving vs. seeking, the rate at

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which drug intake diminishes, the basal brain-levels of drug intake, and other behavioral variables. The behavioral economic data revealed that female animals in estrus administer more cocaine, demonstrate higher baseline brain-drug levels, and demonstrate a three-fold increase in the rate at which cocaine binds its primary molecular target, the dopamine transporter (DAT). These behavioral economic analyses were in line with the hypotheses and data collected from the biochemical analysis. Thus, together with the c-FOS data, the behavioral economic analysis proved to be substantial information to include in a manuscript for publication.

As a whole, the internship allowed me to develop skills in neuroscientific research that includes learning approaches to data analysis and experimental design; performing staining, imaging, and biochemical techniques; surgicizing animals and running behavioral experiments; and writing a manuscript for publication on the research conducted. In addition to the technical skills which I developed, I also gained interpersonal skills through interacting with numerous members of the neuroscience community at seminars and talks, in addition to collaborating with researchers in a professional laboratory setting that will enable me to be able to act as a positive and successful member of a research team in the future. Working every day in upper Manhattan gave me a preview of the schedule I would adopt as a graduate student, balancing research with seminars, talks, and classes in the context of a large research hospital and excellent medical school. I learned how to work autonomously and how to collaborate on multiple projects at the same time, the experience of which will help me compartmentalize and balance my lectures, work study, and other interests as a regular undergraduate at Sewanee.

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Reflecting on the whole, this internship allowed me to gain invaluable experience as a neuroscience researcher, yet also helped me solidify my decision to pursue neuroscience graduate programs that focus on the neurobiology of addiction.