particular dopamine projection pathway terminates in several areas of the frontal and prefrontal cortical areas, which subserve higher-order cognitive functions such as impulse control, rationalization, attention, emotional reactions, working memory, etc. (i.e., the executive functions). The extensive literature in this field suggests that prenatal psychostimulant exposures might disrupt dopamine signaling during critical windows of development resulting in lasting neural deficits. However, the literature in this field also suggests that the resulting anatomical and behavioral alterations would be subtle necessitating specialized techniques to uncover them. The 5CSRTT uses a complex operant learning paradigm to train mice to engage in particular responses to particular stimuli. A mouse must learn to respond (nose poke) to a laminated hole in the cage. A correct response produces a food reward. An incorrect response results in positive punishment (i.e., house lights are turned on). Training progresses as criteria for correct responses are met with incremental time to respond demands placed on the animal (i.e., an increased cognitive and attentional burden). The 5CSRTT ensues after the completion of training whereby the time between the end of one trail and beginning of another is pseudo-randomly set. The analysis of particular types of response errors during this task provides information about numerous cognitive constructs (i.e., executive functions). For example, impulsivity, and, therefore, frontal brain functioning, is assessed from premature responses (i.e, the animal's inability to wait for the stimulus presentation before responding). Perseverative errors (i.e., repeating the same error over and over) provides information about category shifting, etc., which is also indicative of frontal brain functioning. Analysis of adult animals, which received prenatal drug exposures, provides valuable information about the long-lasting, teratogenic effects of the drug on particular dopaminergic circuitry. We will investigate the effects of several psychostimulants, which are also suspected teratogens, using this paradigm including METH, MPD, and AMP. Including female mice in our analysis provides additional, much needed information to the literature, which has been explicitly requested by the National Institute for Drug Addiction.

2. Analysis of behavioral sensitization after adolescent psychostimulant exposures.

Hallmarks of addiction stemming from neural plasticity, include tolerance and sensitization. Both are indicative of an altered neural circuitry induced by drugs. Tolerance refers to a decreased response over time to the same dose of a drug. An example of tolerance is the lessened euphoric effect of a drug over time and can be thought of in

terms of changes in the reward circuits of the brain. Sensitization refers to an increased response over time to the same dose of a drug. An example of sensitization commonly occurring with psychostimulant abuse is behavioral or locomotor sensitization, which is observed as hyperactivity and increased exploratory and stereotyped (repetitive, purposeless) behaviors. Behavioral sensitization results from plasticity in the dopaminergic nigrostriatal pathway induced by the psychostimulants. Hyperactivity, stereotypy and exploratory behaviors (e.g., thigmotaxis, rearing, etc.) will be assessed using an Open Field Activity Chamber. The OFC is a cage with gridded photobeams. As an animal moves through the chamber, beam breaks are recorded as a measure of the amount and pattern of the animal's activity. Therefore, increased activity after subsequent drug exposures is indicative of both neural plasticity and addiction.

Although it is well understood that psychostimulants can produce sensitization in adult animals, it is unclear whether adolescent exposure produces the same effect. Importantly, we will use both low (therapeutic) and high (abuse) doses of prescription ADHD drugs on adolescent mice without ADHD in order to model the current social problems of misdiagnosis, over prescription and abuse of Ritalin and Adderall among adolescents. In addition, we will perform similar studies using METH and cocaine (COC), which are commonly abused in adolescent populations. Mice will receive adolescent exposures to saline, MPD (high or low dose), AMP (high or low dose), COC, or METH and a challenge dose with METH or saline once aged to adulthood (3 months of age). Activity measurements after the challenge will allow for an analysis of long-lasting cross-sensitization. Cross-sensitization refers to behavioral sensitization induced by one drug and demonstrated to other drugs with similar mechanisms of action in the CNS. We wish to find out whether adolescent prescription drug exposures induce a heightened response to a much harder drug even after a significant time of abstinence. In other words, does this adolescent exposure induce a long-lasting gateway effect to much more addictive and dangerous, but similarly acting, drugs like METH? Including female mice in our analysis provides additional, much

Our lab uses a “see one, do one, teach one” approach to student development. Students new to the lab begin their involvement as helpers (see one) on their way to developing the skills they need (do one) which is facilitated by more seasoned students (teach one). These student leaders practice high-level science while developing leadership skills in the lab through personnel and project management. The projects detailed above will involve 6 student leaders in the Fall semester, each responsible for their own project. Furthermore, other students have chosen to pursue scientific evaluation of novel labs they have developed and run in the classroom using the knowledge and skill sets developed while working on these behavioral studies. These educational research projects have been planned for both the fall and spring semesters and will offer invaluable teaching experience for our students interested in education while enhancing the overall academic experience at NGCSU. Additional student leaders will carry on these projects in the Spring. Student leaders must submit detailed project proposals before they begin their work that include an extensive literature review(n)-1(0a)-7(a)-2(dea)-13(n)-1(topr)-6

The model of science and student development described above has been extremely successful in the past. Last year our students received 3 Psi Chi Regional Research Awards at the SEPA conference, 3 Best Presentation Awards at the Georgia Academy of Sciences conference, and a second place finish at the NARC poster session. In addition, two of our students were selected to present at the CUR-sponsored Posters on the Hill event in Washington, DC. We expect our students to accumulate similar accolades this year in recognition of their hard work and scientific achievements. However, it is critical to note that these students would not have had the opportunities described above without the financial support of CURCA. I hope you see that the CUCRA money received went to good use.

III. Budget and Projected Timeline

Timeline:

As described above, all student leaders submit their own, individual project proposal complete with a project timeline. We work closely with the students to ensure that their project and the product it produces are completed within a given semester. Of course the larger projects continue indefinitely and the student often stay in the lab working on them for subsequent semesters. For most projects the student begin by generating the animals they need for their experimentation, then engage in their manipulation (drug exposures) followed by a behavioral assay, analysis and a formal write-up for presentation. Each step is carefully planned with the student leader to avoid other time conflicts (school, holiday, work, etc.) and to be completed within a given semester.

Budget:

The expansion of student participation and research capabilities necessitates that we obtain external funding support. However, continued research until that funding is obtained will serve to enhance our ability to do so. We have included the following budget to conduct this research over the next academic year.

Category	Description	Project	Price	Total
Mice	*Per diem for 9 months (food, bedding, caging, supplies, and animal facility maintenance fees)	**1:~50 2:~100 3:~30	3.82 per diem (9 months)	1031.40
Syringes	All studies require daily injections.	1-3	134.91 (case)	539.64
Gloves	Animal handling is a component of all projects.	1-3	126.08 (case)	756.48
Drugs	***METH, AMP, MPD, CO + processing, shipping and licensing fees.	1-3	832.29	832.29

Day 22-31 and again at 3 months of age). Adult exposures require 10 days of injections.

Additional Equipment/Supplies needed, but already obtained by Drs. Lloyd and Shanks:

1. 5-Hole Operant Chamber, Med Associates Behavioral Analysis Software and Computer Interface purchased from an NGCSU Student Technologies Fees grant awarded to Drs. Lloyd, Shanks, and Robertson.
2. Open Field Activity Chambers (2), Kinder Scientific Behavioral Analysis Software and Computer Interface obtained from a Faculty for Undergraduate Neuroscience Equipment Loan grant awarded to Drs. Lloyd and Shanks.
3. Project 3 (not described in detail above): HD Camera, video editing software, and laptop computers awarded via several NGCSU Leaders in Information Technology Program grants awarded to Drs. Lloyd and Shanks.

4. Dr. Lloyd maintains current Schedule II, II-N, and III licenses through the GA Board of Pharmacy and the Drug Enforcement Agency.