# A Vodcasted, Cross-Disciplinary, Behavioral Neuroscience Laboratory Exercise Investigating the Effects of Methamphetamine on Aggression

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**Abstract:** This article describes a laboratory experience utilizing videos to engage students in hypothesis-driven experimentation in behavioral neuroscience. It provides students with an opportunity to investigate the effects of chronic methamphetamine exposure on aggression in adult mice using a resident-intruder paradigm. Instructors and students only need Internet access to run this lab, which makes it accessible to most institutions, regardless of their facilities or resources necessary to conduct behavioral neuropsychopharmacology experiments. The laboratory experience described here provides instruction and hands-on experience with: 1) developing hypotheses and methodology to test these hypotheses; 2) operationalizing constructs and developing behavioral coding criteria; 3) collecting, analyzing, interpreting, and graphically displaying primary, behavioral data; and 4) working with complex, interdisciplinary ideas. Students who engaged in this laboratory experience demonstrated self-reported learning gains in course-specific outcomes, general and conceptual science learning, and the use of animal models in scientific experimentation.

***Key words**:* laboratory exercise; behavioral neuroscience; animal models; methamphetamine; aggression; vodcast

## INTRODUCTION

There is a recent trend in science education of teaching by engaging students in the process of science and scientific discovery (AAAS, 1990; Handelsman, et al., 2004; AAC&U, 2007). Undergraduate engagement in research, whether through traditional independent research experiences or through its integration into the undergraduate curriculum, is associated with positive student outcomes related to learning, retention, graduation and post-graduate accomplishments, particularly for underrepresented populations (Nagda et al., 1998; Alexander et al., 2000; Foertsche et al., 2000; Seymour et al., 2000; Ishiyama, 2001; Ishiyama & Hopkins, 2001; Ishiyama, 2002; Bauer & Bennet, 2003; Lopatto, 2004; Summers & Hrabowski, 2006; Lopatto, 2007; Ramos Goyette et al., 2007; Brame et al., 2008; Gehring & Eastman, 2008; Miller, 2009; Wu, 2009). Despite their pedagogical benefits, smaller institutions with limited facilities and resources often face challenges in the implementation of research programs and/or the implementation of these experiences into the curriculum (Grisham et al., 2003). The effective use of technology, such as podcasting or vodcasting (i.e., video podcasting), may be able to help bridge this gap.

The laboratory exercise described below involves the use of a behavioral assay to measure aggression using an animal model of drug abuse in the context of several important and controversial issues described herein. Since all laboratory materials are delivered online, there are no special facilities needed to conduct this laboratory, which also makes this a highly efficient laboratory exercise.

### Vodcasting in Education

Vodcasting is a video form of podcasting. Podcasting is a form of downloadable audio files compatible with MP3 players, which is associated with numerous positive learning outcomes (Evans, 2008; Hew, 2009; McKinney et al., 2009; Lloyd & Robertson, *in press*) and has been used for many years by colleges and universities (Hammersley, 2004; Donnelly & Berge, 2006). The newer, enhanced forms of vodcasting provide expanded media options for delivering course content (i.e., the addition of video), which have created a new form of portable learning (Donnelly & Berge, 2006). Unfortunately, there is a large gap between teaching practices and learning theory, which is obviated when the research involves technological innovations for college students (Fernandez et al., 2009; Hew, 2009).

### Development of the Laboratory Exercise

In order to address the need for novel, practical, accessible, and interdisciplinary undergraduate neuroscience laboratories, we developed a behavioral neuroscience laboratory sequence utilizing downloadable video files. Although widely accepted to be an effective pedagological tool, interdisciplinary instruction is not usually a component of undergraduate introductory biology courses. In addition, hands-on neuroscience learning opportunities also tend to be underrepresented in the typical undergraduate biology curriculum (Grisham et al., 2003). Since early exposure and hands-on engagement are key to the development of student interest, we created this interdisciplinary exercise specifically for freshman biology students. Self-report pretest/posttest data described below support the use of this novel laboratory. This vodcasted lab sequence demonstrates the effects of chronic methamphetamine exposure on aggression in the male mouse using a resident-intruder paradigm. The video files we created for this exercise are included as supplemental materials so there is no need for animal housing facilities and scheduled drug licenses to run these labs. We have provided additional supplemental materials including an extensive background (i.e., a review of the literature and novel, primary research data from our lab (see figures in the prelab handout)) and directed student exercises to accompany the video files. Therefore, it is possible for instructors to recreate the same lab experience using only a computer. All supplemental materials are available at: www.northgeorgia.edu/Bioscene.

**Background to the Laboratory Exercise**

*Methamphetamine and the hypothalamic-pituitary axis*

Methamphetamine (METH) is a potent indirect agonist for dopamine (DA), which is associated with oxidative stress, neuroinflammation, neural plasticity and neurodegeneration in the commonly studied DAergic mesocorticolimbic and nigrostriatal pathways (Krasnova & Cadet, 1999). However, the effect of METH on the DAergic tuberinfundibular (TI) pathway is not clear. The TI pathway originates in the arcuate nucleus of the hypothalamus and terminates in the median eminence. The DA released from TI neurons is transported via long portal vessels to the lactotrophs of the anterior lobe of the pituitary gland where it inhibits the release of the hormone prolactin (Ben-Jonathan & Hnasko, 2001), which has numerous organizational and developmental effects on a wide variety of tissues and organs (Hair et al., 2002). In addition to its traditionally recognized role in lactation, prolactin is also a gonadotrophin regulator (Bartke, 1971) that stimulates testicular steroidogenesis (Takase et al., 1990) and spermatogenesis (Hair et al., 2002). The disruption of hypothalamic DA, pituitary DA receptors, or prolactin homeostasis is associated with reproductive disorders and dysfunction (Ben-Jonathan & Hnasko, 2001; Durham et al., 1996; Lucas et al., 1998; Steger et al., 1998; Thomas, Phelps, & Robinson; 1999). A large body of literature demonstrates the potential for pharmacological treatments to affect this HPA-axis pathway. For example, TIDA activity is altered by selective DA agonists (Demaria et al., 2000; Durham et al., 1998; Martignoni et al., 1996), antipsychotics (Dickson & Glazer, 1999; Peabody et al., 1992), antidepressants (Van de Kar, Rittenhouse, Li, & Levy, 1996), analgesics (Bero & Kuhn, 1987; Kreek et al., 1999), atypical neuroleptics (Kapur et al., 2002), and transgenic manipulation of DA function (Ben-Jonathan & Hnasko, 2001; Bosse et al., 1997; Demaria et al., 2000). In relation to stimulant drugs of abuse, cocaine decreases prolactin mRNA in the pituitary, while amphetamines have a direct effect on testicular testosterone production (Tsai et al., 1997; DeMaria et al., 2000).

*Methamphetamine and aggression*

A number of studies link free and total testosterone, prolactin alterations, and disrupted neuroendocrine responses with normal and abnormal aggressive behaviors and traits (Dabbs & Morris, 1990; Dabbs et al., 1995; Banks & Dabbs, 1996; Stalenheim et al., 1998; Wingrove et al., 1999). Although testosterone influences aggression levels in humans and animals (Pope et al., 2000; Kawai et al., 2003; Grgurevic et al., 2008), the exact nature of this relationship is controversial. For example, Mazur & Booth (1998) suggest that testosterone can be both a cause and an effect of aggressive behavior, while a meta-analysis conducted by Book *et al.* (2001) shows a weak positive correlation between testosterone and aggression ($r$=0.14) with a number of potential moderators and third variable explanations. METH abuse in humans is positively correlated with violence, impulsivity, and brain activity indicative of pathological aggression as well as disruptions in social cognitions and interactions, which are further risk factors for aggression (Homer et al., 2008). Furthermore, chronic intermittent METH exposure in mice increases the probability of and decreases the latency to attack an intruder and results in alterations in other forms of social interactions (Sokolov et al., 2004). Our lab has observed significant increases in testicular weight and increased serum testosterone levels in C57Bl/6J mice following chronic methamphetamine exposure (see supplemental material at www.northgeorgia.edu/Bioscene). The DAergic neurotoxicity caused by METH exposure could cause an increase in prolactin release, downstream increased testosterone, and subsequent increases in aggressive behavior.

## METHODS

All materials needed to run the novel laboratory described below can be obtained from the following secure, permanent, university-supported link: www.northgeorgia.edu/Bioscene. We created the following materials for this lab: 1) sixteen vodcasts created from videos demonstrating mouse-mouse interactions in a resident-intruder model of aggression; 2) a prelab handout introducing background information; and 3) a set of assignments related to this laboratory.

**Laboratory Sequences**

The novel laboratory presented here was designed to instruct students towards several general learning outcomes, which included experimental design and methodology, statistical analyses and interpretation, and graphical data presentation. The students participated in a sequence of cross-disciplinary (psychology and biology) laboratory experiences involving hypothesis-driven experimentation at a level appropriate for freshman biology students. The laboratory experience was conducted as follows. In week 1, the students engaged in animal care and use training and were introduced to both the use of animal models in neuroscience research and the behavioral research experience to follow. In weeks 2 and 3, the students learned about and developed behavioral coding criteria and additional research hypotheses focused on the effects of chronic METH exposure on aggression. Small, collaborative groups of students were tasked with downloading, viewing, and coding a subset of predetermined vodcasts of resident-intruder interactions. The students were blinded to the experimental condition and coded the files according to the criteria previously established. In week 4, the students learned about and performed statistical analysis and graphical data presentation of the pooled data collected in week 3.

**Vodcasting and the Resident-Intruder Paradigm**

All animal procedures were performed in compliance with the *Guide for the Care and Use of Laboratory Animals* (Clarke et al., 1996). Adult (3-4 months) male C57Bl/6J mice were injected daily with an i.p. dose of 5mg/kg methamphetamine HCl (n = 7; Sigma-Aldrich, St. Louis, MO) in a 2mg/ml solution or an equal volume of sterile saline (n = 9) for 10 days. These animals were singly housed in standard conditions (shoebox cage; 12hr light/dark cycle; *ad libitum* food and water) in order to establish a territorial home cage (resident animals). Five hours after the last dose, one age and weight matched adult male C57Bl/6J mouse (intruder animals; n = 16) was systematically introduced into each of the resident's cages (Olivier and Young, 2002). The resident-intruder interactions were digitally recorded for 10 minutes (Table 1). Behavioral coding of aggressive behaviors were performed off-line by two independent raters ($\alpha = .97$) blinded to the experimental condition. The following indices of aggression were measured: the latency to first attack; the duration of attacks; and the total number of attacks (Demas et al., 1999; Sokolov et al., 2004). Aggressive behaviors were operationally defined to include: tail rattling, pawing or boxing, chasing, upright posture to gain dominance, persistent non-genital/investigatory sniffing and the coding of

**Table 1**. Video file descriptions and key.

| Video File ID | Treatment | Time to First Attack (sec) | Total Duration of Attacks (sec) | Total Number of Attacks |
|---|---|---|---|---|
| C1-1 | METH | 600 | 0 | 0 |
| C1-2 | METH | 450 | 21 | 9 |
| C1-3 | Saline | 600 | 0 | 0 |
| C1-4 | Saline | 600 | 0 | 0 |
| C2-1 | METH | 600 | 0 | 0 |
| C2-2 | METH | 403 | 21 | 10 |
| C2-3d2 | Saline | 375 | 6 | 4 |
| C2-4 | Saline | 600 | 0 | 0 |
| C3-1b | METH | 533 | 2 | 1 |
| C3-2d1 | Saline | 460 | 3 | 2 |
| C3-2d2 | Saline | 364 | 3 | 2 |
| C3-3d1 | METH | 600 | 0 | 0 |
| C3-3d2 | METH | 231 | 13 | 5 |
| C3-4d1 | Saline | 600 | 0 | 0 |
| C3-4d2 | Saline | 470 | 4 | 3 |
| C3-5 | Saline | 600 | 0 | 0 |

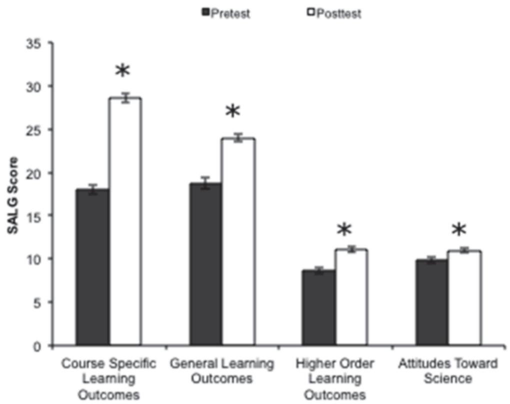


**Fig. 1**. Pretest and posttest SALG construct scores. The novel laboratory experience produced larger self-reported gains in all areas. * $p < .05$

separate attacks required a two second or longer break in fighting (de Boer et al., 1999). The resident-intruder video files were optimized and compressed using iSquint (v1.5.2; Techspansion; http://www.isquint.org), uploaded and served on a University System podcast server, and made available to students through a one-click subscription via a HTML link posted in their course management system webpage.

## RESULTS

The impact of the novel laboratory experience was assessed using a modified version of the Student Assessment of their Learning Gains questionnaire (SALG; www.salgsite.org) using a one group, pretest/posttest design. The 19-item questionnaire assessed self-reported learning across four constructs using a 5-point Likert-type response format (see Table 2). All statistical analyses were performed using PAWS Statistics (v18; IBM SPSS; Somers, NY). Students who engaged in the novel laboratory exercise reported higher values on the posttest compared to their baseline responses for questions related to: course-specific learning outcomes, $t(105) = 14.18$, $p < .001$; general learning outcomes, $t(105) = 6.70$, $p < .001$; higher-order learning outcomes, $t(104) = 4.86$, $p < .001$; and attitudes toward science, $t(105) = 2.47$, $p = .015$ (Figure 1). Summary responses to individual items are listed in Table 2. Since the SALG is a self-report questionnaire, the analyses that follow represent what the student thought they learned from this experience.

## DISCUSSION

Our results suggest that hypothesis-driven experimentation of a scientific and socially relevant topic led to a higher order understanding of the

**Table 2**. Summary of SALG scores by test.

| | Mean (SEM) | |
|---|---|---|
| SALG Question by Construct Assessed | Pretest (n=53) | Posttest (n=54) |
| **Course-Specific Learning Outcomes** | | |
| 1. I have an understanding of how interdisciplinary research provides insight into scientific questions. | 2.91 (0.15) | 3.85 (0.10) |
| 2. I have an understanding of how a hypothesis is tested in an experimental design. | 4.08 (0.10) | 4.59 (0.09) |
| 3. I have an understanding of the relevance of statistical significance in relation to experimental data. | 3.11 (0.15) | 4.13 (0.10) |
| 4. I have an understanding of how t-tests are used to analyze data. | 1.36 (0.11) | 4.04 (0.12) |
| 5. I have the ability to establish criteria to analyze behavioral differences in animals. | 1.92 (0.13) | 4.15 (0.10) |
| 6. I have the ability to accurately disseminate data graphically. | 2.17 (0.13) | 3.87 (0.12) |
| 7. I have the ability to write concise and informative figure legends. | 2.47 (0.14) | 3.93 (0.12) |
| **General Learning Outcomes** | | |
| 8. I am able to identify patterns in data collected from scientific experiments. | 3.30 (0.13) | 4.02 (0.10) |
| 9. I am able to gather quantitative data to answer questions about behavior. | 2.91 (0.15) | 4.13 (0.11) |
| 10. I am able to work effectively with others in an academic setting. | 4.38 (0.09) | 4.50 (0.10) |
| 11. I have confidence that I understand how to identify and quantify behavioral patterns, statistically analyze collected data, and disseminate the data in a figure suitable for publication. | 2.34 (0.16) | 3.70 (0.12) |
| 12. I have confidence that I can understand the realtionship between behavior and biological processes. | 3.06 (0.16) | 4.04 (0.12) |
| 13. I have the ability to work with complex interdisciplinary ideas. | 2.75 (0.15) | 3.59 (0.11) |
| **Attitudes Towards Science** | | |
| 14. I have enthusiasm for interdisciplinary subjects. | 3.57 (0.13) | 3.69 (0.12) |
| 15. I have interest in taking additional interdisciplinary classes | 3.13 (0.14) | 3.39 (0.14) |
| 16. I have a positive view of using animal models to answer scientific questions. | 3.15 (0.17) | 3.93 (0.13) |
| **Higher-Order Learning Outcomes** | | |
| 17. I am capable of using systematic reasoning in my approach to problems. | 3.06 (0.14) | 3.69 (0.13) |
| 18. I am capable of using a systematic approach to analyzing data. | 2.96 (0.13) | 3.72 (0.13) |
| 19. I am capable of using a multi-disciplinary approach to answer scientific questions. | 2.60 (0.14) | 3.72 (0.14) |

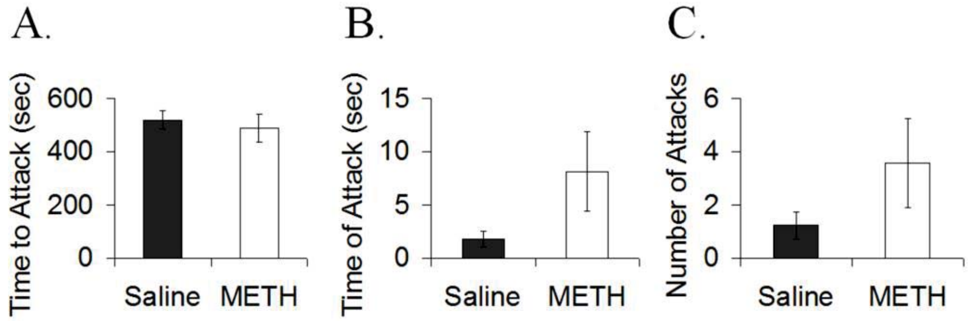


**Fig. 2**. Samples of student results from the laboratory exercise. Students graphically demonstrated the effects of methamphetamine on aggression using three different operational definitions: the number of attacks (A), the time to first attack (B), and the total duration of attacks (C) from the resident-intruder vodcasts.

scientific process without sacrificing fundamental teaching outcomes specific to a course. For example, students learned specific information about the importance of control groups, how to graphically display data, the meaning of statistical significance, and how to operationalize a construct. However, they also learned how to identify and analyze patterns in data sets as well as how to work with and use complex multi-disciplinary ideas and how to use comparative research and systematic reasoning to test hypotheses. Students also showed significant positive changes in their attitudes toward science and experimentation involving animal models. Further, the videos successfully exposed students to experimentation and data collection opportunities, which would otherwise not be available in a laboratory setting. An example of student results following the completion of this laboratory exercise is shown in Figure 2.

We built upon the premise of Grisham et al. (2003) in an effort to meet a demonstrated need of faculty teaching neuroscience with limited resources to provide hands-on learning opportunities for their students. This laboratory exercise also provided an effective means of engaging students in cross-disciplinary behavioral neuroscience as a first year experience. Early exposure to undergraduate research and integrative learning are recognized high impact practices that are effective for meeting explicitly stated goals for excellence in education as well as specialized curricular goals for STEM education (AAC&U, 2002; AAC&U, 2007; Elrod, 2010).

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