

Research in the Rat Lab: Some Thoughts on Undergraduates doing Behavioral Neuroscience Research

Mark C. Zrull

Appalachian State University

One size does not fit all; certainly not in the case of rat labs. So, for the sake of creating some context for what is to follow, consider the Wiley F. Smith Department of Psychology's Behavioral Neuroscience Laboratory (the Lab), which consists of "wet" or histology and microscopy lab space across the hall from the College of Arts & Sciences Animal Facility. This latter space houses rats for the Lab as well as the Lab's behavioral testing facilities—the "classic" rat lab. The Lab has existed for about 14 years, mostly in reclaimed storage rooms, having only been located in its current physical space for the last 3 years, and the histology and microscopy lab is slated to change location in the near future. The faculty investigator has had extramural funding in the past and frequently has competitive intramural funding but has a minimal annual budget for operating the Lab. Appalachian State University has about 14,500 students with over 13,000 undergraduates of whom more than 500 are Psychology majors. Now, assume it's Friday at noon in the Lab.

"So now that everybody's introduced themselves, let's get this going. I know it's Friday, and we all have plans. Steph and Lindsey are the only new folks this semester, which makes nine of you and one of me and Olivia [my graduate assistant]. It looks like most of y'all know Steph and Lindsey from elsewhere. They'll be working on the animal care and welfare training this week. You can help them out but don't give answers to the test items."

"Wait, wait a minute Dr. Z., what's with the y'all?"

"You know about my extreme southern background; if there were more of you, it'd be all y'all. Hey, did y'all notice? It's another semester of Warren and the women. Enough. Before we talk about plans for next week, I wanted to remind you that there'll be Monday morning e-mail reminders about each week's schedule. For a few of weeks I'll attach some readings related to our work. We'll start with re-reading a review of the seizure model we use:

the 1999 Ross and Coleman paper (Ross & Coleman, 1999)."

"I think we have that."

"You do, but we'll go ahead and re-read and discuss them again. I think we could use it. Megan, what about the T-maze plan?"

"I need schedules. We're running five, 2-hour sessions and since Olivia is doing four, I'll need one 2-hour block from each of us except Steph and Lindsey because they aren't certified yet."

"But we'll work them in to the schedule when they finish the test. The rest of you, give Megan your times after this meeting; let's work this out today. You guys have run this before, and I'm leaving it up to you to finish the adult cohorts. It's only a dozen rats. ... So, my plan is to run immunohistochemistry each Wednesday and Thursday, too. Olivia will cut brains on Monday and Tuesday; I think Liz #2 and Jess can select, block sites and do primary on Wednesday, yes?"

"Yep. We got the time. We're running the GABA antibody like last semester?"

"That's the plan Liz #2; the juvenile group is up, which should finish out your honors thesis animals. From y'all's schedules, I'm thinking Megan, Warren, Liz #2 and Margaret will split up the 6-hour run on Thursdays... sound good, doable? We'll work Steph and Lindsey into the schedule so they can start learning how to do this stuff."

"Yes, yep."

"O.K. then; well, the last administrative things I've got are setting up thesis meetings and plans for NCUR [National Conference on Undergraduate Research]. So, here we go. Ginny, you and I will meet each Monday in the lab from noon to one. Liz #1, we'll meet in the lab on Tuesday from 9:30 to 10:30, which gives you time to make your 11 o'clock. Liz #2, we'll meet on Wednesday between noon and one while you're waiting on blocking sites for the GABA tissue. Work for everyone?"

"Yes. Uh, huh."

“Why don’t y’all start to think about making plans for NCUR. We should hear about acceptances in a couple of weeks. I’ll go ahead and reserve hotel rooms...”

While the dialogue is a bit contrived, hopefully it hints that undergraduate researchers in a behavioral neuroscience lab spend time learning about brain and behavior, learning how to do science with their hands, learning about working as a team, and using what they have learned to accomplish joint and/or individual projects. Ideally they learn that being part of a research team and doing neuroscience can be enlightening, rewarding, and fun, too. As in most settings, mentoring in the rat lab is about doing good science with student colleagues with both mentor and protégés gaining from each other.

Undergraduate behavioral neuroscience or biological psychology research often involves work in varied settings and using multiple sets of hands-on skills as well as the various activities common to most undergraduate research. Behavioral neuroscience research involves studying relationships between the brain and behavior with biological psychology having a somewhat broader scope in which relationships between bodily processes and behavior are considered. The focus here is fairly “traditional” behavioral neuroscience research using rats to model phenomena of interest, behavioral experiments with or without a prior neural intervention, and histology to examine neural correlates of observed behavior. A facility to house rats, a location to conduct behavioral experiments, and some “wet” laboratory facility for conducting histology are all needed. Somewhere within these areas, or in a separate location, a place that can be set aside for surgery (if needed for a particular study) is also typical. Ideally, a department, college or university run animal facility for housing rats as well as both behavior and histology laboratories are available. Minimally, facilities and practices should meet local requirements for animal care and welfare, as determined by the Institutional Animal Care and Use Committee (IACUC), and follow National Institutes of Health policy (see National Institutes of Health, 2007; National Research Council, 1996) when rats are subjects.

Care should also be taken to prevent risk to personnel, including undergraduate researchers, and abide by good safety practices and applicable government regulations. For example, instruction in the proper handling of rats and availability of lab coats, protective gloves, and breathing protection (generally simple, filtering face masks are adequate) are needed. Similarly, histological procedures often require organic solvents and other toxic chemicals as well as instruments designed to cut tissue (fingers are tissue)

which means training, gloves, eye protection, lab coats, etc. and having adequate supervision are necessary. When surgical procedures are used, anesthetics and other drugs are used; these substances are controlled and require a license to obtain and/or hold. While state-of-the-art facilities and apparatus are not a requirement, the bottom-line is that doing good student-faculty collaborative research in a “rat lab” requires some spaces that can have some fairly specific uses and some equipment and supplies; the research is done in some sort of lab.

So how does the undergraduate find his or her way into a behavioral neuroscience research opportunity? It can happen in a variety of ways: asking faculty, responding to postings for research opportunities (the “advertising” process is formalized in some departments and colleges/universities), and being recruited by faculty to identify some common ways. While some undergraduates engage in research only in the summer, most behavioral neuroscience labs operate all year long and have year around opportunities for undergraduate research. Given the time needed to learn useful skills that may or may not be taught in a specific psychology curriculum, second semester freshmen or new sophomores make good candidates for beginning researchers in a rat lab. Interestingly, courses in statistics and research methods, that may not be taken until second year and are certainly useful, may not be as important to initiating a successful behavioral neuroscience research experience as for other areas of psychology.

Regardless of how they find their way to a lab, it is important to realize that students may be able to gain valuable research experience without having to engage in every aspect of a specific research program. For instance, some students only wish to run rats and have interest only in behavior under investigation while others really only care about neuroanatomy. The former undergraduates may not want to learn and do surgery or process brain tissue, and the latter may have no interest in dealing with live rats except when anesthetized or... Of course, the most complete experience is had by the student who runs behavioral and histological protocols, and it is important that *all* students make the scholarly connections between brain and behavior. Undergraduates need to be interested in and “well-matched” with the research they do to truly benefit from the experience. There seems to be no point in requiring doing or observing stereotaxic surgery of a student who runs rats well and understands the logic of behavioral experiments following brain lesions, but who faints at the sight of blood. Rather, it seems the role of the faculty member to build a well-functioning research team based on individual student’s interests and, at least to some degree,

aptitudes. Similarly, many undergraduates come to the rat lab with a real interest in investigating an aspect of neuroanatomy. They rarely know exactly what aspect but do know the interest includes perfusing rats and extracting, cutting and processing brains; however, they have an aversion to the extensive rat handling that is needed to run, for example, a T-maze paradigm. As they gain time in the lab, individual undergraduate researchers will gradually develop individual expertise, and when it all comes together a rather high quality research team can emerge. It is probably worth noting that diversity, but with compatibility considered, tends to be important for a quality lab team with each member able to gain from the team and each other member (i.e., a team of all honors students might not be the most efficient or effective).

There are many ways to identify or plan undergraduate research projects in a rat lab. The following discussion assumes a couple of things about undergraduate research. First, the best teaching and best learning occur when a faculty researcher and student are collaborating on a project (see Merkel & Baker, 2002 for a good, general discussion). The addition of other student researchers can make the collaborative process even more powerful. Second, guided-discovery is a much more powerful way to learn than pure discovery (Mayer, 2004). In other words, outlined projects that need to be fleshed out conceptually and make use of known and/or developing skills tend to yield good undergraduate research outcomes. So the value of engaging undergraduates as researchers early in their careers becomes clear: the undergraduate researcher with a year or two of experience can take more responsibility for a project than the student who is new to the rat lab. This guided approach is also efficient considering the need for IACUC approval prior to beginning projects; depending on the particular college or university the approval process can take some time. Similarly, this approach allows for training undergraduate researchers in techniques needed to complete projects well and safely as well as in logical and scholarly skills used to develop a project scientifically.

So assuming the faculty member wishes to have control over the research conducted in his or her lab, what might undergraduate research projects be like in such a behavioral neuroscience lab? One fairly successful approach to running a lab with primarily undergraduate researchers (approximately 6 to 10 at any given time) and often a single M.A.-level graduate student is to conceptualize large projects that yield smaller, “thesis-sized” projects that, in turn, contain a couple of relatively simple studies. In other-words, a program of research works well with

an undergraduate research team. Currently, the major research focus in the Lab has been on the nature of exploratory behavior and simple learning and memory of animals prone to and experiencing bouts of sound-induced seizures at various ages. Seizure-resistant rats are made susceptible to generalized, reflex epilepsy and have seizures induced on a particular schedule by undergraduate researchers. Students work in teams on various projects defined by a particular behavior of interest or age for seizure induction. One individual researcher is responsible for each project, which may yield anything from data for the lab to a presentation at the National Conference on Undergraduate Research (NCUR; e.g., *Learning and performing a task that requires working memory is affected by sound-induced seizures in adult rats*, Waddell et al., 2007) to a senior honors thesis (e.g., *Exploratory behavior in Long-Evans rats after adult audiogenic seizures*, Price, 2007). Teams produced subjects and control groups, and for the thesis project, Ms. Price benefited from her team’s help running open field and object preference tasks. Team members benefited from shared authorship on a related presentation at NCUR. Additional projects result from relevant histology conducted after behavioral testing. Undergraduate researchers perfused animals and processed tissue using immunohistochemistry to visualize GABAergic (a source of inhibition) neurons in the seizure-prone midbrain. Subsequently, cell densities across seizure-prone and control groups were computed using microscopy yielding a submission for the Society for Neuroscience meeting (*Acquired audiogenic seizures increase the proportion of GABAergic neurons in the dorsal nucleus of lateral lemniscus*, Glenn et al., 2007). Finally, projects may evolve serendipitously from a general line of research.

Students have conducted a handful of investigations concerning the mechanics of the acquired reflex epilepsy model used in the Lab (e.g., *Sudden or gradual sound onset differentially affects audiogenic seizure severity in developmentally primed rats*, Dravland, Clapp & Zrull, 2005). In each of these examples, one undergraduate (typically the first author on a product evolving from the project) had responsibility for developing the experiment(s) and organizing team involvement in collaboration with the faculty researcher. Often, with a competent team leader, the faculty researcher has a collaborating scientist role with the lead undergraduate researcher but a technician or consultant role with the team when experiments are being run.

While one size does not fit all as far as specific research goes in the rat lab, undergraduates can do quality behavioral neuroscience research and the opportunity can help them achieve their goals. Working in a rat lab does require learning some unique abilities (e.g., handling rats, possibly doing stereotaxic surgery and intracardial perfusions, microtoming tissue, cleaning slides, doing digital microscopy stereology, etc.) in addition to developing skill in scientific reasoning and research methods (e.g., reviewing literature, designing experiments, doing statistical analyses, etc.) and student preparedness will depend a great deal on the specific curriculum of a particular program. Given the learning curve for student researchers as well as safety considerations and various regulations, working with undergraduates in a behavioral neuroscience lab offers an ideal opportunity for faculty to guide discovery and engage in collaborative researcher with undergraduates. Strong research teams can develop with student-student collaborations becoming common, and a program of research can benefit from having undergraduates in the lab for two or three years. Longer duration relationships afford the opportunity mentoring to truly develop with discussions about life, the future and being a person in addition to learning to do science and function as a scientist. And, of course, with mentoring come some unique opportunities for both the mentor and protégé like eating brains and eggs in Missoula, Montana biker hang-out at 4 a.m. after a long day, and night, of discussing neuroscience and rats.

References

- Dravland, M., Clapp, K., & Zrull, M. C. (2005). Sudden or gradual sound onset differentially affects audiogenic seizure severity in developmentally primed rats. *Impulse*. Online: <http://impulse.schc.sc.edu/Archive2005.lasso>.
- Glenn, E. A., Ostertag, M. F., Adams, M. R., Hodgin, E. L., & Zrull, M. C. (2007, November). Acquired audiogenic seizures increase the proportion of GABAergic neurons in the dorsal nucleus of lateral lemniscus. Poster to be presented at the 37th Annual Meeting of the Society for Neuroscience, San Diego, CA.
- Mayer, R. E. (2004). Should there be a three-strikes rule against pure discovery learning? The case for guided methods of instruction. *American Psychologist*, *59*, 14-19.
- Merkel, C. A., & Baker, S. M. (2002). *How to mentor undergraduate researchers*. Washington, DC: Council on Undergraduate Research.
- National Institutes of Health. (2007). General information. Retrieved May 5, 2007 from Office of Laboratory Animal Welfare Web Site: <http://www.grants.nih.gov/grants/olaw>.
- National Research Council. (1996). *Guide for the care and use of laboratory animals*. Washington, DC: National Academy Press.
- Price, V. (2007). *Exploratory behavior in Long-Evans rats after adult audiogenic seizures*. Unpublished senior thesis. Appalachian State University, Boone, NC.
- Ross, K. C., & Coleman, J. R. (1999). Audiogenic seizures in the developmentally primed Long-Evans rat. *Developmental Psychobiology*, *34*, 303-313.
- Waddell, M. L., Jones, W. S., Snyder, J. L., Price, V.A., (& Zrull, M.C.) (2007, April). Learning and performing a task that requires working memory is affected by sound-induced seizures in adult rats. Poster presented at the 21st National Conference on Undergraduate Research, Dominican University, San Rafael, CA.