Research Statement- Lara D. LaDage, Ph.D.

My research program uses a question-based philosophy centered on the evolution of spatial processing and the neural substrate underlying spatial processing. My approach to research uses three levels of analysis to address questions about the mechanism, development, and function that contribute to differences in the brain and behavior. I believe that I have successfully used this approach to contribute to an integrated understanding of behavior and its effects on underlying brain structure and function in both birds and reptiles. Below, I summarize my research pursuits during my positions as a post doc and a research scientist, as well as my future research goals.

Spatial memory, hippocampal morphology, and neurogenesis

Spatial abilities have been associated with many ecologically relevant behaviors such as territoriality, mate choice, navigation, and acquisition of resources. Spatial memory use, in particular, has been shown to affect the hippocampus, the area of the brain largely responsible for spatial processing. Animals which rely more heavily on spatial processing tend to have larger hippocampi, with more hippocampal neurons, and increased neurogenesis. Further, impairment of the hippocampus results in deficits in spatial memory processing.

As a post doc under Vladimir Pravosudov, I worked on his NIH-funded project concerning the effects of spatial memory and captivity on hippocampal attributes and neurogenesis in chickadees. Although comparative work has shown that differential demands on spatial processing correlates with differences in hippocampal features (e.g., LaDage et al. 2010a), we were also interested in determining if maintenance of the hippocampus requires hippocampal-dependent memory-based experiences and if these experiences were relevant to the recruitment of new hippocampal neurons. We found that reducing memory-based experiences via captivity has a profound negative effect on hippocampal volume (LaDage et al. 2009a), while restricting memory-based tasks within captivity can decrease neurogenesis (LaDage et al. 2010b). From this two-year award, I've produced six first-author manuscripts that are published or in press and several other second- and third-author manuscripts that are either published or in various stages of publication.

Causes and consequences of variation in the hippocampus of individuals utilizing different spatial strategies

The adaptive specialization hypothesis proposes that an evolved behavioral specialization in response to increased spatial demands is reflected by selection for a larger hippocampus, the part of the brain that is heavily involved in spatial processing and memory. Although there is support for the correlation between spatial use demands and variation in the hippocampus, both among and within species, there is little ecologically relevant data as to the causative mechanisms underlying this variation. For instance, what is the contributing role of genetics, experience, hormonal, and maternal effects on the hippocampus? Because the adaptive specialization hypothesis suggests that specialized behavior and correlated increases in brain areas specialized for processing that behavior are naturally selected, it is important to ascertain whether there is a genetic and/or heritable basis to the relationship between the specialized behavior and the change in brain anatomy. Further, can other factors such as experience modulate changes in the brain, outside of those genetically determined?

To answer these questions, I was funded by NSF (#IOS-0918268) to examine the genetic, maternal, hormonal, and experiential basis of variation in the volume, number of neurons and neurogenesis in the putative reptilian hippocampal homologues (dorsal cortex and medial cortex) of male side-blotched lizards (*Uta stansburiana*). Males of the side-blotched lizard come in three different morphs (orange, blue, and yellow) and each morph has evolved to use vastly different spatial niches My previous work (LaDage et al. 2009b) has shown that the dorsal cortices were larger in orange males that had the greatest use of space (highly territorial) and smallest in yellow males with the lowest use of space, while blue males were intermediate. This suggests that space use patterns correlate with brain morphology in this species as predicted by the adaptive specialization hypothesis. However, we have yet to determine if these differences are, in fact, genetic and linked with morphotype or if other factors such as experience, hormones, and epigenetic effects play a role in shaping the morphology of the cortical regions and the regulation of neurogenesis in these brain regions.

To this end, I have just completed selective breeding experiments in the lab to determine if selecting on the genetically-determined morphotype can reproduce the results I found in the field. Also, additional progeny that were produced will be used to examine the effects of spatial use and testosterone on attributes of the dorsal and medial cortices. Next year, I will again be breeding animals based on morphotype to examine maternal effects, in this case estrogen deposition in the eggs, on cortical morphology and neurogenesis in the offspring.

Because the opportunity to causally link behavior and brain structure/function in *Uta stansburiana* is tenable, this causes an influx of new and integrative questions that can be asked in the near future. For example, is differential spatial memory use modulating the changes in hippocampal neurogenesis? Do the genes and the environment interact to produce the medial and dorsal cortical phenotype- what is the relative contribution of particular variables (e.g., experience, maternal effects, stress) to such? Also, I plan to examine the fitness consequences of variance in the cortical regions by performing semi-natural experiments with individuals with manipulated medial and dorsal cortical attributes. Finally, I am also interested in examining the neural basis of spatial processing at a finer scale, by examining the distribution of NMDA receptors within the region of the dorsal and medial cortex.

Due to the highly integrative nature of my research questions, I easily bridge multiple sub-disciplines such as evolution, behavior, ecology, physiology, and psychology. Considering this, the opportunity for collaborative and graduate student research is tremendous. At present, I have an established collaboration with Barry Sinervo at the University of California-Santa Cruz and have had contact with several potential collaborators concerning receptor work. I also foresee the potential for collaboration with several faculty members within the Department of Biology at UC- Riverside.

Citations:

LaDage, LD, Roth II, TC, Fox, RA, and VV Pravosudov. 2009a. Effects of captivity and memory-based experiences on the hippocampus of mountain chickadees. Behavioral Neuroscience, 123, 284-291.

LaDage, LD, Riggs, BJ, Sinervo, B, and VV Pravosudov. 2009b. Dorsal cortex volume in male side-blotched lizards (*Uta stansburiana*) is associated with different space use strategies. Animal Behaviour, 78, 91-96.

LaDage, LD, Roth II, TC, and VV Pravosudov. 2010a. Hippocampal neurogenesis is associated with migratory behavior in adult but not juvenile sparrows (*Zonotrichia leucophrys* ssp.). Proceedings of the Royal Society of London B, *in press*.

LaDage, LD, Roth II, TC, Fox, RA, and VV Pravosudov. 2010b. Ecologically-relevant spatial memory use modulates hippocampal neurogenesis. Proceedings of the Royal Society of London B, 277, 1071-1079.