

Brunjes, P. C.

06/04/87

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PROGRESS REPORT: ONR GRANT N00014-86-K-0342
"Neuroanatomical Studies of Nested Parallel
Information Processing Pathways"

1. Period of Grant Support: 07/01/86-06/30/87

2. Professional Personnel Engaged:

	Title	Date of Service
P. C. Brunjes	PI	07/01/86-06/30/87
L. L. Frazier	Grad. Student	07/01/86-06/30/87
J. Burns	undergraduate	07/01/86-09/01/86
C. Tessitore	Grad. Student	08/01/98-09/01/86

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3. Progress Towards Meeting Goals of Original Proposal.

The application was designed to closely define the circuitry of the olfactory bulb by examining the early development of the structure. We have made considerable progress into completing these goals. Below is a brief summary of the results to date.

The application was divided into two experiments. In the first we proposed to examine the development of topographical connections from the olfactory mucosa to the olfactory bulb, using microinjections of HRP. The bulk of the equipment purchased with ONR money was designed to perform these experiments. Due to a long chain of mix-ups and delays, the equipment did not arrive in Charlottesville until nearly 8 months after the start of the grant. While waiting to begin the first group of experiments, we concentrated our efforts on Experiment 2 and on completing other studies relevant to understanding the development of bulb circuitry. These efforts are described in more detail below.

Experiment 2 was designed to examine the development of relay cells within the bulb. Two studies were proposed. In the first, dendritic growth was to be quantified by examining tissue stained with Golgi techniques. During preliminary work with the tissue we ran across a technique which has been reported to work quite well in the olfactory bulb (Riley, Brain Res. Bull. 1979) and have been working out the staining parameters with it. We also learned of a technique for embedding the Golgi stained tissue in softened glycol methacrylate (P. Lassiter, personal communication) which obviates our use of celloidin, saving the 2 weeks necessary for celloidin infiltration (thus expediting what must be one of the slowest histological preparations yet devised) and avoiding the highly inflammable solvents. At present we are continuing to collect and stain tissue, and have begun to collect data through the production of camera lucida drawings of the

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cells.

Experiment 2b was designed to examine the timing of axonal growth in the various relay cell classes by injecting HRP into the rostral lateral olfactory tract and determining when perikarya of the different classes would first exhibit the label. We have spent a great deal of time working out the variables in this experiment. The first question we had to answer was which approach was more suitable for the injections, the standard dorsal stereotaxic approach or a transorbital one. It appears that the latter is better as it allows direct visualization of the LOT. A second variable is the anesthetic. Given the surgical trauma involved in the HRP injections, we wanted our anesthesia to last the duration of the experiment, and it turns out to be quite difficult to keep newborn pups both anesthetized and alive for the estimated 4-6 hours needed for HRP transport. We think we have solved the problem by using a highly concentrated dose of urethane. Having worked out these parameters, we are now proceeding to collect the needed tissue samples.

While piloting the above experiments, we completed a number of other studies examining early development. Copies of the papers and abstracts have been appended. Each study and its conclusions are described briefly below.

a) An examination of metabolic development in the olfactory bulb. In order to understand the development of bulb circuitry and function one has to be aware of regional differences in growth and activity. One way to assess both factors is to examine regional metabolic activity in developing bulbs. We approached metabolic development by examining levels of a Krebs cycle enzyme, succinate dehydrogenase (SDH), using histochemical techniques coupled with microdensitometry. In the study we assessed both normal patterns of early development and the effects of decreased afferent activity on SDH staining. The results are quite important in that they demonstrated regional differences in early SDH activity, suggesting that there may be gradients of early development, and also that this activity is regulated by the amount of sensory activity experienced by the young organism.

b) An examination of the effects of odor deprivation on olfactory bulb development in a precocial species, Acomys cahirinus. Nearly everything we know about brain development has been gained from studies of animals born in an immature state ("altricial" species). We have been involved for several years in examining early brain growth patterns in a precocial species in order to gain insights into the control of developmental patterns and amount of possible variation. In this study we examined the effects reducing the amount of olfactory experience available

during early life in young Acomys on the development of the olfactory bulb. A tacit assumption throughout the developmental literature is that precocial species, because they are born more mature after a relatively long gestation period, should be less "plastic" than altricial subjects. The results of this study suggest just the opposite--not only does Acomys exhibit a greater response to deprivation than its altricial cousin the laboratory rat, but also a longer period of vulnerability. We feel that the paper has profound implications for general views of developmental constraints and reinforces our finding that Acomys is a particularly suited subject for examinations of early development.

c). A quantitative study of early developmental changes in cellular number and packing density in the olfactory bulb. We have just completed and submitted a large study of the early changes in bulb cellular populations. Once again, the study contains normative data from control olfactory bulbs which is badly lacking, and also an examination of the effects of altered early experience of bulb growth. During the course of the study, over 40,000 cells were measured and keyed into a computer in order to estimate cellular packing density (N_v), and over 37,000 laminar areas were measured in order to determine laminar volumes. Estimates of density were then multiplied times the volume measurements to determine cellular number. The study represents the most thorough and up-to-date study of bulb growth ever reported, and describes changes in bulb cell populations both on a lamina-by-lamina basis and by every major neuronal class and glia.

d). A comparative study of postnatal rates and patterns of myelination in altricial and precocial murid rodents. As a portion of our studies of early brain growth in the precocial mouse Acomys we have examined early myelination in the species. It appears that Acomys has a much different rate of myelin formation; myelination begins much later than normally found in the rat, but subsequently proceeds much more quickly. The study is presently being written up for publication.

e). An examination of early cellular proliferation in the olfactory bulb. Using tritiated thymidine to label the time of last division of cells, we are examining both the establishment of bulb neuronal populations and gradients of early cellular production, and thus bulb maturation. We have found that there is indeed a rostral-caudal gradient of bulb growth, and the proliferative patterns can be regulated by the amount of afferent experience available during early life. The latter finding is quite surprising given that proliferation is commonly regarded as being controlled by internal cellular clocks, not by extracellular, "experiential" variables. The study is

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approximately half-finished, and should be completed by Fall.

In summary, we feel that we have made significant progress in achieving the goals outlined in the original proposal, and look forward to the completion of all projects described.

4. List of Publications

a). Papers in press (copies included)

Cullinan, W. E., & Brunjes, P. C. Unilateral odor deprivation: effects on the development of staining for olfactory bulb succinate dehydrogenase. Dev. Brain Res.

b). Papers submitted for publication (copies included)

Brunjes, P. C. Precocity and plasticity: odor deprivation and brain development in the precocial mouse Acomys cahirinus.

Frazier, L. L., & Brunjes, P. C. Unilateral odor deprivation: early postnatal changes in olfactory bulb cell density and number.

c). Papers in preparation (Abstracts included)

Tessitore, C. T., & Brunjes, P. C. A comparative study of myelination in precocial and altricial murid rodents.

Frazier, L. L., & Brunjes, P. C. Proliferation patterns during postnatal development in the olfactory bulb of normal and unilaterally-deprived rats.

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