

OPTIMIZING NEURONAL TRACER CHEMISTRY TO DETERMINE THE DETAILED TOPOGRAPHY OF BRAIN CIRCUITS RELATED TO NEGLECT

by William Conte

The connections between cortical area AGm and thalamic lateral posterior nucleus LP are key components of the circuitry of hemispatial neglect in a rodent model. The goals of this study are to analyze the neural connections between AGm and LP, and to optimize the retrograde tracing efficiency of 3K BDA.

1. Far medial LP projects to a restricted portion of caudal AGm.
2. Other portions of LP project to rostral, middle, and caudal AGm and to cortical area PPC in a segregated fashion.
3. Optimal retrograde transport of 3K BDA from AGm to LP will occur using acetate buffer at pH 4.0, with a 10 day survival time.

Hemispatial neglect is a neurological condition in which a stroke on one side of the brain affects responding to visual, auditory, or somatosensory stimuli on the contralesional side. These deficits in directed attention are not caused by primary sensory or motor dysfunction. In humans, neglect is most often caused by lesions in the posterior parietal lobes. A patient with neglect syndrome acts as if their contralesional side is nonexistent. This is characterized by the patient failing to recognize stimuli on the contralesional side, and only eating food on the ipsilesional side of a plate. Over 40% of all cases of brain damage caused by stroke result in neglect syndrome, which has a severe debilitating affect on patients and their families.

During this project I will accomplish two things: I will optimize the chemistry of neuronal tracers used for neuroanatomy studies, and determine the specific connections between AGm and LP. Dr. Reep and his colleagues have already developed a rodent model of neglect in order to examine the neuroanatomical circuitry of neglect, and to develop possible pharmacological treatments. During this study, hooded rats will be injected with red, green, and blue 3K BDA in rostral, mid, and caudal AGm. The chemistry of the tracers will be divided into eight different conditions based on a 5 or 10 day survival period, an acetate or phosphate buffer, and a pH of either 4.0 or 7.0. After perfusion and slide mounting, the slides will be examined under a fluorescent microscope. The labeled cells in LP will show a pathway to the specific injection site. BDA is used for both retrograde and anterograde studies, depending on the chemical conditions. Generally, retrograde transport is used with 3k BDA at an acidic pH, and anterograde transport is used with 10k BDA at a neutral pH. Since there is such a small difference between the two conditions, I will attempt to provide a more precise guideline for researchers to use.

Our previous studies with Dr. Reep have determined the existence of neural connections between LP and AGm, but a more detailed topographic map needs to be obtained in order to determine the specific neuronal circuitry that is crucial for neglect and recovery. If my hypotheses are correct, then we will obtain a better knowledge of the circuitry of neglect related to AGm and LP, which can be used in the study of pharmacological treatment research. By optimizing the tracer efficiency, further studies using BDA will yield more accurate and reliable results.