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Program Member Type
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Research Interest

The nervous system generates behavior through the coordinate activity of neural circuits. Our long-term goal is to understand how sex-specific behaviors are encoded by neural circuits. We are pursuing this research in the mouse, which permits a genetic, anatomic and functional analysis of sexually dimorphic behaviors in mammals. Examples of sex differences in mouse behavior include mating, aggression and nursing. Such behaviors can be observed in naïve animals without prior learning, suggesting that the underlying neural circuits are developmentally hard-wired. We exploit this developmental programming to identify and manipulate neurons that influence sex-specific behaviors.

Sexual dimorphisms in behavior can result from sex differences in neuronal connectivity or from differences in neuronal gene expression. Either mechanism can impart sex-specific electrical activity to neural circuits, leading to dimorphic behaviors. One set of projects in the lab focuses on identifying such anatomic or molecular sexual dimorphisms in the brain. Testosterone and its cognate receptor, the androgen receptor, are required for male-specific behaviors. Neurons expressing the androgen receptor are likely to be responsive to testosterone and therefore to influence dimorphic behaviors. Using a genetic approach we have labeled androgen receptor expressing neurons such that we can visualize the cell bodies as well as the processes of these neurons. This study reveals striking sexual dimorphism in androgen receptor expression in discrete brain regions, including previously identified as well as novel areas.

Progesterone and estradiol are required for female-specific behaviors. We are using a similar genetic approach to label neuronal subsets that express receptors for these steroids. We expect to uncover sex differences in several regions expressing these receptors, indicating areas that may influence female behaviors. Several lines of evidence suggest that estradiol signaling is required for both male- and female-specific behaviors. Does estradiol act on distinct brain regions to effect male- and female-specific behaviors? In addition, what is the nature of the interaction between testosterone- and estradiol- signaling in the control of male

behaviors? These and related issues are the focus of developmental studies using a genetic approach.

We plan to use several strategies, including microarray technology, to uncover dimorphic gene expression patterns in the brain. Such studies will highlight additional neuronal groups likely to influence dimorphic behaviors and will also enable us to use these genes as molecular tools to manipulate neurons genetically in future experiments.

What is the behavioral contribution of sexual dimorphisms in the brain? We are designing genetic strategies that afford inducible and regionally restricted ablation or silencing of dimorphic neuronal subsets. In an effort to reveal the pathways in which these dimorphic neurons participate we will utilize established as well as novel genetic trans-synaptic tracers. These experiments will highlight the functional relevance of neuronal dimorphisms and reveal the pathways engaged during sex-specific behaviors. In mice sex-specific behaviors are regulated mainly by olfactory cues and hormonal signals. Our studies should ultimately provide an anatomic and functional link between hormonal and sensory cues and sexually dimorphic behaviors.

Complete Publications [3]

Links
[1] http://profiles.ucsf.edu/nirao.shah
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