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Neuron

Social Control of Hypothalamus-Mediated Male Aggression

Highlights

- PR+ VMHvl neurons can drive aggression in singly housed, resident male mice
- This aggression can occur absent chemosensing, gonadal hormones, or opponents
- PR+ VMHvl neurons do not trigger aggression in socially housed intruder males
- Disabling chemosensing enables PR+ VMHvl-triggered aggression in these males

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In Brief

Yang et al. show that PR+ VMHvl neurons trigger aggression in solitary male mice independent of pheromone-sensing, gonadal hormones, opponents, or social context. By contrast, these neurons can trigger aggression in socially housed intruder males when their pheromone sensing is disabled.

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Social Control of Hypothalamus-Mediated Male Aggression

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SUMMARY

How environmental and physiological signals interact to influence neural circuits underlying developmentally programmed social interactions such as male territorial aggression is poorly understood. We have tested the influence of sensory cues, social context, and sex hormones on progesterone receptor (PR)-expressing neurons in the ventromedial hypothalamus (VMH) that are critical for male territorial aggression. We find that these neurons can drive aggressive displays in solitary males independent of pheromonal input, gonadal hormones, opponents, or social context. By contrast, these neurons cannot elicit aggression in socially housed males that intrude in another male's territory unless their pheromone-sensing is disabled. This modulation of aggression cannot be accounted for by linear integration of environmental and physiological signals. Together, our studies suggest that fundamentally non-linear computations enable social context to exert a dominant influence on developmentally hard-wired hypothalamus-mediated male territorial aggression.

INTRODUCTION

Social behaviors are essential for reproductive success and for success in other domains across diverse human societies. Many forms of social interactions are acquired traits that depend on learning. However, behaviors such as mating and aggression are primal, sexually dimorphic social interactions that are innate in the sense that they can be displayed without prior training, suggesting that the underlying neural circuits are developmentally programmed. Indeed, previous work shows that, in mice and many other vertebrates, sex hormones produced by the gonads during a critical developmental window control the organization of neural pathways underlying these behaviors in a sexually dimorphic manner (Arnold, 2009; Bronson and Desjardins, 1968; McCarthy, 2008; Peters et al., 1972; Phoenix et al., 1959; Wu et al., 2009; Yang and Shah, 2014). The extent to which social cues and internal signals modulate behavioral output elicited by such developmentally wired neural circuits in adult animals is poorly characterized (Fernald, 2015; Insel and Fernald, 2004; Wallen, 1996). In addition, how cues relating to social setting and prior experience are conveyed to neural circuits that control these innate behaviors is not well understood.

It can be difficult to tease apart the relative roles of social cues and internal physiological signals in shaping neural decisions underlying even innate behaviors. This is because salient sensory cues, ethological relevance of social setting, and molecularly defined neural pathways remain to be clearly determined for most behaviors, even in a laboratory setting. Hypothalamus-dependent male aggression in mice provides a suitable platform to study the relative contributions of environment and genetic hard-wiring. Wild male mice are naturally territorial across diverse settings; they attack other males even in the presence of abundant resources and without competition for mates (Berry and Bronson, 1992; Crowcroft, 1955, 1966; Crowcroft and Rowe, 1963; Quadagno, 1968). A successful territorial male will often drive other males into social cohabitation in small areas from which these males rarely attack the territorial male (Crowcroft, 1955, 1966; Crowcroft and Rowe, 1963). Male lab mice are also aggressive, and, as with wild mice, this aggression is purposive and flexible. It is purposive in the sense that a male