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REVIEWS

Acknowledgments

The authors are grateful to members of the Garel laboratory for stimulating discussions and comments on the manuscript. The laboratory is supported by INSERM, CNRS, Investissements d'Avenir implemented by ANR-10-LABX-54 MEMO LIFE, ANR-11-IDEX-0001-02 PSL* Research University, and the ERC Consolidator NImO. S.G. is an EMBO YIP awardee and part of the École des Neurosciences Paris Île de France network.

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https://doi.org/10.1016/j.tins.2018.03.017

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Spotlight

Circuit Architecture Underlying Distinct Components of Parental Care

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Parental care is a key evolutionary innovation that influences the fitness of parents and offspring. How the brain coordinates such a complex behavior remains poorly understood. Kohl and colleagues recently uncovered the organizational principles of hypothalamic galanin neurons and their connections in mice. Their findings revealed a striking picture in which discrete neuronal pools control distinct aspects of parental behavior.

Understanding the evolution and neural mechanisms of complex behaviors remains one of the fundamental aims of biology. While the functional neural architectures giving rise to relatively simple behaviors are fairly well understood [1–3], it is largely unknown whether principles of circuit connectivity and function apply similarly across levels of behavioral complexity. In particular, such principles remain elusive for social behavior, which requires the integration of diverse internal and external inputs and the coordination of context-appropriate behavioral outputs (Figure 1). Recently, Kohl and colleagues provided new insights into the functional circuit architecture underlying parental care in mice [4]. By dissecting the roles of galanin-expressing neurons in the medial preoptic area ($MPOA^{Gal}$), which is known to be key in the control of parental behaviors, the authors shed light on the organizational principles that define the relationships between $MPOA^{Gal}$ subpopulations, their target circuits, and specific aspects of parental behavior.

Kohl and colleagues began by characterizing the anatomical and functional connectivity of $MPOA^{Gal}$ neurons. $MPOA^{Gal}$ input and output projection maps were largely overlapping, revealing extensive reciprocal connections. The majority of inputs were from within the MPOA itself, pointing to prominent local processing. Comparing between neural activity during parenting and non-parenting behaviors, the authors discovered notable activity patterns across various groups of animals. While activity from local inputs increased during parenting in all groups, input activation from outside the MPOA varied based on an animal's sex and reproductive state. For example, fathers and virgin females – but not mothers – exhibited increased input activity from the medial amygdala during parenting, which the authors suggested was related to pheromone-mediated reduction of pup-directed aggression in males and virgin females. Somewhat surprisingly, input connections from oxytocin neurons known to play a role in maternal behavior were absent; however, $MPOA^{Gal}$ neurons in both sexes received inputs from vasopressin-expressing neurons associated with a variety of social behaviors [5]. In contrast to the largely conserved input connectivity, $MPOA^{Gal}$ neuron outputs were sexually dimorphic. Specifically, more $MPOA^{Gal}$ neurons projected to periventricular (PVN) vasopressin and corticotrophin-releasing hormone neurons in males and to PVN oxytocin neurons in females, suggesting a potential mechanism for sex-specific regulation of parental behaviors. Finally, the authors found that $MPOA^{Gal}$ neurons were organized into

distinct subpopulations with shared inputs but largely nonoverlapping target areas.

Given the organization of MPOA^{Gal} neuron outputs, the authors predicted that subpopulations with distinct projection targets might mediate distinct aspects of parental behavior. In general, the entire population of MPOA^{Gal} neurons had high activity levels during pup-directed (but not non-pup-directed) behaviors in mothers, fathers, and virgin females. But strikingly, as summarized next, the behavioral outcomes of this activity were specific to distinct MPOA^{Gal} subpopulations. Optogenetic stimulation of periaqueductal gray (PAG)-projecting MPOA^{Gal} neurons increased pup grooming and pup-directed sniffing in both sexes and suppressed pup-directed attacks in infanticidal virgin males. Conversely, optogenetic inhibition of PAG projections reduced pup grooming and sniffing. Activation of ventral tegmental area (VTA)-projecting MPOA^{Gal} neurons increased the motivation to seek out pups while inhibition of these projections decreased this motivation. Importantly, the effects of PAG-projecting and VTA-projecting MPOA^{Gal} subpopulations were specific to pups, as neither subpopulation influenced social interactions with adults. By contrast, activation of medial amygdala (MeA)-projecting MPOA^{Gal} neurons did not affect pup interactions but inhibited social interactions with other adults, perhaps representing an indirect mechanism by which parental care is increased via reduction of non-parental behaviors. Taken together the results of Kohl and colleagues demonstrate a remarkable functional architecture in which specific MPOA^{Gal} neuron subpopulations receive diverse inputs that are likely to mediate the integration of diverse cues relating to parental behavior and project specific outputs to a variety of target regions, each mediating unique aspects of parental behavior.

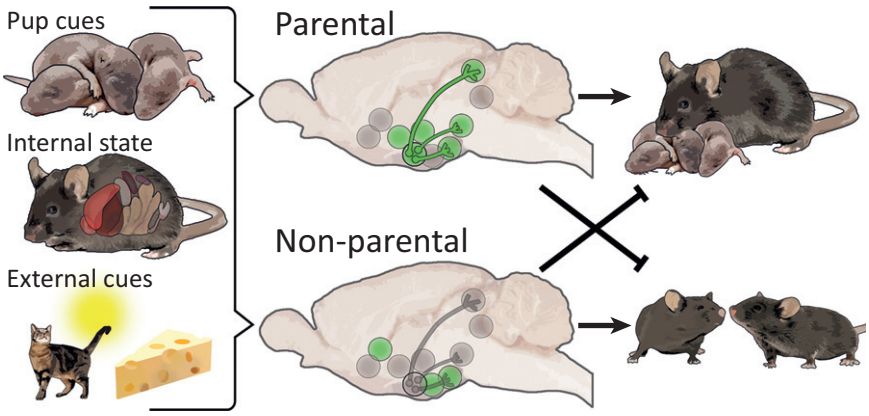

Figure 1. Neural Pathways for Parental Behavior. Neural circuits integrate offspring cues, internal physiological state, and environmental information to initiate parental behavior (left panel). Subpopulations of galanin neurons in the medial preoptic area project to various brain regions that control distinct components of parental behavior (middle panel; bold circle in the brain represents the medial preoptic area with different galanin subpopulations projecting to the medial amygdala, ventral tegmental area, and periaqueductal gray). The work by Kohl and colleagues suggests that tuning of activity in the circuit (neuronal activation indicated by green in the middle panel) drives complex behavioral outcomes and decisions between parental care and other social behaviors (right panel).

The study by Kohl and colleagues raises several important questions regarding the function of the MPOA^{Gal} circuit in mammals. Infanticide and caretaking vary with genotype, sex, and experience even within mice [6]. Kohl and colleagues used laboratory mice that display parental behavior in both males and females. In particular, males display a time-dependent change in behavior toward pups, where care behavior increases and infanticide decreases in the specific time window following mating that coincides with parturition [7]. This is in contrast to wild mice, in which males and females will typically kill unfamiliar pups [6]. Explorations of how activity in the MPOA^{Gal} parental circuit is synchronized with mating to induce a behavioral switch from aggression to infant care in laboratory mice and how mouse domestication has shifted the overall tuning of the circuit toward increased parental care would be valuable future directions. In light of the current study, understanding how the genome specifies parental care and whether principles governing the functional architecture of the MPOA^{Gal} parental circuit apply generally in rodents and other mammals is one of the next frontiers.

While best understood in mammals, parental care has evolved independently across nearly all forms of animal life [8]. A critical extension of the questions raised by this work is the degree to which this circuit architecture is functionally conserved across vertebrates. The location and connectivity of hypothalamic galanin, arginine vasopressin, and oxytocin neurons are evolutionarily conserved across vertebrates [9]. Given this widespread circuit conservation, the evolution of parental care across species may rely more on altering circuit activity than changing the underlying circuit architecture. Moreover, the location, connectivity, and function of a diversity of neuropeptides and neuromodulators related to additional forms of social behavior (e.g., mating, aggression) are known to be conserved similarly to those involved in parental care across vertebrates [10]. Thus, selection on the tuning of neural circuits with functional

architecture similar to that described by Kohl and colleagues for MPOA^{Gal} neurons may prove to be a guiding principle in the evolution of social behaviors. This also suggests preadaptation for behavioral evolvability, where altering the tuning of highly conserved circuits can lead to evolutionary gains (and losses) of complex social behaviors. Comparative work across species will give insights into the evolution of circuit tuning where circuit activity thresholds that elicit specific behaviors are adjusted within and between species, thereby driving natural variation in social behavior.

Defining the principles of circuit architecture that promote parental care and other social behaviors is critical to understanding the maintenance, development, and evolution of complex behavior. The work by Kohl and colleagues provides a striking example of how discrete components of social behavior can be regulated by subpopulations of the same neuron type in the vertebrate brain. These findings lay the groundwork for new research to understand how these circuits are tuned by an individual's experience as well as by the broader evolutionary processes that modify activity in conserved neural circuits to promote increasingly complex behavioral systems.

Acknowledgments

This work was supported by grants from the National Science Foundation (DBI-1608997 to E.K.F. and IOS-1557684 to L.A.O.).

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https://doi.org/10.1016/j.tins.2018.04.003

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