

W. Sun (et al.)

Reviving-like prosocial behavior in response to unconscious or dead conspecifics in rodents

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Editor's summary

In emergency situations, humans often exhibit instinctual “first aid” behaviors toward others. Whether and how other species show prosocial behaviors toward others is unclear. In two independent studies, W. Sun *et al.* and F. Sun *et al.* showed that mice exhibit stereotyped behaviors toward unconscious conspecifics, escalating from sniffing and grooming to licking of the head and tongue pulling, which accelerated recovery from unconsciousness (see the Perspective by Sheeran and Donaldson). The activation of neurons in the medial amygdala and oxytocin-expressing neurons in the hypothalamic paraventricular nucleus was required to trigger these behaviors. The results elucidate different aspects of a previously unrecognized prosocial behavior in mice and its underlying neurobiological mechanisms. —Mattia Maroso

Structured Abstract

INTRODUCTION

When humans encounter someone unconscious, they often respond with emergency reactions aimed at reviving that person. However, it remains unclear whether animals naturally exhibit any specific behaviors when faced with an unconscious peer.

RATIONALE

Anecdotal observations of various animal species in the wild have documented behaviors toward peers that have collapsed as a result of sickness, injury, or death. These behaviors include touching, grooming, nudging, and sometimes even more intense physical actions such as striking. Although these actions toward incapacitated conspecifics are reminiscent of human emergency responses involving intense sensory stimulation, it remains difficult to determine the precise nature of these behaviors, how common they are within a species, and the neural mechanisms behind them. In this study, using laboratory mice under controlled conditions, we examined whether animals naturally display any stereotypic behaviors in response to and directed toward their unresponsive social partners, which would allow us to address the above questions.

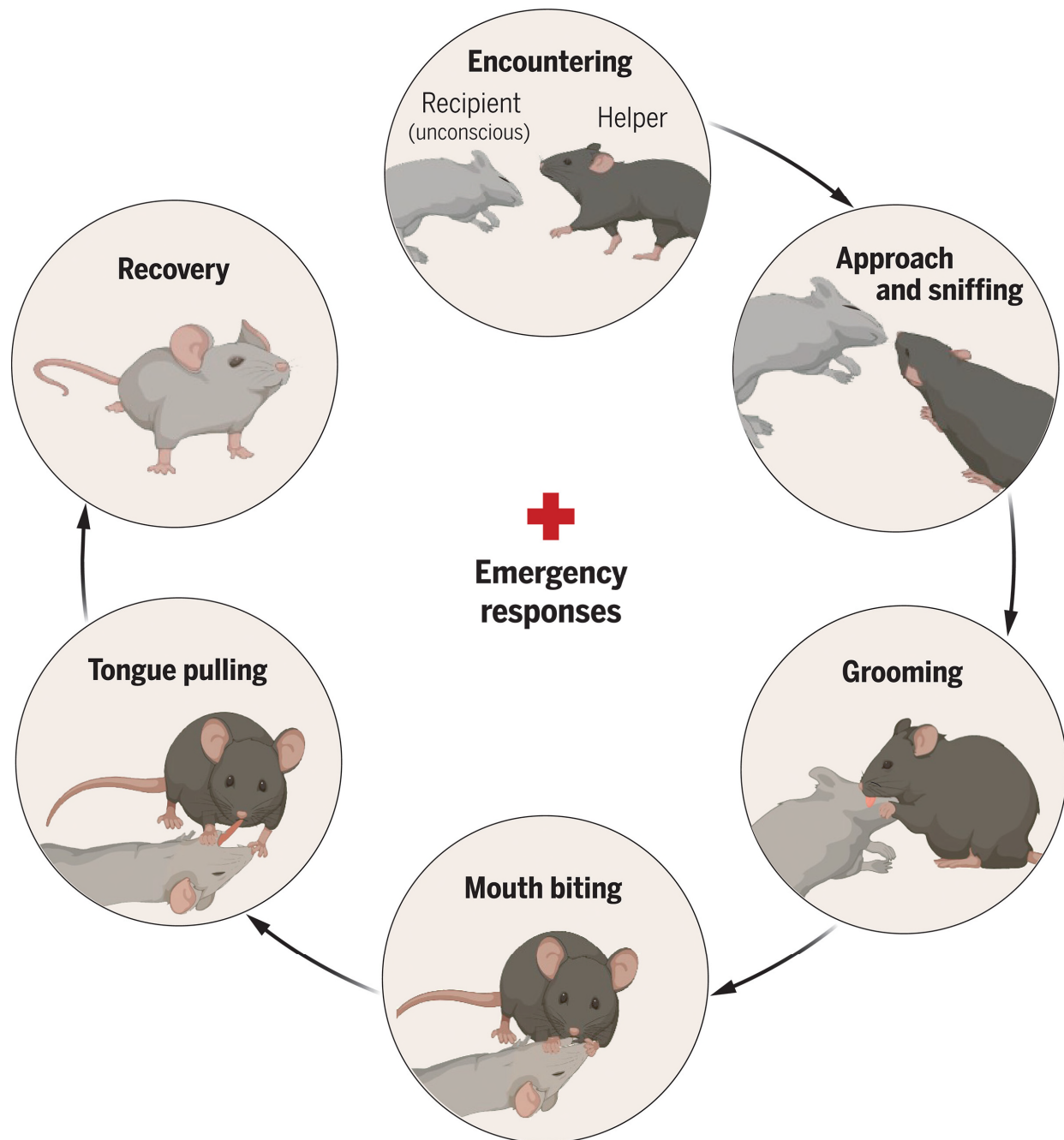
RESULTS

Behavioral monitoring combined with a machine learning–based annotator showed that when mice encountered a familiar social partner in a state of unconsciousness caused by anesthesia, they displayed distinct and consistent behaviors toward the partner, escalating from sniffing and grooming to more forceful actions such as biting the partner’s mouth or tongue and pulling its tongue out. The latter intense actions were also observed in mice interacting with a dead familiar partner but were rarely seen when the partner was active or simply sleeping. These behaviors emerged after prolonged immobility and unresponsiveness of the partner and ceased once the partner regained activity, suggesting that they were triggered by observing unresponsive states of others. These behaviors were strongly influenced by familiarity, being more pronounced in familiar pairs, and were unlikely to have been motivated by a desire for reciprocal social interaction or curiosity about something new. The consequences—including clearance of foreign objects from the mouth, improved airway opening, and hastened recovery—suggest reviving-like efforts. Electrophysiological recordings and microendoscopic calcium imaging showed that oxytocin neurons in the hypothalamic paraventricular nucleus as a population exhibited increased activation in the presence of unconscious, compared with active, familiar partners, suggesting that the activity of these neurons can distinguish between the different partner states. Additionally, increased activity was observed in distinct subpopulations of the oxytocin neurons during specific behavioral actions. Furthermore, optogenetic activation of these neurons promoted reviving-like behaviors, whereas inactivation of them or blocking oxytocin signaling through ventricular administration of oxytocin receptor antagonists impaired the behaviors.

CONCLUSION

Our study reveals a stereotypic set of behaviors in mice directed toward unresponsive familiar peers that appear to facilitate the regaining of responsiveness. Similar to other prosocial behaviors, these behaviors rely on the oxytocin system, which is essentially conserved across

vertebrate species. Our findings thus suggest that animals exhibit reviving-like emergency responses and that assisting unresponsive group members may be an innate behavior widely present among social animals. Such behavior likely plays a role in enhancing group cohesion and survival.



Mouse behaviors toward an unconscious peer.

Mice exhibit a stereotypic set of behaviors when encountering an unconscious social partner, reminiscent of human emergency responses. The behavioral reactions escalate from sniffing and grooming to intense stimulatory actions such as mouth biting and tongue pulling during extended periods of unresponsiveness. These reviving-like actions facilitate the recipient's recovery. [Figure created with BioRender.com]

Abstract

Whereas humans exhibit emergency responses to assist unconscious individuals, how nonhuman animals react to unresponsive conspecifics is less well understood. We report that mice exhibit stereotypic behaviors toward unconscious or dead social partners, which escalate from sniffing and grooming to more forceful actions such as mouth or tongue biting and tongue pulling. The latter intense actions, more prominent in familiar pairs, begin after prolonged immobility and unresponsiveness and cease when the partner regains activity. Their consequences, including improved airway opening and clearance and accelerated recovery from unconsciousness, suggest rescue-like efforts. Oxytocin neurons in the hypothalamic paraventricular nucleus respond differentially to the presence of unconscious versus active partners, and their activation, along with oxytocin signaling, is required for the reviving-like actions. This tendency to assist unresponsive members may enhance group cohesion and survival of social species.

