This Week in The Journal

Oxytocin Promotes Cooperation by Promoting Punishment

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(see pages 5930–5943)

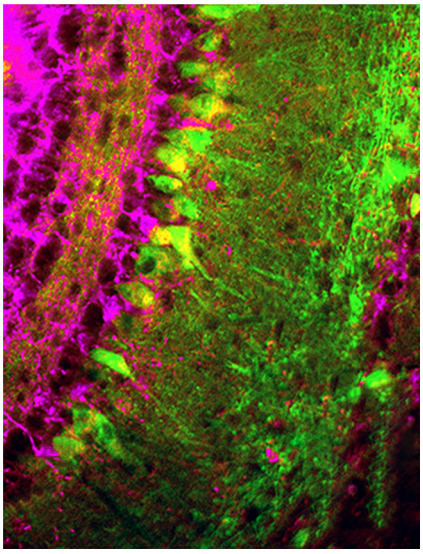
Cooperation allows groups to gain rewards that would be difficult to obtain by individuals working alone. To sustain cooperation, groups often punish members that try to reap rewards without contributing sufficient effort. Remarkably, a single hypothalamic neuropeptide (oxytocin) promotes both cooperation and the willingness to punish selfish behavior. And Li et al. show that administering oxytocin to a few well-connected individuals can increase cooperation levels throughout a group.

Volunteers were assigned to networks that played multiple rounds of economic games. Each network contained a few central players that interacted with relatively large subsets of other players, and several peripheral players that interacted with fewer others. Before the games began, central players received either oxytocin or a placebo. In one game, players assigned to be investors had to trust other players (trustees) to give them a fair return on investments. Central players were always investors, and those that received oxytocin invested more money (indicating more trust in trustees) than those that did not. Knowledge of this apparent trust did not affect subsequent behavior of peripheral investors or trustees, however.

In another game, players designated as proposers were given money to split with players called responders. Responders could reject splits they deemed unfair, in which case neither player would receive anything. All central players were designated responders, and those that received oxytocin demanded a more equitable split than those that did not. The resulting punishment of unfair splits not only caused proposers to offer more money on subsequent rounds, but also led peripheral responders to demand more, until finally proposers offered to split the money evenly.

In a third game, each player chose to cooperate or defect and then were allowed to punish defectors. Players who received oxytocin were more likely to cooperate and more likely to punish. Additional analyses indicated that higher levels of punishment caused other players to cooperate more and to punish defection more, leading to an overall increase in cooperation.

These results, further supported by computer simulations, suggest that elevated levels of oxytocin in a few well-connected individuals can increase cooperation within an entire group, not because oxytocin increases cooperation by the well-connected individuals, but because it increases their propensity to punish noncooperation.



Using CRISPR to inactivate $K_V1.3$ in olfactory bulb M/T cells (pink) increases olfactory discrimination and reduces weight gain in male mice. See Kolling et al. for details.

Olfactory Bulb Neurons Influence Whole-Body Metabolism

Louis John Kolling, Roberta Tatti, Troy Lowry, Ashley M. Loeven, James M. Fadool, et al.

(see pages 5966–5990)

Olfaction helps animals locate food, judge its quality, and enjoy eating it. Surprisingly, olfaction can also influence how food is metabolized by the body. This has been suggested, for example, by studies in mice lacking the voltage-sensitive potassium channel $K_V1.3$. Unlike WT mice, $K_V1.3$-null mice did not gain weight when fed a moderately high-fat diet. This resistance to diet-induced obesity was accompanied by an increase in olfactory sensitivity and was eliminated by removing the olfactory bulb. Pharmacological inhibition of olfactory bulb $K_V1.3$ channels also conferred resistance to diet-induced obesity. Kolling et al. now extend these results by using *in vivo* CRISPR gene editing to inactivate $K_V1.3$ selectively in mitral and tufted cells (M/T cells), the primary output neurons of the olfactory bulb.

As expected, inactivating $K_V1.3$ increased the excitability of M/T cells. This was accompanied by an increase in odor discrimination as assessed by an odor habituation test. More remarkably, inactivating M/T $K_V1.3$ in male mice prevented many of the effects of consuming a moderately high-fat diet. In particular, although mice lacking $K_V1.3$ and control mice consumed similar numbers of calories, those lacking $K_V1.3$ gained less weight, had less abdominal fat, and had lower serum levels of leptin (a hormone produced by adipose tissue) than controls. In addition, liver triglycerides were significantly lower and glucose clearance was faster when $K_V1.3$ was inactivated in M/T cells. Finally, mice lacking $K_V1.3$ ate smaller meals during the day (but not the night) and had a significantly lower respiratory exchange ratio (suggesting greater fat metabolism) during the day relative to controls.

Short-term silencing of M/T cells using designer receptors exclusively activated by designer drugs also altered metabolic indicators in male mice. In a 4 h window after designer drug injection, olfactory discrimination was reduced, as were food consumption, oxygen consumption, and energy expenditure during the night.

These results confirm that changing the activity of olfactory bulb output neurons alters olfactory discrimination and leads to changes in metabolism. Most notably, increasing excitability of these cells increases olfactory discrimination and decreases fat accumulation. Future work should investigate whether metabolic changes result from changes in odor discrimination per se or from altered output to the targets of M/T cells.

This Week in The Journal was written by Teresa Esch, Ph.D.
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