
Temporal–orbitofrontal pathway for integrating reward and perceptual novelty

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Résumé

Humans and other primates interact with the world by observing and exploring visual objects. They especially desire to interact with objects associated with both future rewards and novelty. Despite the importance of object value and novelty, and their behavioral interactions in our daily lives, little is known about how the brain controls decisions in which agents consider both reward and novelty. To study this issue, we focused on the perirhinal cortex (PRH), an area involved in novelty detection that we recently linked to signaling predictions of future novelty to guide novelty seeking behavior (Ogasawara et al., 2022, *Nature Neuroscience*). Notably, PRH strongly projects to the orbitofrontal cortex (OFC), a core region for processing the value of objects and decision offers. We hypothesized that the PRH–OFC pathway critically contributes to the behavioral interaction of novelty and reward in decision making. To assess this, we trained monkeys with a task consisting of several contexts. In the first context, five offers predicted future novel versus familiar objects with five distinct probabilities (% of novel/familiar objects: 0/100, 25/75, 50/50, 75/25, 100/0). Obtaining novel objects was associated with large rewards, while obtaining familiar objects predicted small rewards. Oppositely, in a second context, five other offers also predicted novel objects with the same five probabilities, but here, novel objects were associated with small rewards instead of big rewards, while familiar objects were associated with big rewards rather than small rewards. Hence, in the first context, novel objects had a high reward value, while in the second, they had a low reward value. When given an option to choose among these

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offers, monkeys consistently chose offers more with high expected reward and high expected novelty over offers with high expected reward and low expected novelty, even if their reward probabilities were the same. We next tested whether and how the PRH-OFC pathway contributes to this boosting of reward value by novelty. To do so, we injected an AAV viral vector expressing hM4Di in PRH and performed chemogenetic disruption of the pathway by injecting DCZ into OFC where hM4Di was expressed on PRH axons. This changed the monkeys' preferences, altering the interaction of novelty and reward in their decisions. Our data suggests that the PRH-OFC pathway causally contributes to decisions guided by both reward and novelty, such as those we and other primates often make in our daily lives.