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The Roles of the Orbitofrontal Cortex and Related Brain Regions in Decision-Making in Rodents and Primates

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Abstract: Decision-making is a behavior involving many neuronal processes that is crucial for animals to maximize benefits for survival. The orbitofrontal cortex (OFC) is a brain region known to play critical roles in decision-making in both rodents and primates, and it functions in conjunction with several other brain regions in both species to fulfill decision-making needs. Here we review studies on the specific roles of the OFC and related brain regions in decision-making in rodents and primates, to gain insights on how distinct neural activities in several brain regions functionally contribute to the complex processes required to make a choice. The prefrontal cortex (PFC), the anterior cingulate cortex (ACC), and the striatum work in combination with the OFC to perform the basic processes involved in decision-making, while the basolateral amygdala (BLA) and the hippocampus are implicated together with the OFC in specialized types of decision-making. The specific functions of these brain regions in rodents and primates reveal both preserved and evolved aspects of decision-making mechanisms along the evolutionary lineage.

Keywords: Orbitofrontal cortex, decision-making, reward, choice, outcome.

1. Introduction

Decision-making, the process of evaluating choices to determine the best strategy that maximizes benefits, is a complex behavior involving a series of processes that is essential for animals to ensure survival and maintain well-being. Animals make informed decisions by assigning subjective values to available options, comparing these values to identify the optimal choice, and finally, planning and executing the actions based on the evaluation[1].

The OFC is a brain region in the PFC that is primarily responsible for decision-making. The OFC hosts a variety of neuronal processes that contribute to decision-making, including and not limiting to encoding the integral value of a reward[2], updating reward value based on choice outcome[3], and integrating information previously learned in isolation to guide decision-making strategies[1]. Moreover, the OFC has functional connections with various regions across the brain, each contributing unique yet interconnected roles to decision-making. While the separate roles of the OFC and related brain regions in decision-making have been extensively investigated in previous literature, an integrated overview comparing their distinct roles and how they collectively contribute to the decision-making process remains underexplored. In addition, mechanisms of decision-making in rodents and primates, which are the two models for studying this behavior, have drastic anatomical and functional differences. Therefore, examining these differences in rodents and primates separately

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is essential for understanding species-specific neural circuitry and evolution trajectory of decision-making.

To achieve a comprehensive understanding of how different brain regions of rodents and primates contribute to distinct aspects of decision-making, this paper reviews the roles of the OFC in decision-making processes with the PFC, the ACC, the striatum, the BLA, and the hippocampus. The PFC is an extended structure responsible for executive functions, social cognition, and emotion regulation, containing several sub-divisions involved in decision-making[4]. For example, the ventromedial prefrontal cortex (VMPFC) updates reward values to guide value-based decision-making[5]. The ACC is a limbic structure within the PFC implicated in processing emotion, memory, and actions. It receives information from the OFC about the value of a choice and generates behavioral responses to choices together with the midcingulate motor area[6]. The striatum, a component of the basal ganglia, is responsible for reward processing and behavioral control. It is involved in several neuronal pathways that have essential roles in both reflexive and rational decision-making[7]. The BLA, a subcomponent of the amygdala, is pivotal for behavioral response to emotionally significant events and fear processing. It has bidirectional connections with the OFC and is implicated in adaptive decision-making and the formation of outcome-specific reward memories[8]. Lastly, the hippocampus is a limbic structure critical for the formation of spatial and episodic memories and spatial navigation. It is involved in model-based decision-making and guides choices through encoding memories of past reward values[9].

This review synthesizes findings on the roles of the OFC and its associated brain regions in decision-making across rodents and primates, to providing insights into the distributed neural processes in the brain that underlie this complex behavior. The goal of this review is to elucidate how neuronal pathways in different brain regions and across different species collectively enable the complex decision-making process.

2. Methodology

A comprehensive literature search was conducted using Pubmed and Google Scholar in June 2024. To identify studies that are relevant to the scope of this review, the keywords “OFC”, “[name of a brain region]”, “decision-making”, and “rodent”/“primate” are connected using the Boolean operator “AND”. For example, the query “(((OFC) AND (prefrontal cortex)) AND (decision-making)) AND (rodents)” is used to find studies on the roles in decision-making of the OFC and the PFC in rodents. Studies published in peer-reviewed journals between 2009 to 2024 that have rigorous methodology, obtain statistically significant results, and make conclusions relevant to the scope of this study are included. Studies that are non-peer-reviewed, published before 2009, or present the same findings as a previous study are excluded.

3. The role of the OFC and related brain regions in decision-making in rodents

3.1. The OFC and the PFC

Although decision-making strategies are facilitated by the OFC, the prefrontal cortex (PFC) is likely responsible for executing the action required to obtain a reward based on the choice outcome. Hong et al. (2019) [2] discovered that the OFC and the medial prefrontal cortex (mPFC) showed distinct neuronal activities in response to rewards and during actions in risky decision-making. The authors trained rats for a rat gambling task (RGT) where they choose between a high probability of receiving a small reward or a low probability of obtaining a large reward. Electrodes were then implanted in the ipsilateral OFC and mPFC of rats that consistently preferred the large reward. Rats were subsequently tested on another RGT task where they chose between a small reward associated with a lower probability of punishment or a larger reward with a higher probability of punishment. Rats

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chose the larger reward significantly less after it became associated with punishment. In the OFC, a specific subset of neurons exhibited increased firing frequency in response to the preferred choice, while another group of neurons showed increased firing intensity with larger reward size. This indicates that the OFC encodes the overall value of a choice by integrating information about reward size, probability, and risk, thereby determining and updating decision-making strategies as the value changes. In the mPFC, a subset of neurons was excited by rewards but inhibited during the execution of decision-making actions. This pattern of neuronal activity suggests that the mPFC may play a role in encoding choice outcomes and in maintaining attention or controlling behaviors required for obtaining a reward.

Sul et al. (2010) [3] also examined the roles of the OFC and the mPFC in decision-making processes. In this study, rats were trained using a modified 8-shaped maze on a two-armed bandit task, in which reward probabilities change within one session. Tetrodes were implanted in the mPFC and lateral OFC of rats to record single-neuron activity in these brain regions. The authors found that neural signals related to animals' choice manifested after the choice behavior was completed, neural signals related to choice outcomes increased significantly immediately after the outcome was revealed, and signals related to decision value showed similar temporal patterns in both the mPFC and OFC. In conclusion, while the rat mPFC is involved in controlling behavior, it is likely not engaged in action selection due to the absence of neural signals before a choice.

3.2. The OFC and the ACC

The ACC has crucial roles in encoding the value of a choice by integrating information about the effort required to obtain a choice with the value of reward. Fatahi et al. (2020) [10] demonstrated that both the OFC and ACC are involved in effort-based decision making. The researchers implanted bipolar recording electrodes into the left ACC and the OFC of rats individually. Then, the rats performed a T-maze decision-making task, choosing between high effort for a large reward and low effort for a small reward. Wavelet analysis revealed increased neural synchronization in the ACC and the OFC in theta and low beta frequency bands when animals preferred the larger reward with high effort, and a high gamma synchrony between the ACC and the OFC. These results indicate that neural synchronization between the ACC and OFC is crucial for effort-based decision-making, with the ACC likely evaluating the trade-off between effort and reward size to assist decision-making.

3.3. The OFC and the striatum

The striatum receives and processes reward information from the OFC to guide decision-making strategies. Gore et al. (2023) [1] found that the OFC and the dorsomedial striatum (DMS) are both involved in economic decision-making. In this study, rats performed a behavioral task in which they choose between two options based on a visual cue indicating the type and quantity of rewards for each option. Optogenetic inhibition of the OFC or DMS of rats was conducted when the rats evaluated the cues. The findings suggested that inhibition of the OFC and the DMS both interfered with economic decision-making. Specifically, choice prediction in the OFC precedes that in the DMS, and inhibition of axonal projections from the OFC to the DMS impaired decision-making related to reward volume, but not reward type preferences. Thus, the DMS receives reward quantity information from the OFC, while additional output pathways from the OFC may convey reward type information.

3.4. The OFC and the BLA

The BLA encodes choice values by integrating reward and punishment information, which is then relayed to the OFC to generate a decision-making strategy based on all past outcomes. Zeeb and Winstanley (2013) [11] found that the connection between OFC and BLA is important for both encoding the expected value of each choice and updating choice pattern in response to changes in reward value. The authors performed contralateral lesions of the OFC and the BLA in rats; then trained them for a RGT in which a rat makes a nose-poke in an illuminated hole to obtain a food reward, with each hole offering a different maximum number of rewards per trial. Subsequently, rats underwent satiety manipulations and were re-tested on the RGT again. The study found that rats with lesions learned the optimal strategy at a slower rate. Additionally, the choice preferences of lesioned rats were not altered by satiety manipulations, whereas choice preferences of control groups were. These results show that communication between the OFC and the BLA is vital for updating decision-making strategies based on choice outcome and for adapting decision-making strategies based on changes in reward values. Their findings suggest that input from the BLA may contribute to encoding the state information of each choice in the OFC.

Moreover, Orsini et al. (2015) [12] investigated the distinct roles of the OFC and the BLA in adaptive decision-making with risk of explicit punishment. In their study, rats received bilateral lesion of either the BLA or of the OFC. Rats were tested on a risky decision-making task before and after surgery, where they choose between a small food reward with no punishment or a large food reward with a certain probability of punishment. Post-surgery, rats with BLA lesions chose the large risky reward considerably more frequently, whereas rats with OFC lesions chose the large risky reward considerably less frequently even at low probability of risk. Moreover, rats with BLA lesions had shorter latencies and rats with OFC lesions had longer latencies to make the risky choices. Thus, the BLA may be responsible for integrating information about the risk of punishment with the reward value, potentially receiving this information from upstream structures. A potential explanation for the risk-aversion induced by OFC lesion is that OFC facilitates model-based decision-making in which probability of punishment is calculated using an internal model based on past experiences. Consequently, OFC-lesioned rats may exhibit model-free behavior, making decisions solely based on outcome of the previous choice and avoiding risk even when the probability of risk is minimal.

3.5. The OFC and the hippocampus

The hippocampus is implicated in associative learning in memory-guided decision-making. Lin and Zhou (2024) [13] showed that the rodent OFC and hippocampus play essential roles in learning associations between environmental stimuli and reward. The researchers trained mice to learn distinct sequences odors, each associated with a reward. The four odor sequences form two sequence structures, or how the sensory stimuli are related to the outcome. Calcium imaging data revealed that both the OFC and the hippocampus have neural activities that distinguish between sequences paired under the same sequence structure, which is evidence for the formation of associative memory. Specifically, similar signals were found in the OFC for sequences that had similar expected outcome, and signals that differentiate sequences based on the temporal order of odor cues were found in the hippocampus. Hence, the authors conclude that the OFC and the hippocampus have distinct and complementary activities that jointly produce associative learning.

4. The role of the OFC and related brain regions in decision-making in primates

4.1. The OFC and the PFC

The primate PFC is implicated in representing aspects of choice values and generating choice strategies. Rudebeck et al. (2017) [14] investigated the roles of the OFC and the ventrolateral prefrontal cortex (VLPFC) in encoding the valuation of outcomes in decision-making. Monkeys were assessed on two behavioral tasks: one tested their ability to adjust strategies based on updated reward probabilities, and the other evaluated choices made based on reward desirability. Performance on the behavioral tasks of unoperated monkeys, monkeys with lesion in the OFC, and monkeys with lesions

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in the VLPFC were evaluated. The authors found that the OFC and the VLPFC have dissociable roles in evaluating choices: the OFC and not the VLPFC guided choices by encoding the desirability of a reward, while the VLPFC and not the OFC represented the changing probabilities of outcomes. The findings suggest that separate signals from the OFC and VLPFC may converge in the mPFC to guide decisions.

Cai and Padoa-Schioppa (2014) [15] further examined how the VLPFC and the dorsolateral prefrontal cortex (DLPFC) are involved in transforming decisions into actions. Monkeys performed a behavioral task in which they make choices based on the abstract representations of options without direct action-outcome associations. Recording of neural activity found that the OFC encoded the value of a chosen reward before information about the action required to make the choice was available, suggesting that it makes abstract representations of choices. The VLPFC and DLPFC initially encoded outcomes in goods space but then encoded the spatial location and represented the action plan for obtaining a choice. Hence, the researchers concluded that the VLPFC and DLPFC transform decisions into action plans and then produce actions via projections to motor structures.

4.2. The OFC and the ACC

The OFC and the ACC exhibit distinct yet complementary roles in decision-making, particularly in encoding choice outcomes based on different types of associations. The ACC is a part of the mPFC in primates. A study by Luk and Wallis (2013) [16] investigated how the ACC and the OFC participate in stimulus-outcome associations and action-outcome associations. Rhesus monkeys were trained for a two-phase behavioral task composed of alternating blocks: in the stimulus-outcome block, the monkeys selected an image associated with its preferred reward; then, in the action-outcome block, the monkey repeatedly moved a lever to one side to receive more units of the preferred reward. The activities of single neurons in the ACC and the OFC were measured as the monkeys performed the two tasks. The researchers found that a small number of neurons encode for the predictor-outcome association in both brain regions, but their roles differ. The OFC showed stronger activity in stimulus-outcome associations, while the ACC exhibited greater activity in action-outcome associations. These results indicate a division of labor between the two regions, with the OFC and the ACC encoding different types of associations . Additionally, the authors suggested that complex interactions between the OFC and various brain regions contribute to decision-making, challenging the notion that a downstream process integrating reward value with effort value is solely responsible for making a choice.

Furthermore, functional connectivity between the OFC and the ACC in primates is implicated in producing the motor output for decisions. Balewski et al. (2023) [17] investigated how neural connectivity between the OFC and ACC allows for the encoding of a choice response based on the value of each option as represented in the OFC. Two macaque monkeys performed a binary choice task in which they were either free to choose one of two presented images or are forced to choose one image, with each image associated with a different probability of reward. Electrodes were implanted in the OFC and the ACC, and the activities of single neurons were measured overtime. The authors found that activities of ACC neurons were affected by the OFC particularly during the encoding of the more valuable option. Specifically, ACC neurons displayed increased ramping activity when the OFC encoded the more valuable option for a longer duration and more frequently. This suggests that the ACC may bias its encoding toward generating a choice response associated with the more valuable options. The results are coherent with previous evidence showing that the ACC encodes for motor control following fluctuating value signals encoded by the OFC. Additionally, the authors proposed that the OFC-ACC interaction, along with contributions from other regions such as the lateral prefrontal cortex, collectively produce the motor output of a choice response.

4.3. The OFC and the striatum

The striatum and the OFC collaboratively encode expected value in economic decision-making in primates. Yamada et al. (2021) [18] showed that the central OFC (cOFC) and the ventral striatum (VS) had distinct roles in representing the expected value of a choice. In a visually cued lottery task, monkeys chose between two pie charts, each indicating a different probability and magnitude of a fluid reward. Neural activities of the cOFC, medial orbitofrontal cortex (mOFC), dorsal striatum (DS), and VS were collected when the monkeys evaluated the choices. Analysis of neural population data found that the cOFC and the VS both showed stable signals that encode for expected value, whereas signals in the mOFC and the DS were weaker. Moreover, expected value signals in the cOFC and the VS displayed distinct temporal patterns, indicating that the encoding of expected value was partially overlapping yet distinct process in these regions. The authors hence conclude that the OFC-striatum circuit is implicated in the computation of expected values in primates.

Additionally, the striatum and the OFC work together to produce a distributed value representation to guide decision-making. A study by Ebitz et al. (2020) [19] explored how neuronal circuits in the OFC, VS, and DS process rules to make choices. In the study, macaques performed a cognitive set-shifting task, in which they chose specific symbols with various colors and shapes. In each trial, the researchers set a single correct shape or color feature, and only choices that matched the correct feature were rewarded. Neural recordings revealed that representation of choice features during rule-based decision-making was expanded across the OFC, VS, and DS, evoking similar neural activities that were distributed among these regions. In contrast, representations of non-rule-based decisions were compressed, enabling rule-relevant information to dominate decision-making. Additionally, sparser population activity was observed in the VS during rule-based decision-making but in the DS and the OFC during non-rule-based decision-making. The results reveal that computational cost of decision-making is lowered in rule-based contexts due to expansion of rule-relevant dimensions in all the studied brain regions.

4.4. The OFC and the BLA

The BLA has previously been found to play a critical role in encoding value representations during decision-making in primates, similar to its function in rodents[11]. A study by Jezzini and Padoa-Schioppa (2020) [20] investigated the specific roles of the OFC and the BLA in encoding value in economic decision-making in rhesus monkeys. Monkeys were trained to select one of two visual patterns, each associated with a different combination of juice rewards. Neural recordings from the amygdala and OFC during the task revealed that the BLA robustly encoded the subjective value of a choice and the values of individual juices. In contrast, the OFC had a significantly smaller number of neurons with less sustained activity encoding for the value of a choice. This study shows that the BLA may have a more prominent role in value representation and reward expectation than the OFC in primates.

4.5. The OFC and the hippocampus

The primate hippocampus is responsible for making context-dependent choices in decision-making tasks that require memory of past experiences. Mizrak et al. (2021) [21] showed the collective roles of the OFC and the hippocampus in memory-guided decision-making in humans. In the study, participants learned to associate several categories of food stimuli with either a “like” or “dislike” reaction of a customer in the imagined context of purchasing products from several grocery stores. Then, participants performed a binary decision-making task by selecting the correct reaction of the customer with a presented food type in a specific grocery store context while undergoing fMRI imaging. The choices involved in the behavioral task were categorized into two different task

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structures (i.e. context-dependent and context-independent choices). Although participants were not explicitly informed on the two categories, fMRI data showed distinct roles for the OFC and the hippocampus. The OFC represented the overarching task structures whereas the hippocampus encoded choice-relevant information that differentiate between context-dependent and context-independent choices.

5. Discussions

This paper has reviewed the roles of the OFC and related brain regions in decision-making across rodents and primates. In both species, the OFC plays a central role in encoding reward values, integrating information, and producing decision-making strategies.

The prefrontal cortex exhibits species-specific differences in decision-making roles. The rodent mPFC is considered as analogous to the primate VLPFC, and they are both responsible for encoding the outcomes of choices. Nonetheless, while the rodent mPFC is involved in controlling the behavioral response to a choice and not responsible for action selection, the primate VLPFC produces action plans for decisions. The ACC is specialized in assessing and executing actions needed to acquire a reward. In both rodents and primates, it forms associations between action and outcome. Evidence from neuronal recordings highlights the functional connection between the ACC and the OFC, showing that these regions interact to generate the motor output of making a choice. The ACC may have downstream connections that produce the behavioral response of making a choice. The striatum plays a key role in economic decision-making alongside the OFC. The rodent DMS guides decisions related to reward volume, while the primate VS is similarly involved in outcome evaluation by encoding the expected value of reward in collaboration with the OFC. Moreover, the primate VS and DS have distributed functions in processing rules together, guiding rational decisions in contexts that require economic decision-making.

The specific contributions of the PFC and the striatum to decision-making vary across species, suggesting potential evolutionary distinctions in neural circuitry. In primates, the more extensive PFC, compared to rodents, supports more specialized functions that are distributed across sub-divisions, such as VLPFC and DLPFC, which are responsible for transforming decisions into action plans. In contrast, the rodent mPFC handles more general behavioral control. Also, the primate striatum is larger and has more extensive neural architecture than the rodent striatum, allowing for distributed functions in combination with the OFC in reward expectation and rule processing, which are absent in rodent striatum.

The OFC, the PFC, the ACC, and the striatum may form a functional network responsible for the principal processes in decision-making. The OFC encodes the expected value of a reward and is connected to structures in the striatum that contribute to assigning values to rewards to guide economic decisions. Once a decision is made, the PFC generates a plan for the course of action or controls the decision-making behavior. Then, the ACC produces a motor output to complete choice selection.

The amygdala and the hippocampus may be considered as secondary regions to the decision-making network that are responsible for specific types of decision-making. The BLA encodes reward values of a choice in both rodents and primates. Lesion studies in rodents reveal the role of BLA in updating decision-making strategies in contexts involving satiety and punishment, whereas recordings of neural activity in the primate BLA and OFC discover that the BLA is responsible for encoding the subjective value of a choice. The BLA receives inputs of sensory information to process the emotional significance of a stimuli and initiates behavioral responses to fear[22], possessing the necessary sensory inputs and neuronal pathways to assign subjective value to a reward and aid in the formation of decision-making strategies together with the OFC. Moreover, the hippocampus supports memory-guided decision-making in both rodents and primates. The hippocampus forms associative memory based on temporal sequence of stimuli in rodents and represents choice-relevant information based on memorized contexts in primates. The hippocampus processes episodic memories, so it contributes to decision-making tasks that require the integration of complex sequences of stimuli.

6. Conclusion

This review highlights both shared mechanisms and species-specific adaptations in the neural processes underlying decision-making across rodents and primates. Several brain regions function in conjunction with the OFC to perform the complex behavior of decision-making in rodents and primates. In sum, decision-making involves functional contributions from multiple specialized regions distributed across the brain. Along the evolutionary lineage, both rodents and primates show this pattern of neural activity, reflecting an intricate communication of distributed neural systems evolved to adapt to varying environmental and behavioral demands.

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