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Contrasting reward signals in the orbitofrontal cortex and anterior cingulate cortex

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Damage to the orbitofrontal cortex (OFC) and anterior cingulate cortex (ACC) impairs decision making, but the underlying value computations that cause such impairments remain unclear. Both the OFC and ACC encode a wide variety of signals correlated with decision making. The current challenge is to determine how these two different areas support decision-making processes. Here, we review a series of experiments that have helped define these roles. A special population of neurons in the ACC, but not the OFC, multiplex value information across decision parameters using a unified encoding scheme, and encode reward prediction errors. In contrast, neurons in the OFC, but not the ACC, encode the value of a choice relative to the recent history of choice values. Together, these results suggest complementary valuation processes: OFC neurons dynamically evaluate current choices relative to the value contexts recently experienced, while ACC neurons encode choice predictions and prediction errors using a common valuation currency reflecting the integration of multiple decision parameters.

Key words: anterior cingulate cortex; decision making; neurophysiology; orbitofrontal cortex; prediction error; reward

Studies using functional magnetic resonance imaging (fMRI) typically show activation of the orbitofrontal cortex (OFC) or anterior cingulate cortex (ACC) when investigators manipulate factors relevant to decision making such as reward size,[1,2] proximity to reward delivery,[3,4] outcome likelihood,[5] and even abstract factors such as trust.[6,7] Neurophysiological studies reveal that neurons encoding such parameters are prevalent in both the OFC[8–12] and ACC.[13–16] Neuropsychological studies show that damage to either OFC[17–21] or ACC[22–26] produces impairments in decision making. In contrast, damage to other parts of the frontal cortex, such as the lateral prefrontal cortex (LPFC), typically impair other cognitive processes, but leave decision making intact.[27,28] Despite this abundance of evidence that the OFC and ACC are critical to the neural implementation of decision making, their precise contribution to the process remains unknown. In this paper, we review a series of experiments that we have performed in order to differentiate the roles of the OFC and ACC.

Multidimensional decision making

Our first experiment examined whether OFC and ACC neurons encoded different types of decision parameters.[29] We trained two monkeys on a multidimensional choice task that involved making choices between 30 different pictures. Each picture was associated with a different behavioral outcome. The outcomes associated with different sets of pictures varied in terms of either their payoff (volume of juice delivered), effort (number of lever presses necessary to earn a specific quantity of juice), or probability (probability that a specific quantity of juice would be delivered). We simultaneously recorded neuronal activity from the OFC and ACC, as well as the LPFC. Figure 1 illustrates the activity of three neurons when the subject evaluated choices of different value, across the three different decision variables. Neurons encoded value across the different decision variables in diverse ways. For example, the neuron in Figure 1A increased its firing rate as the probability

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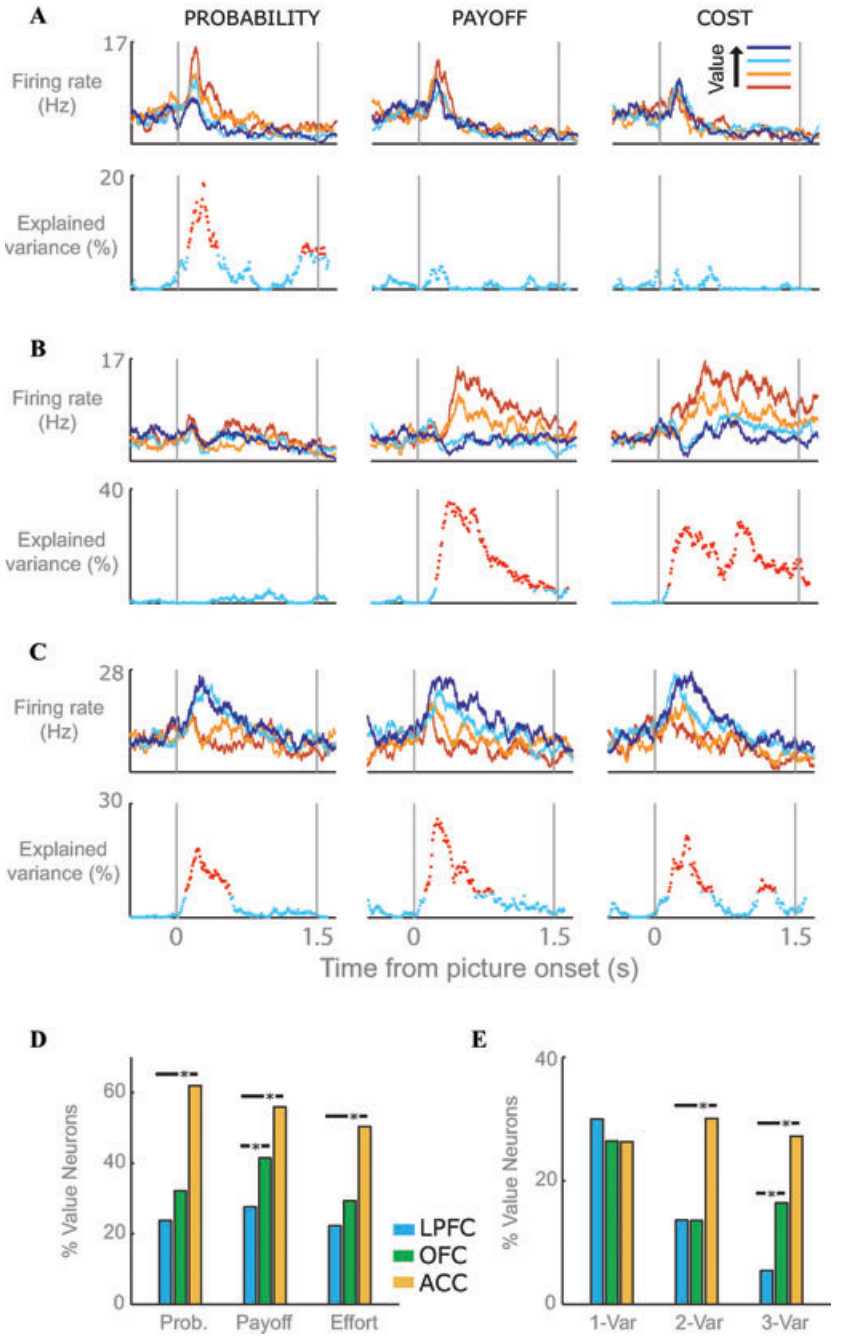

Figure 1. (A) A neuron that encoded the value of the probability pictures. It showed an increase in firing rate as the value of the choice decreased. The top row of plots consists of spike density histograms sorted according to the value of the choice. The vertical lines relate to the onset of the pictures and the time at which the subject was allowed to make his choice. The lower row of plots indicates the percentage of variance in the neuron's firing rate that can be explained by the value of the choice as determined by a linear regression. Red data points indicate time points where the value of the choice significantly predicted the neuron's firing rate. (B) A neuron that encoded the value of the payoff and cost pictures, but not the probability pictures. It showed an increase in firing rate as the value of the choice decreased. (C) A neuron that encoded value for all three decision variables, showing an increase in firing rate as value increased. (D) Percentage of all neurons selective for value for each decision variable. The ACC contained the most neurons encoding each variable. (E) Percentage of all neurons selective for value as a function of number of decision variables encoded. ACC and OFC neurons tended to multiplex decision value across two and three decision variables.

of reward decreased but did not encode decisions involving payoff or effort manipulations. Other neurons encoded the value of choices for two of the decisions but not the third (Fig. 1B), while still others encoded value across all three decision variables (Fig. 1C).

There was no evidence that the OFC or ACC preferentially encoded one of the decision variables. In all brain areas, we saw neurons that represented every decision variable and every combination of decision variables (Fig. 1D). However, there were differences between the areas. The prevalence of neurons encoding a single decision variable was similar in all areas, but neurons encoding two or three decision variables were more prevalent in the OFC and ACC than in the LPFC (Fig. 1E). In addition, we noted that some neurons increased their firing rate as the value of the choice increased (e.g., Fig. 1C), while others increased their firing rate as the value of the choice decreased (e.g., Fig. 1A and B). In fact, there was an approximately equal number of neurons that increased their firing rate as the value increased (49%) as increased their firing rate as the value decreased (51%), with no specific topographic distribution of these neurons. In other words, neighboring neurons encoded the same value parameter by using opposite encoding schemes. When we examined the average amount of value information encoded by the positive and negative valence populations, we found that all value information at the population level averaged to zero.[30] These results have important implications for neuroscientific investigations of decision making, as methodologies that average the neuronal response across populations of neurons (e.g., fMRI and event-related potentials) may not be sensitive to detect these value signals. Summing together neurons with equally prevalent but opposing encoding schemes would average out this information. This highlights how the spatial and temporal resolution of single unit neurophysiology can contribute to our understanding of the neuronal mechanisms underlying decision making.[31]

These results were the first to contrast directly the encoding of decision-related information in the ACC, OFC, and LPFC. They show that the areas do not differ in the nature of the decision variables that they encode: neurons encoding probability, payoff, or effort were equally prevalent in all three areas. However, the key difference was whether neurons encoded a multiplexed representation of decision-related information. This was most prevalent in the ACC and least prevalent in the LPFC. A multiplexed representation may allow the integration of the individual components of a decision and underlie the critical contribution of the ACC and OFC to decision making. Integrating the various components of a decision into a more abstract measure of value could be useful when decisions involve comparison of widely divergent outcomes. Neuroimaging results are consistent with a role for the OFC in this process. The medial OFC is activated in humans when they are making comparisons between goods whose attributes are not directly comparable (e.g., a USB key vs. a box of chocolates).[32] Furthermore, patients with large lesions encompassing the OFC and the adjacent ventromedial prefrontal cortex alter the way in which they choose to acquire information when making complex decisions. The patients prefer to compare all the attributes of a single available option (in this case, an apartment) rather than evaluating across all available options on an selected set of attributes (for instance, the price or number of bedrooms).[18]

Range adaptation of value signals

Our results so far showed that there was no difference between OFC and ACC neurons in the type of decision information that they encoded. Furthermore, although ACC encoding tended to be stronger, activate more neurons, and was more likely to multiplex across value parameters, there was little to suggest that these signals played a different functional role in the two areas. However, when we looked in more detail at the value signals, differences began to emerge.

One problem with a neuronal representation of value is that neuronal firing rates can only range between about 0–100 Hz, but the value of an outcome can vary by many orders of magnitude. For example, we can quickly transition from choosing what house to buy, to choosing what to order for lunch. How can neurons represent such dramatically different values? One possibility is that, rather than representing value on an absolute scale, neurons could represent the value of an outcome relative to a restricted set of other potential outcomes.[33,34] This would require neurons to adapt their dynamic firing rate range depending on the choice environment. When you are choosing between houses, the neurons would adapt

their range so that large changes in absolute value would be needed to modulate firing rates. When you are choosing lunch, the neurons would adapt their range so that small changes in absolute value would modulate their firing rate.

If these ideas are correct, then encoding of the choice's value may depend on the local history of choices. If the subject has experienced a sequence of low-value choices, neurons will adapt so that small absolute differences in value will be able to change their firing rate. In contrast, if the subject has experienced a sequence of high-value choices, large absolute differences in value will be needed to change neuronal firing rates. Figures 2A and B illustrate a neuron showing trial-by-trial range adaptation. This neuron increased its firing rate as the value of the current choice increased (left-most plot). Additionally, when the trials are sorted by the previous trial's value (N − 1), firing rate increased both as the current trial value increased and as the previous trial value decreased (four rightmost plots). In other words, the neuron showed a higher firing rate as the value of the current trial increased, but this effect was magnified when the previous trial had been low value, exactly as one would expect from range adaptation.

At the population level, range adaptation should be evident as a negative correlation between the effect of the previous trial value and the effect of the current trial value on neuronal firing rates. Figure 2C shows that such a correlation did exist, but only in the OFC.[30] This correlation emerged 300 ms into the current choice, consistent with when the current choice would be evaluated. We could also look at two trials in the past (N − 2). Here, the effects were weaker but still significant in the OFC (Fig. 2D). Thus, OFC neurons were not simply encoding the value of the current choice relative to the previous choice, but rather were modulating their firing rates according to the local history of choices.

Frontal coding of prediction errors

So far, we have only considered neuronal activity during the evaluation of the choice options, where neurons encode the value of the expected outcome of the choice. A critical question is what happens if the value of the actual outcome is not what the animal was expecting because, for an organism to learn, it is imperative that it modifies its behavior when outcomes are not as expected. To investigate this, we focused our analysis on the probability trials, since the payoff and cost trials did not involve unexpected outcomes.

Many neurons responded to the receipt of the delivery of the reward in a way that depended on the subject's prior expectancy of receiving a reward. An example is shown in Figure 3A. This neuron showed an increase in firing rate when the subject received a reward, but only when the subject was least expecting it—that is, when the probability of receiving a reward was 0.3 or 0.5. When the probability of receiving a reward was 0.7 or 0.9, the neuron showed little response. In addition, the neuron showed little response when the monkey did not receive a reward, irrespective of the subject's prior expectancy. In other words, the neuron appears to respond whenever something happens that was better than the animal expected. Such a signal is referred to as a positive prediction error and is similar to that seen in dopamine neurons.[35] These signals are very important in models of learning, since they enable an organism to adapt its future behavior to maximize reward.[36] Some prefrontal neurons showed the opposite response, that is, a negative prediction error, and encoded when events occurred that were worse than expected. For example, the neuron in Figure 3B encoded events that were worse than expected. It did not respond to reward delivery, but rather responded when no reward occurred, particularly when the subject was expecting to receive one (i.e., on those trials where reward occurred with a probability of 0.9). Similar signals have also been observed subcortically, specifically in the lateral habenula.[37]

A second type of neuronal encoding was similar during both the presentation of the pictures and the receipt of the actual outcome. For example, the neuron in Figure 3C responded to the least valuable pictures during the choice phase and then showed the same pattern of encoding during the outcome phase when the subject received a reward. It is important to note that the events occurring at the outcome phase were identical across all trials: the subject was receiving a drop of juice. However, the neuron's response was different depending on the subject's prior expectancy of receiving the reward, with the neurons appearing to replay the original prediction.

We subsequently quantified the proportion of neurons that showed these different patterns of selectivity across the three different prefrontal areas (Fig. 4A). The proportion of neurons that encoded value only during the choice phase was consistent

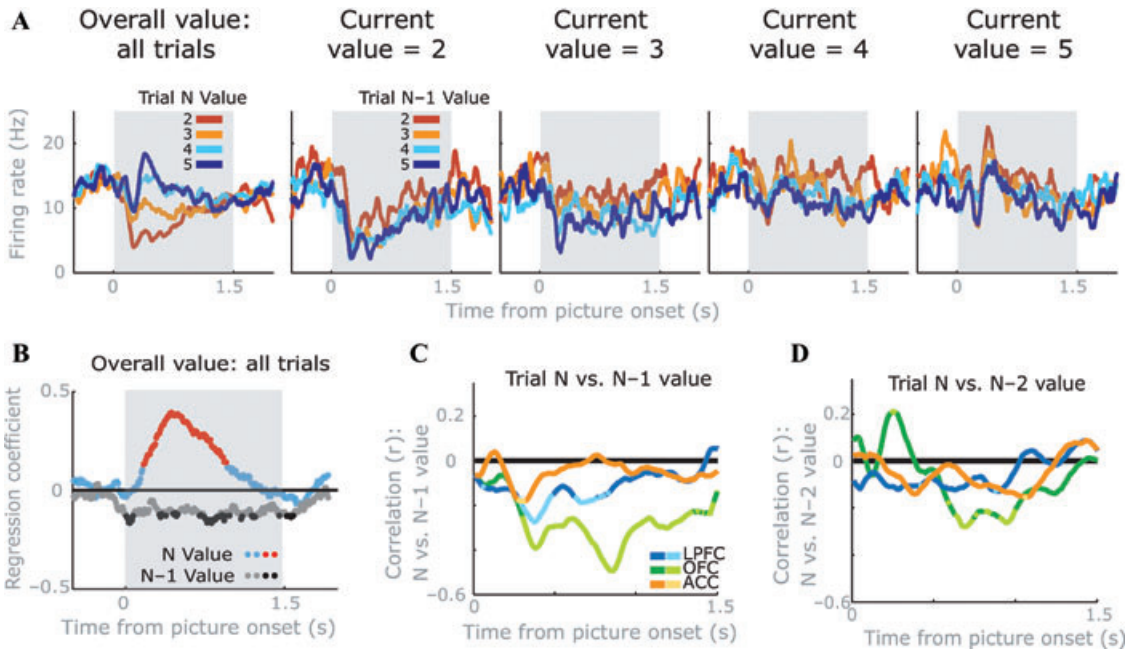

Figure 2. (A) An OFC neuron encoding current and past trial choice value. This neuron increases firing rate as current choice value increases (left-most plot). Additionally, when the trials are sorted by the N − 1 trial value, firing rate increases both as the current trial value increases and as the previous trial value decreases (four right-most plots). Thus, this neuron is modulated by the difference in the current and past trial value. (B) Dynamics of the encoding shown in A as determined from the coefficients of a regression model to quantify the influence of the value of the current and immediately preceding trial on the neuron's firing rate. Significant bins for current and N−1 value are shown by red and black symbols, respectively. Mean correlation (r) between regression coefficients for encoding value of the (C) current and previous trial or (D) current and two trials ago. Brighter colors signify the bins where the correlation was significant ($P < 0.01$).

across all three areas. However, the ACC differed from both the OFC and LPFC in that it contained many neurons that encoded value during both the choice and outcome phases.[30] Among these neurons, there was an even split between those that encoded value in a manner similar to a prediction error and those that replayed the choice value signal. Both types of signal could be useful for learning since they provide a link between the actual outcome and the predictions at the time of the choice. Other groups have found that ACC neurons can also encode a saliency signal (i.e., whether an outcome was unexpected irrespective of whether it was better or worse than expected)[38] as well as "fictive" error signals, neuronal responses to outcomes for actions that one did not take.[39] This emphasis on the importance of the ACC for learning is consistent with other conceptualizations of ACC function. For example, human neurophysiological results suggest that midline frontal areas are important for monitoring the outcome of one's actions. This is most commonly described in relation to the error-related negativity,[40] a negative electrical potential that is associated with the occurrence of errors. However, it is becoming increasingly apparent that midline frontal potentials can also be evoked by unexpected positive events[41] consistent with a more general role in learning.[42]

We noticed two other properties of ACC neurons. First, the direction of value encoding at the time of the choice distinguished the type of signal that would be encoded at outcome—prediction error versus value replay (Fig. 4B). ACC neurons that encoded positive prediction errors were significantly more likely to show a positive relationship between firing rate and probability during choice. In contrast, neurons that encoded a value replay signal on rewarded trials were significantly more likely to show a negative relationship between firing rate and probability during choice. Thus, if an outcome selective neuron coded reward probability positively at choice, then it flipped sign and encoded a

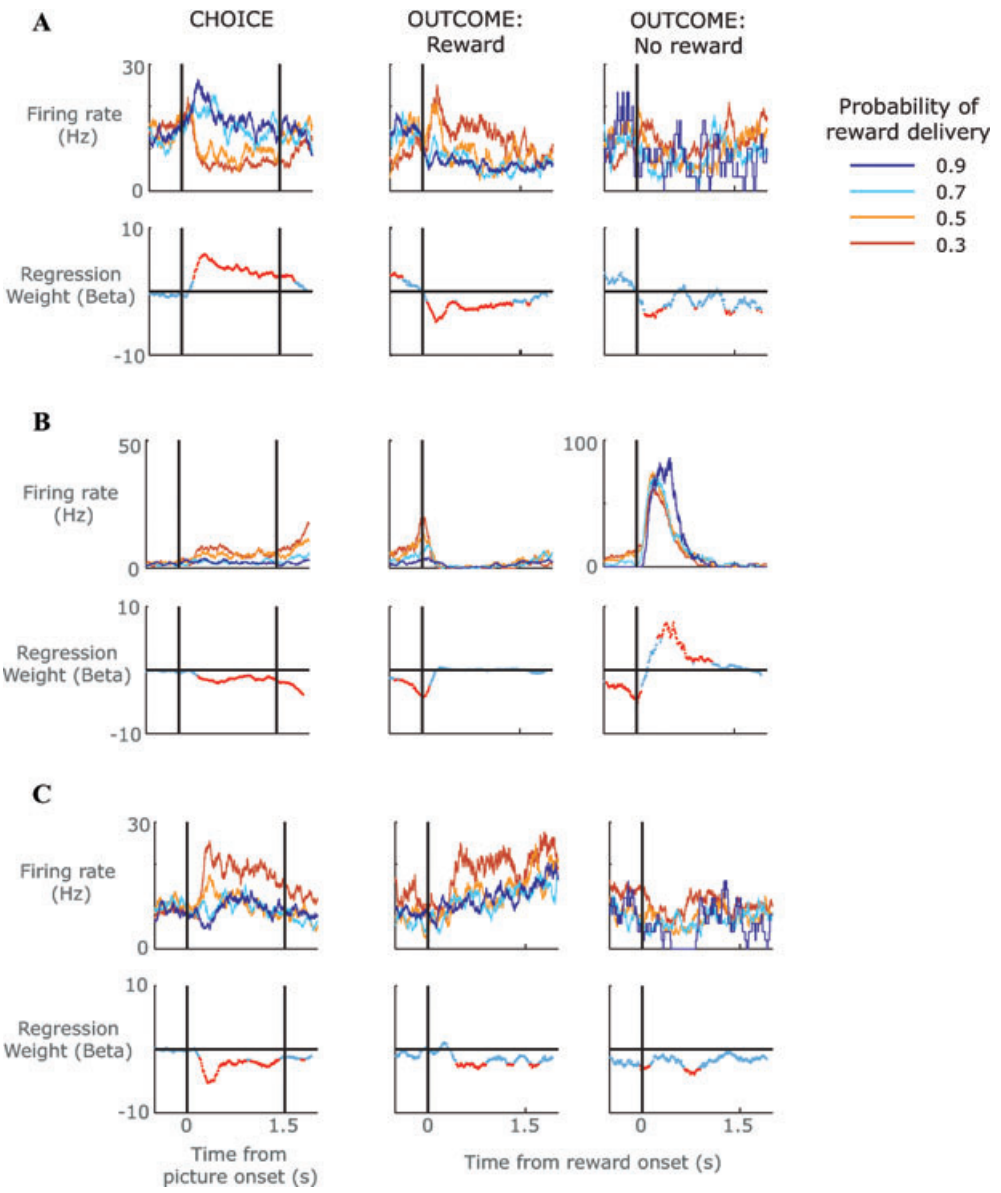

Figure 3. (A) The top row of plots consists of spike density histograms sorted according to probability of reward delivery, as indicated by the pictures. The three plots show activity during the choice phase, the outcome phase when a reward was delivered, and the outcome phase when a reward was not delivered. For the choice phase, the vertical lines relate to the onset of the pictures and the time at which the subject was allowed to make his choice. For the outcome phase, the vertical line indicates the onset of the juice reward. The lower row of plots indicates the results of a regression analysis, testing the relationship between the neuron's firing rate and the probability of reward delivery at each time point. Red data points indicate time points where the probability of reward delivery significantly predicted the neuron's firing rate. The neuron encoded a positive prediction error—that is, it responded when events occurred that were better than expected. The neuron responded during the choice phase when pictures appeared that predicted reward delivery with high probability. It also responded during reward delivery, but only when the subject was least expecting to receive the reward. It showed little response when the subject did not receive a reward. (B) A neuron that encoded a negative prediction error—that is, it responded when events occurred that were worse than expected. The neuron responded when pictures appeared that predicted reward delivery with low probability, showed little response to the delivery of reward, and responded when reward was not delivered, particularly when the subject was expecting to receive a reward. (C) A neuron that replayed the signal observed during the choice phase at the time of reward delivery. During the choice phase the neuron showed its highest firing rate to the pictures that predicted reward delivery with low probability. This same signal occurred again at the time of reward delivery.

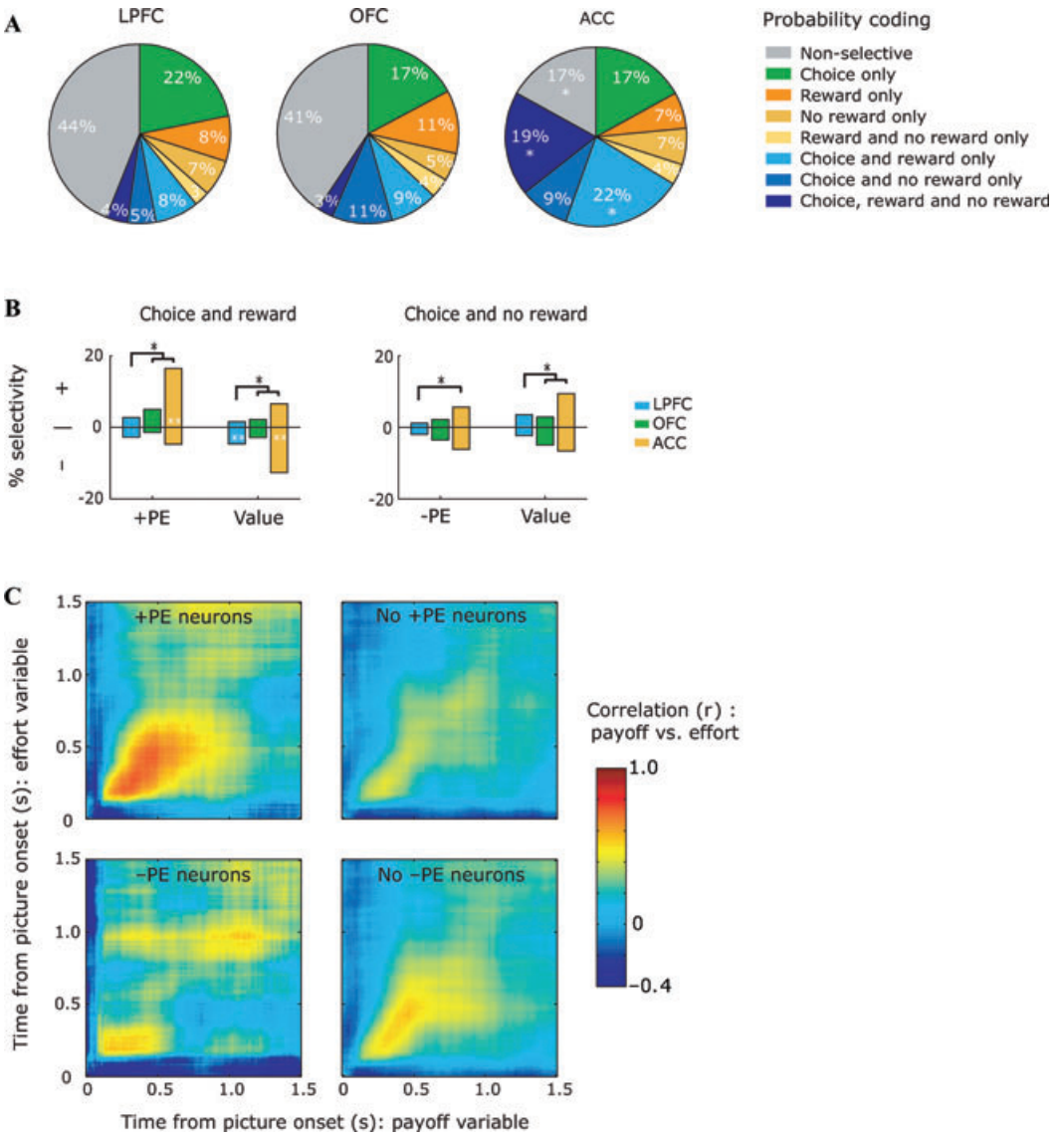

Figure 4. (A) Prevalence of neurons encoding probability during different task events (choice, rewarded outcomes, and/or unrewarded outcomes). Asterisks indicate that the proportion in the ACC significantly differs from that in the LPFC and OFC (chi-squared tests, $P < 0.05$). More ACC neurons encoded reward probability during both choice and outcome phases (blue shading). (B) Bar plots summarizing the different schemes encoding the probability of receiving a reward. Prediction error (PE) neurons encode probability in opposite directions during the choice phase and outcome phase, while value neurons encode probability in the same direction during both phases. Neurons are sorted on the *y*-axis according to whether they encode probability during the choice phase with a positive or negative relationship (+ or −). Single black asterisks indicate significant differences between PFC areas (chi-squared tests, $P < 0.05$). Consistent with the plots in A, ACC neurons are more likely to show encoding during both the choice and outcome phases of the task. Double white asterisks indicate that the proportion of neurons showing positive or negative encoding was significantly different from the chance 50/50 split (binomial test, $P < 0.05$). Position of white asterisks indicates the larger population. In the ACC, neurons that encoded probability during the choice with a positive relationship were more likely to encode a positive prediction error at outcome. Neurons that encoded probability during the choice with a negative relationship were more likely to replay the value signal at outcome. (C) Neurons that encoded probability during choice are sorted into four groups, depending on whether these neurons did or did not encode a positive or negative prediction error during outcome. Plotted is the correlation of their value encoding on payoff trials with the value encoding on effort trials. Neurons that encoded probability during the choice phase and a positive prediction error at outcome showed a significant correlation with value encoding on payoff and effort trials.

prediction error at outcome, but if it coded probability negatively at choice, then it encoded a value signal at outcome. While the relationship between firing rate and value at the time of choice predicted the type of outcome signal when examined at the single neuron level, because of these opponent coding schemes, value information averaged to zero at the population level.

Second, ACC neurons that encoded all three decision variables during the choice phase were more likely to encode positive prediction errors during the outcome phase. To demonstrate this, we sorted neurons that encoded probability during choice into two groups, depending on whether these neurons did or did not encode a positive or negative prediction error during outcome. There is no *a priori* reason why one group should be more likely to encode information about payoff and effort than the other group. However, we found a very strong correlation between the encoding of payoff and effort information for the group of neurons that encoded positive prediction errors, but no correlation for the other groups (Fig. 4C). This specific subpopulation of ACC neurons uses a common value currency (abstracted across probability, payoff, and effort) for computations related to representing expected values at choice, and discrepancies from those expectations at outcome. Furthermore, this correlation began as early as 200 ms after the start of the choice epoch, suggesting these neurons are multiplexing choice value early enough to reflect a role in the decision process.

Taken together, these results suggest that there is a special population of neurons in ACC that multiplex value across decision variables, do so with a positive valence, and encode positive prediction errors. This suggests that the ACC encodes decision value and positive prediction errors using a common value currency.

Future questions

An important question for future research is whether ACC neurons are involved in decision making. Specifically, does ACC value encoding during the choice phase reflect valuation of the options, in the same way that we think it does in the OFC? An alternative possibility is suggested by the fact that ACC activity during feedback matches that at choice. For example, if a neuron responded to rewards that were better than expected, it also tended to respond when the choice was between better than average alternatives (e.g., Fig. 3A). This raises the question of whether we should reinterpret our original conclusions regarding ACC activity during the choice phase as encoding differences between the value of the present options and the average choice value (i.e., a choice prediction error) rather than the value of the choice per se.

Studying decision making requires presenting subjects with choices. This is typically done in such a way as to minimize other cognitive processes, such as learning, that might confound the interpretation of neural activity related to decision making. Choices are randomized, independent of one another, and, in humans, frequently trial unique. However, even with these precautions in place, subjects are still able to learn. They are learning the range and average value of the choices that the experimenter might present. Consequently, although activity during the choice may reflect predictions about the outcome of the choice alternatives, it could equally reflect a prediction error, encoding the current options relative to the other potential choices the subject might have expected. For instance, if a subject has extensive experience with three equally probable choices valued at 0, 1, and 2, the average value of a choice in this experiment is 1. An offered choice of 2 is better than expected and could produce a prediction error at the time of the offer. This shows that if you were to focus solely on neuronal activity during the choice phase, you would not be able to differentiate neurons encoding prediction errors from those encoding the value of the chosen stimulus. Yet these signals have very different implications for the larger question of how the brain computes value-based decisions.

Conclusion

Although value signals are strongly encoded in both OFC and ACC, it is also clear that they serve different roles in the two areas. OFC value coding appears to be directly related to the choice process. It encodes many of the variables relevant to the choice and it shows adaptive coding of the choice valuation based on the local choice history. Yet OFC neurons did not encode a prediction error at outcome, so this cannot be characterized as a general discrepancy signal. In contrast, the ACC appeared to have a more "downstream" role, since it appeared to be more important for evaluating the consequences of the choice. Such

signals could play an important role in learning, enabling the modification of future choices. In addition, whereas neurons encoding specific decision parameters were equally prevalent in the OFC and ACC, neurons that encoded all three decision variables were primarily in the ACC. Furthermore, these neurons used a unified coding scheme of positive valence and encoded positive prediction errors on rewarded outcomes. This suggests that both choice value and prediction error coding—at least within many ACC neurons—is based on a common valuation scale reflecting the integration of individual decision variables.

Formal decision models suggest that determining an action's value requires the integration of the costs and benefits of a decision, thus generating a single value estimate for each decision alternative.[43] This net utility signal can be thought of as a type of neuronal currency that can facilitate comparison of very disparate choice outcomes.[43] However, such a valuation system operating in isolation would make learning about individual decision variables problematic. It would not be possible to update the value estimate of individual variables (e.g., effort costs in isolation of reward benefits) if the only signal the valuation system received was in terms of overall utility. It may be optimal for the brain to encode two types of choice value signals; a variable-specific value signal that represents why an option is valuable and a net utility signal that reflects the integrated net value of the option.

In conclusion, our results show complementary encoding of value between the ACC and OFC. The ACC encodes value on a fixed scale using a common value currency and uses this value signal to encode prediction errors: how choice outcomes relate to prior expectancies. In contrast, the OFC encodes the value of choice options in an adaptive way that is dynamically adjusted based on the recent value history of choice environments.

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Conflicts of interest

The authors declare no conflicts of interest.

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