

Partially dissociable roles of OFC and ACC in stimulus-guided and action-guided decision making

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Khani A. Partially dissociable roles of OFC and ACC in stimulus-guided and action-guided decision making. *J Neurophysiol* 111: 1717–1720, 2014. First published January 8, 2014; doi:10.1152/jn.00323.2013.—Recently, the functional specialization of prefrontal areas of the brain, and, specifically, the functional dissociation of the orbitofrontal cortex (OFC) and the anterior cingulate cortex (ACC), during decision making have become a particular focus of research. A number of neuropsychological and lesion studies have shown that the OFC and ACC have dissociable functions in various dimensions of decision making, which are supported by their different anatomical connections. A recent single-neuron study, however, described a more complex picture of the functional dissociation between these two frontal regions during decision making. Here, I discuss the results of that study and consider alternative interpretations in connection with other findings.

orbitofrontal cortex; anterior cingulate cortex; dissociation; decision making; single neuron; stimulus; action; outcome

THE GOAL OF COST-BENEFIT COMPUTATIONS is to maximize the economic value of a choice, a process often referred to as utility maximization by economists. Using external (e.g., environmental cues) and internal (e.g., memory of past experiences) input, the prefrontal cortex (PFC) supports adaptive behavior in decision making by considering a multitude of decision variables, including costs, quality, quantity, the subjective desirability of the expected outcome at the time of decision, and the appropriateness of the outcome based on the current needs and goals. The orbitofrontal cortex (OFC) and the anterior cingulate cortex (ACC) are the two primary frontal areas that have been implicated in reinforcement-guided decision making in a dynamic environment under varying circumstances. The OFC encodes the expected value of decisions and makes this information available for other PFC areas to use in planning and adopting strategies, whereas the ACC encodes action values and monitors the outcomes of actions. Whenever an outcome suggests a change in the value of a choice, the OFC and ACC signal that a decision needs to be revised based on the changed circumstances. Reversal learning is a special example of this process.

Interest has recently been growing in the functional specialization of distinct frontal regions in different aspects of decision making. The OFC and ACC display dissociable functions in several dimensions of decision making (Lee et al. 2007; Rushworth et al. 2007). The differing anatomical connections of the OFC and ACC with high-level sensory and motor

systems have prompted the suggestion that the OFC and ACC make distinct contributions to decision making by representing sensory stimulus reinforcement and action reinforcement, respectively (Rushworth et al. 2007). A number of studies have demonstrated such a dissociation in human patients with focal frontal damage (Camille et al. 2011) and in monkeys with circumscribed lesions in either the OFC or the ACC (Rudebeck et al. 2008). These lesion studies showed that the OFC and ACC are essential for optimal decision making that depends on stimulus-outcome (SO) and action-outcome (AO) associations, respectively. However, it is not yet clear how underlying neural activity supports such a regional specialization in function. In addition, lesion studies may be unable to further characterize subregional functional specializations of the PFC. Luk and Wallis (2013) recently investigated whether a dissociation between the OFC and ACC in encoding SO and AO associations holds at the level of single neurons.

Luk and Wallis (2013) designed two analogous decision-making tasks that required either SO or AO associations and simultaneously recorded neural activity in both the OFC and ACC in monkeys. They placed a particular emphasis on separating the cuing of possible decision options from the animal's response. The tasks consisted of two distinct phases: a predictive sampling phase in which the subject either was presented with two sequential pictures (SO) or performed two sequential actions (AO), with each event predicting a specific juice reward; and a choice phase in which the animal had to choose between a leftward or a rightward lever movement on the basis of the outcomes that were associated with the two events in the sampling phase (Fig. 1). In the SO task, two pictures that had been presented sequentially in the sampling phase were presented side by side in the choice phase, and the monkey had to choose the lever movement that would lead to the preferred outcome. The use of this two-phase task design and simultaneous recording from both frontal regions enabled the authors to separate the underlying neural activity associated with preparation for decision making from that associated with the decision itself and to analyze corresponding neural activity in both regions under the same circumstances. Such a design avoids complications in interpretation that arise when comparing the results of single-neuron studies conducted during separate experiments or in different laboratories that use different tasks.

To study the encoding of AO and SO associations, Luk and Wallis (2013) examined neural activity starting from the onset of the first reward and continuing until the end of the first delay (Fig. 1). They found weak support for dissociated encoding of SO and AO associations in the OFC and ACC, respectively. In

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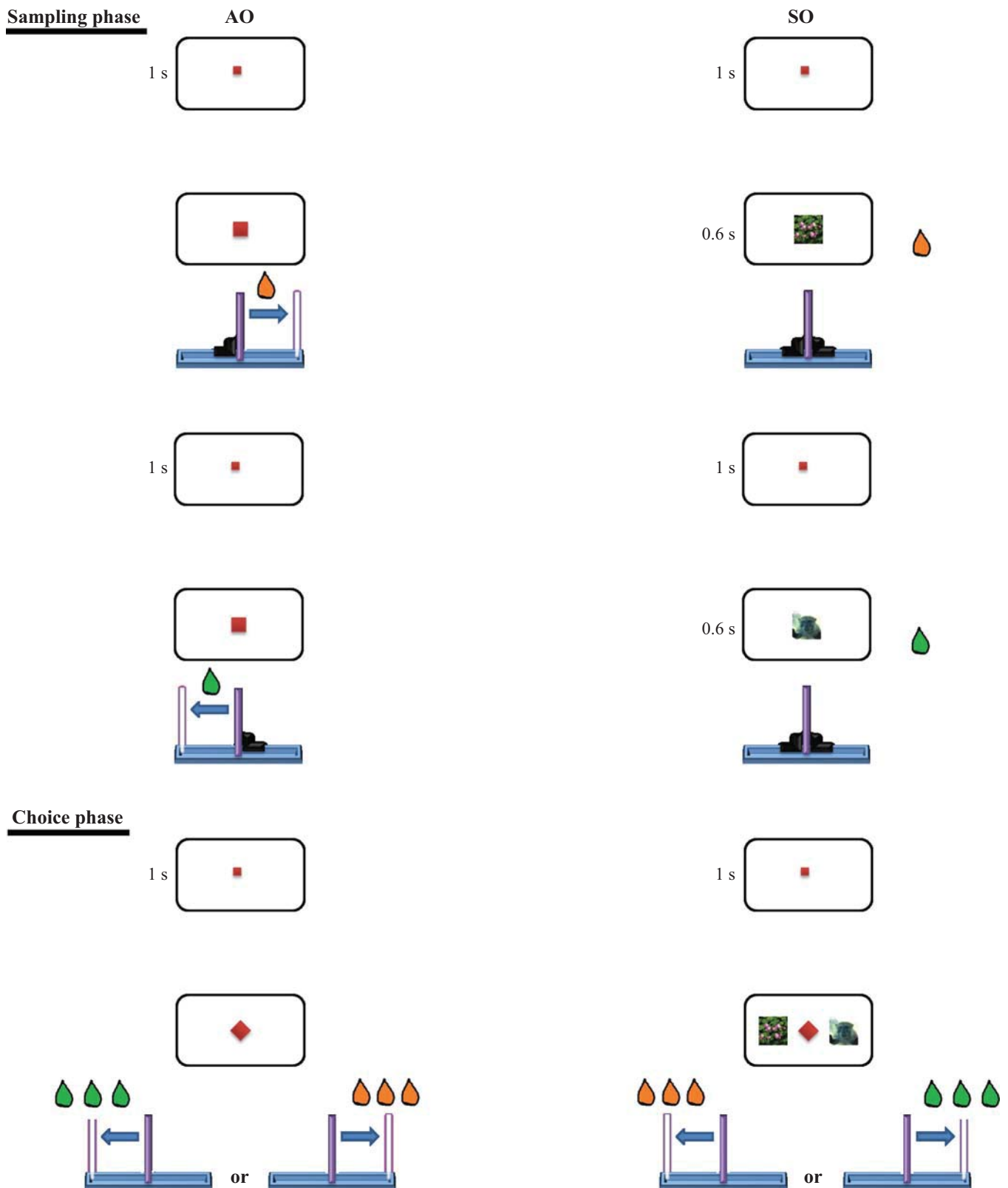


Fig. 1. The sequence of steps for a trial in action-outcome (AO) and stimulus-outcome (SO) tasks. Every trial was composed of two phases: a sampling phase in which the monkey became familiar with two different outcomes (juices) associated with two different actions (AO task) or two different stimuli (SO task), and a choice phase in which the animal had the chance to choose a larger amount of one juice from two sampled juices. As shown, the volume of the final choice juice (0.77 ml delivered during 1.25 s) was almost three times greater than that of the sampling juice (0.25 ml delivered during 0.4 s). In the sampling phase, the juice was delivered so that its offset coincided with the offset of stimulus presentation (SO task) or immediately after the detection of lever movement by the monkey (AO task). During the choice phase in both tasks, the monkey had to demonstrate his choice by a lever movement. For the SO task, the monkey moved the lever toward the stimulus that was associated with the preferred reward in that trial.

both regions, only a small proportion of neurons encoded predictor \times outcome interactions. This proportion was significantly above chance in the OFC during the SO task and in the ACC during the AO task. A comparison between the areas showed no significant difference in distinct tasks between the two brain regions; moreover, an examination of Table 1 in the Luk and Wallis paper shows no significant difference in task selectivity for each area.

Luk and Wallis (2013) also examined neural activity during the choice phase, which comprised the time between the onset of the second reward delivery and the chosen action (i.e., the median of the subject's reaction times for each task in each session). They showed that a significant number of neurons encoded the chosen action during this period. Statistical tests on the neuronal populations that solely encoded the chosen action with no significant interaction with the stimulus or outcome revealed a double dissociation in the prevalence of action-selective (the action necessary to make a choice; i.e., choice-selective) neurons in the two brain areas. Choice-selective neurons were significantly more prevalent in the ACC than in the OFC in the AO task, whereas choice-selective neurons were significantly more prevalent in the OFC than in the ACC in the SO task. This strong encoding of the choice with a clear regional dissociation contrasts with the rather weaker encoding of the SO and AO associations and highlights the importance of a robust representation of the action that is necessary to achieve the subject's final goal, the choice outcome. The animals performing the tasks in this study used a clear preference between the rewards as a basis for decision making. Whether neuronal populations in the OFC and ACC would encode the choice in such a robust manner in tasks that require decisions to be made under more uncertain conditions (e.g., in probabilistic settings) should be investigated in future studies. Finally, the authors found that over one-half of the neurons in both the OFC and ACC encoded the experienced reward, and this finding could be used by the PFC to update values and to guide future decisions. The experienced reward was encoded primarily in a task-specific but not area-specific manner. In all their analyses, Luk and Wallis (2013) used a sliding window to compare the neural activity that represented different parameters and the interactions among them. This method is useful for comparing neuronal populations with different baseline activities and with a dynamic range of firing rates because it allows researchers to measure neuronal selectivity independently of the absolute firing rate (Kennerley et al. 2011). An additional complementary set of analyses using a modified principal component analysis method could prove useful for determining the contribution of each parameter to the variability of the observed neuronal activity (Machens 2010).

The findings of Luk and Wallis (2013) add to the current debate regarding the distinct contribution of the different frontal lobe regions in decision making. In particular, their findings shed further light on the results of an earlier lesion study in monkeys by Rudebeck et al. (2008). These two studies used similar tasks but with some notable differences. Rudebeck et al. (2008) used stochastic reward contingencies in which decision making and learning were mixed. By contrast, Luk and Wallis used a two-phase task design that required active updating of value in every trial. To make the two tasks (AO and SO tasks) as similar as possible in all parameters except the association, Luk and Wallis required their subjects to perform

the same actions to demonstrate their choice in both tasks. The earlier work by Rudebeck et al. found that the ACC but not the OFC is critical for decisions that are based on AO associations and that the OFC but not the ACC is critical for decisions that are based on SO associations. At first glance, the demonstration by Luk and Wallis of a weak dissociation in the encoding of SO and AO associations provides little support for the existence of a dissociation between the OFC and ACC in using SO and AO associations to guide behavior, as shown by Rudebeck et al. However, at least two explanations can relieve the apparent disparity between the two studies. First, the "relative dissociation" of encoding associations in two brain regions that was shown by Luk and Wallis explains the moderate but significant impairment in decision-making tasks without complete disruption in performance that was shown by Rudebeck and colleagues. Second, an alternative interpretation of the results of the lesion study by Rudebeck et al. is that the task-specific impairment in decision making is largely due to the context-specific impairment in choice coding, or "making a choice," rather than an impairment in encoding the SO and AO associations. The greater prevalence of neurons encoding the action demonstrating the animal's choice and the dissociation between the areas for the two tasks presented in the Luk and Wallis (2013) study provide strong support for this alternative interpretation.

The specific task design or the specific window of time in the task chosen for the analyses of the SO and AO associations and the manner in which the authors included the stimulus parameter in their analyses might explain why Luk and Wallis (2013) did not observe a large number of neurons encoding associations. The authors analyzed neuronal responses during the first part of the sampling phase, that is, from the onset of the first reward delivery until the end of the first delay. However, associations are learned during the sampling phase and are probably stored more robustly in other frontal regions (e.g., the dorsolateral PFC), as the authors suggested. Therefore, it would be more appropriate to look for representations of the SO and AO associations during the choice phase rather than during the sampling phase. Although this would be difficult for the AO task in the current task design, it would be possible for the SO task. In fact, there is relatively strong encoding of stimulus-choice (stimulus-response) and stimulus-choice-outcome associations during the choice phase in both the OFC and ACC (Luk and Wallis 2013, their Table 2). The strong stimulus-response coding in both the OFC and ACC in the markedly dynamic task employed by these authors can be partially guided by SO association coding.

The manner in which Luk and Wallis (2013) included the stimulus parameter in their analyses is a possible reason for the lack of significant encoding of the SO association in the choice phase (as shown in their Table 2). The authors used the spatial position of the pictures as a stimulus parameter rather than the identity of the chosen stimulus, while the performance of the task enabled the monkeys to learn to associate the pictures with the rewards during the sampling phase. Therefore, in addition to the current analyses used by the authors, an alternative analysis taking into account the chosen stimulus would be very informative. Assume stimulus no. 1 and stimulus no. 2 are presented side by side in the choice phase of the task. Two configurations are possible if, like the authors, we include the spatial position of the stimuli as a factor. In the first configu-

ration, stimulus no. 1 would be on the left and stimulus no. 2 would be on the right, and in the second configuration, the positions would be reversed. An interaction analysis between these two configurations as stimulus factor and the choice (leftward or rightward movement), which also has a spatial component, would ensure that an exact stimulus is considered for every trial. A left or right stimulus position combined with a left or right action would specify which of the two stimuli is chosen. For example, a leftward choice in the first configuration would mean stimulus no. 1 is chosen. In contrast, an interaction analysis between these two configurations as stimulus factor and a parameter with a nonspatial nature such as the outcome would not clearly define the chosen stimulus. For example, stimulus no. 1, which was associated with apple juice (the outcome) in a given trial, could be presented in either configuration (left or right), but the interaction between the outcome and spatial position of the stimulus would not represent the chosen stimulus in the analysis of the SO association. However, the association between the outcome and the stimulus was learned regardless of the next stimulus position in the choice phase. This manner of including the stimulus parameter in the analyses might explain the discrepancy between the strong coding of interactions when the identity of the chosen stimulus was defined by the presence of another spatial parameter (i.e., $S \times A$ and $S \times A \times O$) and the lack of a significant $S \times O$ interaction in the analyses used by Luk and Wallis (2013, their Table 2). Thus, the new analysis suggested here, in which the stimulus identity (stimulus no. 1 or 2) is used as stimulus factor in the $S \times O$ interaction analysis, may reveal a significant $S \times O$ interaction, thus underscoring the role of encoding of the SO association “during decision making.” It would also be interesting to plot the time course along which the $S \times O$ interaction is encoded, in a similar way to how the authors plotted the time course along which the chosen response was encoded (Luk and Wallis 2013, their Fig. 6) and to determine whether encoding of the SO interaction precedes that of the chosen response.

In summary, the findings of Luk and Wallis (2013) provide insight into the roles of single neurons during the different phases of decision making and have the potential to stimulate new studies for better understanding of the specific contributions of the OFC and ACC in decision making at the level of single cells. Variations in the authors’ novel task design (e.g., replacing the spatial left/right action with one having less

spatial polarity in the SO task or integrating the task with probabilistic settings) would offer new experiments that may afford better understanding of prefrontal function in decision making. An important property of prefrontal neurons is functional reconfiguration (Duncan 2001). The different functions and roles of frontal areas in decision making cannot be encompassed in a single paradigm, and different paradigms, including variations of the task design used by Luk and Wallis, should be employed to address how underlying neural coding in varying circumstances enables adaptive decision making.

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DISCLOSURES

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AUTHOR CONTRIBUTIONS

A.K. analyzed data; A.K. prepared figures; A.K. drafted manuscript; A.K. edited and revised manuscript; A.K. approved final version of manuscript.

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