

Spotlight

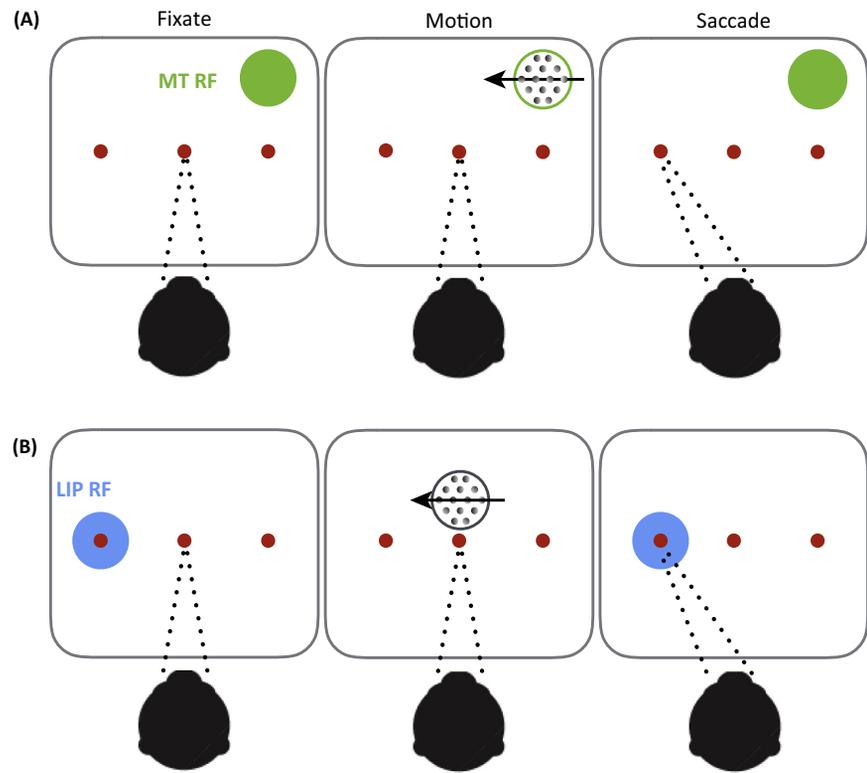
Where Are Perceptual Decisions Made in the Brain?

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Recently, Katz and colleagues report the effects of silencing neurons in two brain areas during a perceptual decision-making task. In a landmark result, silencing neurons in the visual cortex impaired performance but silencing neurons whose activity correlates to the decision had no effect.

Decision-making is the process by which sensory input is transformed into perception and action. An elegant approach to the puzzle of understanding the neuronal mechanisms underlying perceptual decisions was pioneered by Newsome, Movshon and colleagues using a now widely-studied paradigm, which we refer to as the noisy motion perceptual decision task (Figure 1). In their original studies, Newsome and colleagues recorded from neurons in visual area MT that selectively respond to visual motion while monkeys indicated their perception of stimulus motion via a saccadic eye movement. Their results revealed that individual MT neurons' activity correlated with subject's decisions about motion direction (Figure 1A). This was true even when the stimulus was entirely noise and the monkeys were forced to make guesses about the direction of motion [1]

A critical question raised by these experiments was how, then, is this motion information read out from MT neurons to guide the eye movement choices? Shadlen, Newsome and colleagues reasoned that a likely candidate was area LIP, to which MT neurons project and which is known to be involved in planning saccadic eye movements. Since LIP neurons were known to be involved in saccade planning, rather than placing



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Figure 1. Noisy Motion Perceptual Discrimination Task. Monkeys are presented with a visual motion stimulus in which a field of dots appears to move either left or right; the monkeys have to report the direction of stimulus motion with a saccadic eye movement—typically with a leftward or rightward saccade for leftward or rightward motion, respectively. The amount of ‘noise’ in the stimulus is controlled by altering how much the dots appear to move in the same direction. The visual motion percept is generated by integrating the motion stimulus over time and across the field of dots. As expected, monkeys’ decisions are less accurate for noisier stimuli. (A) In the MT configuration the noisy motion stimulus is placed in the response field (RF) of the MT neurons under study and the saccade targets elsewhere. (B) In the LIP configuration one of the saccade targets is placed in the RF of the LIP neurons under study, the other saccade target is placed in the opposite visual hemifield and the noisy motion stimulus is placed centrally.

the motion stimulus in the neuron's response field (RF; as was done in the MT experiments), an alternative configuration was used in which one of the saccade targets, again, instead of the motion stimulus, was placed in a neuron's RF (Figure 1B). Neuronal recordings revealed that, unlike MT neurons, LIP neurons' activity was correlated with both the monkeys' trial-by-trial choices and reaction times [2,3]. Computational modeling suggested the animals' perceptual decision was made by the gradual accumulation of motion information in area LIP, offering a seductive view into otherwise private deliberations [3].

Given the weight of this evidence, and other work showing that silencing LIP neurons biases monkeys' eye movement choices [4], we might expect that silencing LIP neurons during the noisy motion task also alters perceptual decisions. However, until recently, studies aiming to silence LIP neurons during performance of this task, and thereby identify a direct role for LIP in perceptual decisions, have been missing. But no more. Recently, Katz and colleagues [5] reported the effects of injecting small volumes of the GABA agonist muscimol to reversibly silence neuronal activity in MT and LIP as monkeys perform the noisy motion task. Consistent with earlier

lesion work [6], silencing MT produced a clear and significant impairment in performance on the noisy motion task. Remarkably, silencing LIP neurons during the noisy motion task had no effect. What might have seemed to be a confirmatory experiment has delivered, in a sense, a landmark null result.

By their nature, null results are hard to defend. This makes Katz and colleagues' achievement all the more impressive. To show they successfully silenced LIP neurons and to estimate the extent and degree of inactivation, they made simultaneous electrophysiological recordings before, during and after every inactivation session. To further mitigate concern, during each inactivation session the authors also demonstrated a positive effect of LIP silencing on a free-choice saccade task. After silencing LIP neurons in one hemisphere, monkeys were less likely to choose targets presented in the contralateral visual field (a region of visual space represented by the silenced neurons). This is a very important control. It shows that the muscimol injections into LIP were behaviorally significant, with similar effects as reported in previous work, and highlights how the lack of a behavioral effect of silencing was restricted to the noisy motion task. Another advantage of Katz *et al.*'s work is that the silencing was done reversibly using a drug, unlike excitotoxic lesions used in [6] or aspiration, both of which are permanent. As a result, we can rule out long-term reorganization as a potential confound. To address the concern that different motion stimuli involve different mechanisms of motion integration, Katz *et al.* also tested stimuli employing different kinds of dot motion and did not observe an effect.

This study is likely to shake up a long-standing and influential view of LIP's role in decision-making and prompt more scrutiny of existing models. A natural conclusion is that the new evidence casts doubt on the hypothesis that motion information is accumulated by LIP neurons to

make the decision in this task. If so, other cortical areas may play a more direct role in the decision process during this task, such as other nearby posterior parietal and superior temporal areas, the frontal eye fields, lateral prefrontal areas and sub-cortical structures like the basal ganglia. Caution is, however, warranted when attempting to ascribe any unitary function (or lack thereof) to a particular brain area. LIP may still play an important role in perceptual decisions. One possibility is that LIP is more involved in making perceptual decisions during other kinds of tasks – particularly tasks which requiring greater cognitive demands or flexibility than the noisy motion task [7]. For example, a recent work showed that extensive training on a categorical decision task engages decision-related mnemonic encoding in LIP beyond that observed prior to learning [8]. LIP may also be more involved in other variants of the noisy motion task, such as a 'reaction time' version of the task in which monkeys report their decision as rapidly as possible rather than following a delay period as in Katz *et al.* study. Future work examining neuronal activity in a wider range of decision-making tasks, and during learning, is needed to understand decision-related mechanisms more generally, and whether different decision tasks rely on distinct or common mechanisms.

Muscimol acts slowly, over minutes, potentially giving neurons in other brain regions time to compensate. Katz and colleagues closely examined behavior for changes even immediately after the injection. This said, while they recorded at the injection site, they did not record in other regions to rule out the possibility that more rapid, compensatory changes occurred to maintain performance in response to the LIP silencing. Networks are robust to perturbations and can compensate within seconds [4]; thus, rapid compensation may mask a role for LIP neurons in perceptual decisions. In any case, because LIP neurons display coherent patterns of activity with neurons nearby and in other

areas [9,10], it seems unlikely that silencing LIP neurons will have no impact on neurons in the regions to which they project. Ideally, we need to convert the current null finding into a positive result. Decisively addressing this network concern will require rapid, reversible inactivation combined with large-scale neuronal recordings distributed across the decision circuits. This combination of tools is already working in rodents and is emerging in primates. Thus, sophisticated network experiments may explain why silencing LIP neurons does not alter perceptual decisions during the central noisy motion task (Figure 1B).

The detailed correlations previously observed between LIP neuronal activity and perceptual decisions during neurophysiological recordings suggests other factors could also be in play [3]. For example, Shadlen and colleagues originally assumed a saccade-related role of LIP in mediating perceptual decisions in the noisy motion task, which motivated them to place the saccade targets, rather than the motion stimulus, inside LIP neurons' RFs. However, it has long been known that LIP neurons respond selectively to visual stimuli within their RFs, even in the absence of saccades. This leaves open the possibility that LIP neurons are more involved in forming decisions about visual stimuli when those stimuli are placed in their RFs. Recent work has shown that LIP neurons encode monkeys' categorical decisions about visual stimuli more strongly when they are shown inside compared to outside neurons' RFs [7], and that this decision related encoding was distinct from saccade-related encoding [11]. Additional causal evidence for a role of LIP in evaluating visual stimuli comes from a study reporting a visual discrimination deficit when silencing LIP neurons, but only for stimuli placed within the inactivated region of space [12]. This highlights LIP's role in analyzing stimuli and/or directing attention toward stimuli within their RFs. An interesting follow-up to the Katz study will be to silence LIP

using the same stimulus configuration under which MT was tested; namely, by placing the motion stimulus, not one of the saccade targets, in the RF (Figure 1A).

By using reversible inactivation to reveal a dissociation between decision-correlated neuronal responses and their causal impact on behavior, the Katz study presents an important challenge to understanding the mechanisms of perceptual decisions. Deploying emerging new approaches for large-scale monitoring and precise manipulation of neuronal activity across brain networks that span the sensory-motor continuum offers new opportunities to meeting the challenge. The coming years offer a particularly fruitful

period in uncovering neural circuit mechanisms of decision-making.

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