

How Confident Do You Feel?

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In this issue of *Neuron*, Fetsch et al. (2014) show that microstimulation of motion-sensitive neurons in the visual cortex (MT/MST) of primates mimics the addition of sensory information for which the stimulated neurons are selective. Such microstimulation increases the confidence that monkeys have in their decisions about motion direction.

Confidence in our decisions is affected by the amount of evidence available to make them. Decisions based on ambiguous information are accompanied by a sense that our choice might not be correct (Bach and Dolan, 2012; Beck et al., 2008). An outcome of seven heads out of ten flips, for example, is not sufficient information to decide about the fairness of a coin (or a coin flipper [Gelman and Nolan, 2002]), and we would be better off by not committing to a yes/no categorical answer. However, a coin landing 70 heads out of 100 flips can be called unfair, and we can have great certainty about our answer. Thus, although the proportion is the same in both examples, a larger amount of evidence makes us more confident about our choice.

We now know that the perception of certainty that accompanies choices is also experienced by other animals, such as rats and monkeys. Clever behavioral methods have shown that these animals will bet for a large reward when they are confident about a choice and that they would choose a smaller but certain reward when the available evidence ambiguously points to the options.

In this issue of *Neuron*, Fetsch et al. (2014) make use of a postdecision wager task (Kepecs and Mainen, 2012; Persaud et al., 2007) in which monkeys could choose the correct of two options, and get a large reward, or choose a third “sure bet” option and receive a smaller but certain reward. The monkeys observed a patch of noisily moving dots on a computer monitor and had to make an eye movement to indicate whether the dots were moving preferentially to left or to the right. Only correct choices

were rewarded when monkeys decided to look at the left or the right target, and they always received a smaller reward when choosing the centrally positioned sure bet target. Thus, monkeys not only had to decide whether the dots were moving to the left or to the right but also whether the sensory evidence was strong enough to discard the smaller reward and risk for one of the two choices.

The behavioral results show that the monkeys sometimes chose the smaller reward offered by the sure bet option and they did this preferentially on trials in which the motion information was weak. This is consistent with the notion that monkeys chose the sure bet when they were not sure about the direction of motion. However, the crucial behavioral result was that the proportion of correct responses increased in the group of trials in which the sure bet was available, and this was true even for weak motion stimuli. This is a key result because it implies that they did not choose the sure bet indiscriminately on low-strength amplitudes—a behavior that would have not changed the proportion of correct responses. Instead, the fact that performance improves indicates that monkeys preferentially discarded those trials in which sensory information (or its readout) was unreliable.

What is the neuronal mechanism underlying the sense of confidence that allows monkeys to identify unreliable decisions? Recent experiments show that, for decisions communicated with eye movements, a neuronal correlate of confidence might be represented in the same neurons that accumulate the sensory evidence used to select the saccadic movements

that communicate the choices (Kiani and Shadlen, 2009). These neurons, located in the lateral intraparietal area (LIP), change their firing rate in proportion to the strength of motion stimuli, reflecting the accumulation of sensory evidence in favor or against a particular saccadic eye movement. The experiments show that monkeys choose the sure bet when the accumulated evidence does not reach beyond a threshold value. These parietal neurons, thus, encode in their firing rate a decision variable that can be used to make decisions and also reflect the confidence in a straightforward manner: the decision to answer left or right is determined by the sign of the change in the activity, and the confidence is encoded by how far the activity moves away from the starting point, taking into account elapsed time (see Figure 1).

In the new study on this issue of *Neuron*, Fetsch et al. (2014) aimed to test a direct implication of the previous results: if the accumulation of sensory evidence underlies decision making, then a manipulation of sensory evidence will affect choices and, importantly, also will affect the confidence subjects have on their decisions. To test this association, Fetsch et al. (2014) artificially activated neurons in the motion-sensitive areas MT/MST by means of microstimulation. Microstimulation allows the experimenter to activate neurons by injecting low-current pulses through an electrode tip placed within the cortex. This is a powerful technique that allows neuroscientists to test possible causal links between neuronal activity, perception, and behavior. Previous results have shown that microstimulation of sensory

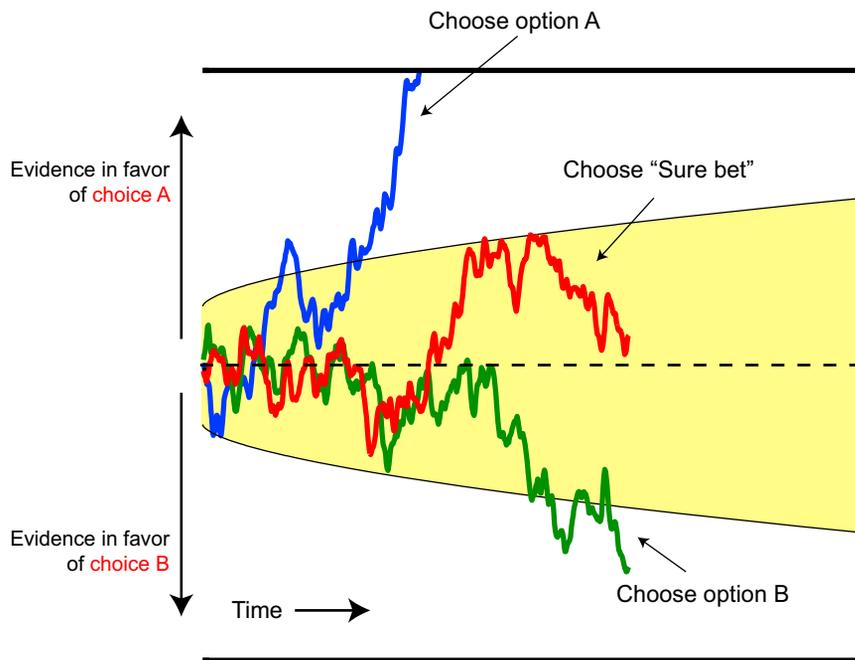


Figure 1. An Accumulation-to-Bound Model Incorporating a Confidence Threshold

A decision is made when the accumulated evidence hits a bound (blue trace). If the stimulus turns off and the accumulated evidence ends within the yellow area, subjects do not commit to a categorical choice and instead choose a “sure bet” option (red trace). If the stimulus turns off and the evidence is large enough, subjects make a choice based on the sign of the ending point (green trace).

neurons can be used to modify (Salzman et al., 1990), or even altogether substitute (Romo et al., 1998), sensory evidence.

That microstimulation was able to modify the amount of sensory information was a firmly established experimental result. But how is confidence affected by microstimulation? Could microstimulation affect the confidence that monkeys experience in their decisions? The effect of microstimulation on confidence is not a trivial question to ask. Microstimulation in areas MT/MST directly activates a group of high-level visual neurons, bypassing the natural flow of visual information. A moving object within the visual space generates a cascade of activity that, in its most direct route, travels from the retina, through the lateral geniculate nucleus of the thalamus, V1, V2, to finally reach MT and MST. Neuronal networks calculating confidence might require access to the neuronal representation of motion in any number of those processing nodes.

In the key experimental manipulation, Fetsch et al. (2014) microstimulated the motion-selective neurons of MT/MST in randomly selected trials of the postdeci-

sion wager task. The results show the artificial activation of neurons contributed to the sensory evidence for which the neurons were selective for. When leftward-selective neurons were stimulated, the monkeys chose the left choice more often, just as if motion in that direction was stronger. These results confirmed previous experiments showing that microstimulation biases the monkeys' choices toward the direction preferred by the stimulated neurons and that this shortens the time monkeys take to make a decision favoring that direction.

The novel and exciting finding, however, was that the confidence reports of the monkeys changed in agreement with the hypothesis that microstimulation added or subtracted sensory evidence: when the preferred direction of the stimulated neurons agreed with the visual motion, monkeys chose the sure bet less often, as if the sensory stimulus was stronger and they were more certain of their choices. Conversely, they chose the sure bet more often when microstimulation activated neurons that provided motion information opposing the direction of the real stimulus.

A somehow enigmatic finding is that monkeys seemed to be unable to detect the presence of microstimulation. It is important to note that microstimulation adds motion information that reduces the monkeys' sensibility in the direction opposite to the stimulated neurons, shifting the discrimination curves, and reducing the amount of reward that monkeys could get. The monkeys reacted to this with an opposite direction bias, somehow compensating for the additional motion information introduced artificially. However, the results show that the compensating bias was present in trials with, and also without, microstimulation. Had the monkeys been able to detect the presence of microstimulation, they could have compensated for the artificial motion information but only on the microstimulated trials. This result is enigmatic because it is known that monkeys can be trained to detect the presence of microstimulation in several cortical areas. A plausible interpretation for these conflicting results is that microstimulation induces a perceptual phenomenon that monkeys can be trained to respond to but that artificial percept is not distinguishable from the natural stimulus or behavioral conditions that normally activate the stimulated neurons. Future experiments are needed in which monkeys could be explicitly asked to distinguish microstimulation-induced percepts from natural stimuli.

To formally test the assumption that microstimulation acted like additional motion information, Fetsch et al. (2014) made use of the accumulation-to-bound model (see Figure 1) (Palmer et al., 2005), incorporating the electrical stimulation as an additional parameter that increased the strength of motion information in the direction preferred by the stimulated neurons. Remarkably, the fitted model not only explained the shift in the proportion of sure bet choices but also predicted, with astonishing accuracy, the shift in the left/right choices induced by microstimulation.

If, as the model fittings suggest, microstimulation affects choice and confidence by acting like an increase in motion information, then the results should be replicated by introducing an actual increment in the strength of the real sensory stimulus. That was exactly what

Fetsch et al. (2014) found in this control experiment: an offset in the motion coherence of the real stimulus biases the monkeys' choices and confidence ratings just like microstimulation did.

In an elegant control experiment, Fetsch et al. (2014) sought to break the system apart. Instead of using low currents to stimulate a small patch of neurons with similar preferred orientations, the authors now injected a large amount of current that recruited a wider population of neurons including disparate preferred motion directions. This widespread activation resulted in a large increase in the number of sure bet choices, indicating that monkeys experienced noisy motion information and less confident decisions. The result illustrates at least two important issues. First, it demonstrates that monkeys are capable of reporting a large decrease in confidence and, second, it shows that the behavioral consequences of microstimulation are exquisitely dependent on the selectivity of the stimulated neurons. Large stimulation currents, instead of injecting additional information, indiscriminately recruit neuronal popula-

tions whose contributions can mask subtle sensory representations.

The results reported by Fetsch et al. (2014) demonstrate that the mechanisms that read sensory evidence have access to the additional information added by microstimulation at the level of MT/MST. Future experiments should be aimed to identify the downstream neuronal circuits that read this evidence to decide whether to choose a safe bet or to risk for a larger reward. Importantly, these circuits must have learned, during behavioral training, the association between the amount of accumulated evidence and the likelihood that a given answer will be correct. What are the neuronal correlates of this learning? The answer will likely include the orchestrating functions of the frontal cortices, and also the modulatory effects of subcortical projection systems (de Lafuente and Romo, 2011; Schultz, 2013).

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Oscillatory Substrates of Fear and Safety

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Oscillatory activity in the basolateral amygdala (BLA) is critical for emotional behavior. In this issue of *Neuron*, Stujenske et al. (2014) describe novel dynamics of BLA theta-gamma-coupled neuronal oscillations associated with conditioned and innate fear.

Neuronal theta (4–10 Hz) and gamma band (30–80 Hz) synchrony, which can be detected in the neocortex and associated areas of mammals including humans, subserves several cognitive functions. Notably, these two oscillatory bands can interact with each other, and their interplay represents a fascinating area of investigation. During specific sensory and cognitive experiences, the power of the gamma rhythm is modulated

by theta oscillations, as theta provides an ideal substrate of timing, suitable to define the onset of a stimulus. Specifically, the theta-gamma code could be relevant for the recall of a memory linked with salient stimuli, such as a reward or a noxious stimulus. Phase-amplitude cross-frequency coupling (CFC) between theta and gamma is an index of the modulation of the gamma power by the phase of the theta oscillations (Canolty et al.,

2006). Stronger CFC can be detected in the hippocampus when an animal learns the association between an item and its spatial context (Tort et al., 2009).

The BLA, hippocampus (HPC), and medial prefrontal cortex (mPFC), three interconnected brain structures involved in fear and anxiety, display synchronized theta oscillations correlated with fear memory (Seidenbecher et al., 2003). Although it is known that BLA gamma