How the brain makes decisions and its importance for human health

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Decision making in everyday life
Why care about how the brain makes decisions?

Importance for human health and well being
The personal impact of brain disorders

High functioning, friendly, successful.

In late 50s, personality started changing dramatically. Unfriendly and easily agitated. Poor decisions. Lost job.

At 60, diagnosed with frontal-temporal dementia (FTD).

Needed full-time professional care by age 63.

Passed away at age 65.

Story of my Dad
Why focus on neural mechanisms?

To find potential targets for clinical interventions that can improve decision making impairments
Experimental approach
Experimental approach

Extended Data Figure 7

Chemically sharpened fibre optics allow extensive inhibition during acute and chronic recordings from cortical regions expressing eNpHR3.0.

a, Image of a chemically sharpened 50 μm core, 125 μm cladding fibre.

b, Light spot produced by a blunt and sharpened fibre 2 cm above the floor of a cylindrical container 10.5 cm in diameter.

c, Laser power output from a blunt and sharpened fibre as a function of angle relative to the fibre optic tip. 25 mW input power. Power meter was 2.86 mm from the fibre tip.

d, Single trace of an acute recording of spontaneous activity in anesthetized primary somatosensory cortex (S1, 1.5 mm posterior, 2.8 mm lateral from Bregma) expressing eNpHR3.0. Laser illumination period, 500 ms, marked by the green bar.

e, Location of acute recording units (single and multi) in anaesthetized S1 relative to fibre tip and cortical surface. The level of inhibition was measured from ten repeated 500 ms laser illumination periods, delivered every 5 s. Percentage reduction displayed next to partially inhibited units. Unit in d indicated with an asterisk.

f, Example multiunit activity from the FOF of a rat performing a memory guided orienting task. The 2-s laser illumination period initiated at cue onset, resulted in 97% inhibition of spiking activity for both trials where the rat made left or made right responses.

g, Multiunit spiking activity (from f) aligned to laser onset (top) and laser offset (bottom). Spiking activity is strongly inhibited, 16 ms after laser onset and recovers, 60 ms after laser offset.
To quantitatively probe the dynamics of decision-making, we developed a class of tasks in which subjects are concurrently presented with noise associated with the addition of new sensory evidence. The method allowed us to measure, for each trial's pulse timing to distinguish between different positions in the trial. The resulting data are analyzed with models of evidence accumulation that use the richly detailed information of each trial's pulse timing. The method is particularly powerful as a tool for revealing the internal properties of decision-making. The method is generalizable to a variety of phenomena in biology, from spiking in single neurons to behaviors in humans on a computer.

Optimal accumulation of evidence for decision-making in rats

Figure 1: Rat decision making task

- Water valve
- Nose in center port
- Nose in side port
- Center LED
- Probability of correct response
- Probability of rightward response
- Stimulus duration (sec)
- Difficulty = r_1:r_2 (clicks/sec)

Table 1: Rat's behavior

<table>
<thead>
<tr>
<th>Difficulty</th>
<th>Prob. correct</th>
<th>Prob. rightward</th>
</tr>
</thead>
<tbody>
<tr>
<td>3:1</td>
<td>0.5</td>
<td>0.6</td>
</tr>
<tr>
<td>7:1</td>
<td>0.5</td>
<td>0.6</td>
</tr>
<tr>
<td>13:1</td>
<td>0.5</td>
<td>0.6</td>
</tr>
<tr>
<td>27:1</td>
<td>0.5</td>
<td>0.6</td>
</tr>
</tbody>
</table>

Datasets

- 1 auditory dataset
- 3 visual datasets

Methods

- Chronometric curves for an example rat's behavior
- Psychometric curves (fits to a 4-parameter logistic function for each subject; see methods) for rat subjects.

Acknowledgments

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Brain networks for decision making
Neural responses supporting decisions

- Sensory evidence
  - Strong rightward
  - Weak rightward
  - None rightward

![Graph showing relative neural response for rightward choice over time during the decision.](image)
Influencing decisions by altering brain activity

Figure 6. Optogenetic inactivation reveals that dorsal striatal activity causally contributes to decision formation throughout the accumulation process but not before nor after.

(a) Coronal section of the left hemisphere showing the expression of eYFP-eNpHR3.0 in the left dorsal striatum. Optical fiber localization and 750 μm estimated inactivation radius are indicated by the red circle.

(b) Raster plot (bottom) and peri-stimulus time histogram (top)
Using rats to study attentional deficits

N = 60 rats