

Vision: Depth perception in climbing mice

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Summary

Depth perception helps animals interact with a three-dimensional world. A new report in *Current Biology* presents a novel paradigm to study depth perception in naturally climbing mice and links their behavior to binocular disparity signals in primary visual cortical neurons.

Main text

We perceive the visual world around us as three-dimensional. However, the projections of visual objects on the retinas in our eyes are two-dimensional. How does the brain infer depth from 2D retinal images? One major cue is provided by the slightly different views in our two eyes. The eyes' horizontal separation creates small spatial offsets — known as binocular disparities — in the retinal images, enabling the brain to infer the distance of objects (Figure 1A). Binocular disparity has been investigated in detail in species with forward-facing eyes, such as humans and non-human primates. In primates, visual cortex contains binocular neurons that receive inputs from two eyes and respond preferentially to specific disparities¹. Binocular neurons that encode disparity are also found in mouse visual cortex². However, compared to humans and non-human primates, mice have much more laterally placed eyes and a smaller binocular zone (Figure 1B). This raises the question whether the mouse, which has become a popular species to study vision, relies on binocular cues for depth perception. In a report in this issue of *Current Biology*, Boone, Samonds and colleagues³ provide new insights into this question by linking depth discrimination in naturally climbing mice with disparity encoding in mouse visual cortex.

The authors developed a new approach to study depth perception in mice that was inspired by the classic visual cliff task⁴, in which animals are placed on a glass plate above platforms at different depths. Animals instinctively move to the “safest” platform that is closest to the glass and avoid deep “visual cliffs”, demonstrating their perception of depth. In mice, the standard visual cliff task typically engages the lower part of the visual field with little overlap between the two eyes. The binocular field is larger in the upper part of the visual field (Figure 1C), extending in front and above the animal's head. Boone, Samonds *et al.* therefore reasoned that orienting the head towards the ground would

engage a larger part of the binocular field. The authors exploited the fact that mice are natural climbers and introduced a vertical pole above the visual cliff. Mice were placed at the top of the pole and naturally climbed down, with the head pointing down towards the platforms (Figure 1D). They found that mice reliably descended to the shallow platform (2.5 cm below the glass plate) when the distance with the other platforms exceeded 10 cm.

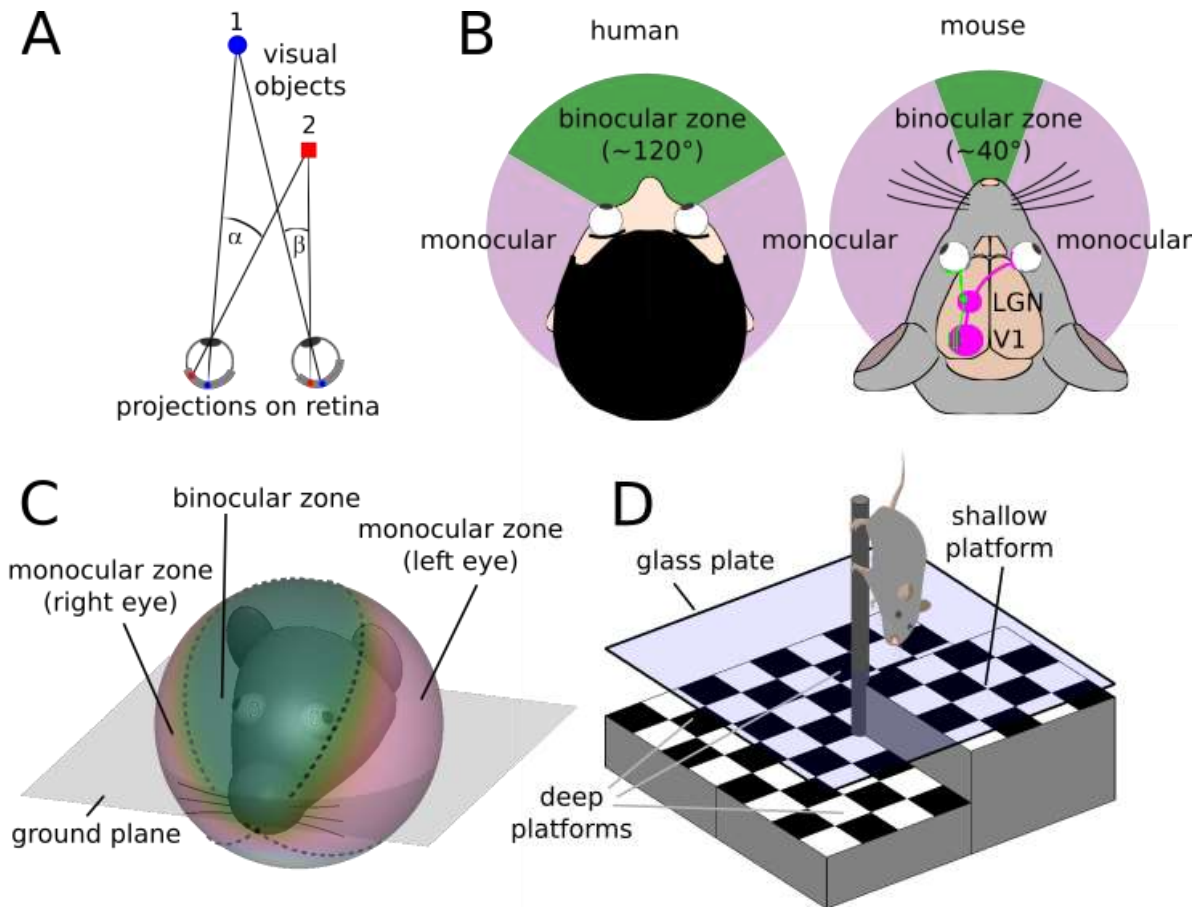


Figure 1. Depth perception using binocular disparity in freely-moving mice. (A) Binocular disparity can be used to infer depth, by comparing the difference in angles of the projections of two visual objects on both retinas. (B) Binocular and monocular fields in humans (left) and mice (right). Mice have a comparatively small binocular field in front of the head (~40 degrees) compared to humans (~120 degrees). Green indicates the region of visual space that is seen by both eyes, the purple region is seen by only one eye. A simplified schematic of the visual pathway is shown for mice: neurons in primary visual cortex receive input from two eyes via the thalamus (LGN) and encode binocular disparity. (C) Binocular and monocular fields reconstructed for a mouse moving parallel to the ground. The binocular field is largely confined to the part of visual space above the ground. Same color coding as in B. Data modified from Meyer *et al.* (2020). (D) Pole descent cliff task. Mouse descends from pole towards a glass plate covering four

platforms of different depths. Mice rely on input from both eyes to descend towards the shallow platform. Adapted from Boone, Samonds *et al.* (2021).

Are mice using binocular cues, in particular binocular disparity, during this pole descent cliff task? As disparity requires input from both eyes, the authors repeated the same experiments in mice with one eye sutured closed. In contrast to mice with binocular vision, mice performing the task with only monocular input did not preferentially descend to shallower platforms, even when the difference in depth was as large as 60 cm. Mice with only one open eye did not take longer to descend the pole, suggesting that eye closure did not impair climbing performance. Other monocular depth cues such as “motion parallax”, which relies on different speeds of close and far objects on the retina when an animal is moving, could in principle still be used by these mice. These experiments therefore indicate that mice use binocular depth cues to identify the “safest”, most shallow platform.

Next, the authors investigated the link between depth discrimination of mice in the pole descent task and the response properties of neurons in the primary visual cortex (V1). V1 is a brain area that is important for integration of input from the two retinas, arriving via the thalamus. To test whether V1 could encode depth information in the pole descent task, the authors used two-photon imaging to measure neural responses of binocular V1 neurons in a separate group of head-fixed mice. First, binocular disparities associated with different platforms depths were estimated using behavioral data from freely-moving mice. Based on these disparities, stimuli were generated and presented to the head-fixed mice using a polarization-preserving screen and polarization filters in front of the two eyes, using techniques similar to those used in 3D cinemas. This approach allowed the authors to estimate “neural discrimination” performance, indicating how well binocular disparities could be discriminated based on V1 responses. Strikingly, neural discrimination performance was similar to the behavioral performance of freely-moving mice.

A challenge with naturalistic tasks is that it is not always clear when the animal is making a decision. The pole descent cliff task enabled the authors to determine when mice were choosing the platform by measuring the angle of the mouse on the pole (indicating to which of the four platforms the mouse was turning during descent, Figure 1D). Mice only turned to the shallow platform when reaching the bottom part of the pole, about 5 cm above the platform. Neural discrimination in head-fixed mice was relatively robust against variations in viewing distance. However, closer viewing distances caused a wider range of disparities and therefore better neural discrimination. This provides a possible explanation for why mice made their minds up late. To confirm this idea, the authors forced climbing mice to make depth discriminations from further away, by increasing the distance between the glass plate and both the shallow and deep platforms but keeping the absolute depth difference between platforms constant. Consistent with the neural data, behavioral discrimination was worse for further viewing distances.

Finally, the authors examined whether changes in alignment of the two eyes in freely behaving mice would impair neural depth discrimination performance. Mice make rapid, saccadic eye movements during gaze shifts^{5,6}. Saccade sizes can differ across the two eyes, with larger differences in freely-moving compared to head-fixed mice (the latter

were used for the neural disparity measurements). Boone, Samonds *et al.* therefore analyzed data from a previous study that tracked eye movements in freely-moving mice⁵. They simulated the effects of eye movements on perceived disparity in the pole descent cliff task and on neural discrimination. Neural discrimination was comparable for the middle 50% of observed saccade sizes. Such robustness to eye movements could be very important for accurate depth discrimination during naturalistic conditions.

The study by Boone, Samonds *et al.* is part of an emerging line of research that exploits naturalistic behaviors, such as defensive⁷ and hunting behaviors⁸, to study visual processing in freely behaving mice. Major advantages of using innate behaviors are that they do not require extensive animal training and that results can be more easily generalized to the “real world”. However, there are also major challenges to monitor visual input and motor outputs that modify visual processing, such as eye and head movements. Additionally, certain experimental techniques are difficult to perform in freely-moving animals. Boone, Samonds *et al.* therefore linked behavioral performance in a naturalistic task in freely-moving mice to neural data collected in head-fixed animals with precisely controlled visual input. Discrimination based on binocular cells in V1 matched depth discrimination in freely-moving mice, and responses were relatively robust to variations in viewing distance and eye movement. This supports the idea that binocular V1 neurons contribute to depth discrimination during naturalistic behavior – a prediction that can be further tested in future work.

Recent technological advances expand the way we can measure and manipulate behavior and neural activity. For example, precise tracking of an animal’s location⁹, including head and eye positions^{10,11}, enable reconstruction of an animal’s visual input¹⁰. Using these tools, it would be interesting to investigate to what extent the orientation of the head towards the ground in the pole descent task is counter-acted by eye movements as previously reported in rodents^{5,10–12}. Perhaps the greatest difficulty for studying visual processing in freely-moving animals is control of the visual stimulus. Recently developed head-coupled large-field projection systems^{13,14} provide a promising approach to dissociate the impact of different visual cues, such as motion parallax, on depth perception when an animal is climbing down the pole. These tools could be used in conjunction with large-scale neural recording techniques^{15,16} to measure the activity of disparity-sensitive neurons in visual cortex. The ability to manipulate genetically defined local cell populations and inter-areal neural projections¹⁷ in freely-moving mice permits dissecting the roles of these circuits in visually-guided behaviors, including the precise contribution of primary and higher visual areas to depth perception^{18,19}.

The “old method of watching and wondering about behavior”²⁰ favored by ethologists is helping us gain fundamental insights into the neural basis of visual perception. New tools are making it easier to measure and manipulate naturalistic behavior and neural activity in freely-moving mice. The timely study by Boone, Samonds and colleagues provides a rich, naturalistic behavior to help understand the neural mechanisms of depth perception.

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