

Menkes disease suggest that long-term rescue therapies might be developed by the delivery of a wild-type version of the ATP7A into the ventricles of the brain.

Concluding remarks

While iron and zinc have long been known as metal ions that are important for life, it is clear that Cu is also a critical metal in biology. Given that Cu is also a potentially dangerous toxin exploited by immune cells and that Cu dysregulation causes human disease, the homeostasis of this metal ion must be under exquisite regulatory control. Many questions remain to be deciphered with respect to Cu's role in biology, including an articulation of the entire constellation of Cu-dependent processes, how hosts and microbes interact with respect to Cu, how cells and organs distribute and communicate their Cu status, and precisely how Cu dysregulation contributes to human disease.

Further reading

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Changing expectations about speed alters perceived motion direction

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Our perceptions are fundamentally altered by our knowledge of the world. When cloud-gazing, for example, we tend spontaneously to recognize known objects in the random configurations of evaporated moisture. How our brains acquire such knowledge and how it impacts our perceptions is a matter of heated discussion. A topic of recent debate has concerned the hypothesis that our visual system ‘assumes’ that objects are static or move slowly [1] rather than more quickly [1–3]. This hypothesis, or ‘prior on slow speeds’, was postulated because it could elegantly explain a number of perceptual biases observed in situations of uncertainty [2]. Interestingly, those biases affect not only the perception of speed, but also the direction of motion. For example, the direction of a line whose endpoints are hidden (as in the ‘aperture problem’) or poorly visible (for example, at low contrast or for short presentations) is more often perceived as being perpendicular to the line than it really is — an illusion consistent with expecting that the line moves more slowly than it really does. How this ‘prior on slow speeds’ is shaped by experience and whether it remains malleable in adults is unclear. Here, we show that systematic exposure to high-speed stimuli can lead to a reversal of this direction illusion. This suggests that the shaping of the brain's prior expectations of even the most basic properties of the environment is a continuous process.

We tested two groups of six participants, across five consecutive days, on their ability to report the motion direction of a field of parallel lines oriented at 70 degrees from

horizontal (Figure 1A) that either moved perpendicular (‘up’ and to the right, 20 degrees) to the lines (50% of trials) or oblique (‘down’ and to the right, –20 degrees) to the lines (in the other 50%), as we varied stimulus contrast (high = 53% or low = 8%) and duration (133, 266 or 532 ms). Each session contained a short test block (216 trials), a long ‘training’ block (720 trials) and a final test block (216 trials). The test blocks were always conducted with low stimulus speeds (4 deg/s). The training block differed across groups, with a high-speed group performing the task with stimuli moving at 8 deg/s (16 times the previously estimated prior speed [1]) and a low-speed group at 4 deg/s. We reasoned that exposure to such stimuli might lead the observers to implicitly update their expectations towards faster speeds, leading to a decrease in the direction bias in all conditions, and possibly a reversal of the illusion for the high speed group when tested with lower speeds (Figure 1B).

Consistent with previous findings [4], we found that initial perception of motion direction was accurate for both groups at high contrast (see Figure S1 in the Supplemental Information), and biased towards perpendicular judgments at low contrast (Figure 1C). The low-speed group showed a small within-session effect ($p = 0.046$, corresponding to the vertical displacement between dashed and solid lines in Figure 1C); however, the illusion was unaltered across sessions ($p = 0.52$). For the high-speed group, the initial perpendicular bias gradually diminished until the illusion reversed and the motion direction was most often perceived as being more oblique. Interestingly, this group exhibited both a fast (within-session; $p = 0.0047$) and a slow (across-sessions; $p < 0.001$) learning component. The fast component is a type of perceptual adaptation in which the perceptual system adapts to current perceptual conditions (for example [5]) and then is reset. The slow component resembles perceptual learning, where the lack of a significant effect in the low-speed group is consistent with the need for a learning threshold to be exceeded for perceptual learning to occur [6]. These results provide the first evidence that basic sensory

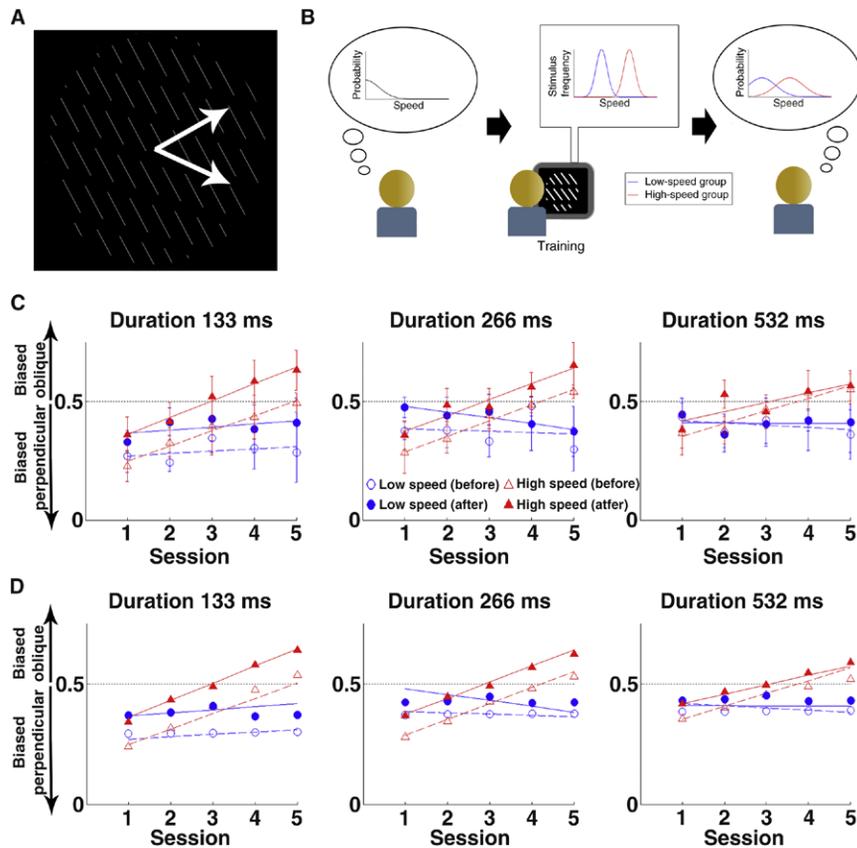


Figure 1. Schematic illustration of the experiment and results. (A) The stimulus used in the experiment. The entire line field translates rigidly along either of the two directions shown by the white arrows (the latter are not part of the stimulus). (B) A cartoon of experimental hypothesis. Left: initially subjects have a prior favoring low speeds. Middle: the low-speed group was exposed to low speeds (blue), while the high-speed group viewed faster speeds (red). Right: training will lead the high-speed group to shift their prior expectations towards higher speeds (red) compared to the low-speed group (blue). (C) Results: proportion of oblique perceptions (p_o) in low-contrast condition, for three trial durations. Each point is the p_o for the first (empty symbols) or last (filled symbols) test block of the session, for the high-speed (red) or the low-speed (blue) group. Lines correspond to linear fits to each block/group combination. Error bars denote between-subjects SEM. (D) Fits from Bayesian model of motion perception (points) can account for the behavior of the two groups (lines, corresponding to the linear fits in C).

knowledge such as the speed of stimuli in the world can be changed in a long-lasting manner.

We modeled our results using a Bayesian model [2], which suggests that motion perception can be described as an optimal estimation of object velocities under the assumption of local measurement noise and an *a priori* preference for slower speeds. This model satisfactorily fits our results by assuming that the speed prior shifts towards higher speeds with exposure (Figure 1D and Supplemental Figure S2), with a mean of 0 deg/s at the start of the first experimental session and 6.2 deg/s by the end of the last session for the high-speed group. The prior of the low-speed group started at 0 deg/s and showed

little change — achieving only 0.63 deg/s by the end of the last session. As such, our results support the previously proposed Bayesian models of motion perception and provide the first experimental evidence that our knowledge of the speed of stimuli plays a causal role in direction discrimination.

Overall, our results are consistent with the hypotheses, first, that naive subjects expect to see slow speeds, and thus perceive the direction that corresponds to the slowest speed under conditions of uncertainty, and second, that subjects exposed to high-speed stimuli gradually shift their expectations towards higher speeds and thus perceive directions consistent with faster speeds more often.

Generally, our results show that expectations that are thought to result from a lifetime of sensory inputs remain plastic. Previous studies found that expectations that ‘light comes from above’ [5] can be reset in the short term, particularly if they conflict with inputs from other modalities (such as tactile inputs). Here, we found that even basic aspects of motion processing, such as perceived direction, can be changed in a long-lasting manner. Moreover, they occur through an implicit statistical learning [7–10] procedure where no guidance was provided to subjects regarding the stimuli’s motion-directions. This suggests that the brain is constantly revising even its most basic assumptions about the environment even without explicit information regarding the true properties of the stimuli in the world.

Supplemental Information

Supplemental Information contains two Figures, Supplemental Results and Supplemental Experimental Procedures and can be found with this article online at doi:10.1016/j.cub.2011.09.013

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