Chicks go left for less, right for more

Most humans think of numbers as being ranged along a horizontal line, called the mental number line (MNL), with smaller values located to the left and larger values to the right. Relativity is a fundamental characteristic of the MNL: for example, in the numerical range of 1–9, 9 is located on the right, whereas in the numerical range of 9–18, 9 is on the left.

The origin of the MNL is unclear. Human infants as well as certain animal species (including Clark's nutcrackers and rhesus macaques) seem to share a tendency to count up from left to right, perhaps reflecting a common spatial-numerical association. But the existence of a MNL has so far only been demonstrated in adult humans.

Rosa Rugani and colleagues at University of Padova and at University of Trento (both in Italy) designed a new strategy for testing the presence and relativity of a MNL in animals. They used 3-d-old domestic chicks (*Gallus gallus*), first teaching them

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to locate food hidden behind a small card marked with a certain number of dots (the target number). Once each chick learned to do this, it was shown two identical cards, one on its left side and one on its right side, both marked with the same number of dots, which was different from the target number. Each chick underwent two tests: in the first, the two cards were marked with a smaller number of dots than the target, and in the second, the two cards were marked with a larger number of dots than the target. The investigators recorded which card (left or right) each chick inspected first. Across a series of experiments, chicks spontaneously associated numbers smaller than the target with the left card and numbers larger than the target with the right card (*Science* **347**, 534–536; 2015). Furthermore, the association of a certain number with the left or the right card depended on the relative magnitude of the number with respect to the target. Chicks that were trained with a target number of '5' associated the number '8' with the right card, whereas chicks that were trained with a target number of '20' associated the number '8' with the left card.

The results show that the tendency to map numbers of increasing magnitude from left to right along a MNL can be observed in animals, leading the authors to suggest that it "may be a universal cognitive strategy."

Monica Harrington

MOUSE MODEL TO CLARIFY OVARIAN CLEAR-CELL CARCINOMA

Ovarian clear-cell carcinoma (OCCC) is an aggressive form of cancer. Although its incidence is not high, accounting for 5–20% of all epithelial ovarian cancers (EOCs), it has a poorer prognosis, higher recurrence and lower survival than other EOC types, particularly when diagnosed at advanced stages. A better understanding of OCCC development and progression could lead to improved treatments and outcomes for those affected, and a new tool for studying OCCC holds promise for delivering this necessary insight. Scientists at University of North Carolina (Chapel Hill) recently announced the creation of a genetically engineered mouse model of OCCC that recapitulates the disease in humans. The model could be used to test potential therapies and to identify disease markers for diagnostic screening.

The scientists, led by Terry Magnuson, looked for genes that were frequently mutated in human OCCC and found that *ARID1A* (a tumor suppressor gene) and *PIK3CA* (a proto-oncogene) were both mutated in about 33% of cases. The mutation in *ARID1A* resulted in loss of function, whereas the mutation in *PIK3CA* resulted in activation. Magnuson's team recreated each mutation in mice and found that neither mutation alone caused tumor growth, but mice carrying both mutations together rapidly developed ovarian tumors (*Nat. Commun.* **6**, 6118; 2015). "When ARID1A is less active than normal and PIK3CA is overactive, the result is ovarian clear cell carcinoma 100 percent of the time in our model," Magnuson said in a press release. "It's an extremely aggressive model of the disease, which is how this form of ovarian cancer presents in women," he continued.

The team showed that the two mutations cooperated to promote tumor growth by spurring the overproduction of interleukin 6 (IL-6), an inflammatory cytokine. Treatment with an antibody against IL-6 suppressed tumor growth in mice with mutations of both ARID1A and PIK3CA. Treatment with BKM120, a drug that blocks PIK3CA, also inhibited tumor growth, prolonging the lives of these mice. BKM120 is being studied as a treatment for other cancers.

In addition to evaluating potential treatments, the mouse model could be used to develop a test to screen for OCCC. Ronald Chandler, first author on the published report, explained, "If we can find something measurable that's downstream of ARID1A…then we could use it as a biomarker of disease. We could create a way to screen women. Right now, by the time women find out they have [OCCC], it's usually too late. If we can find it earlier, we'll have much better luck successfully treating patients."

Monica Harrington