Abstractions

LAST AUTHOR

Tissue pH is a potent indicator of many disease states, including cancer, inflammation and infection. Yet there is no non-invasive way to image it in the clinic. Although magnetic resonance imaging is a powerful tool with which to visualize the body's soft tissue architecture, its sensitivity for imaging tissue chemistry has been low. Biochemist Kevin Brindle at Cancer Research UK's Cambridge Research Institute and his colleagues show on page 940 that they can markedly increase that sensitivity — and document the lower tissue pH associated with tumours in mice.

How does this technique image pH?

We knew tissue chemistry could be imaged if we could increase sensitivity. Normally, when atoms with a magnetic moment — such as carbon-13 — are put into a magnetic field, the 'spins' of their nuclei align themselves with it. But the interaction between the magnetic field and the nuclear spins is very weak, so the spins jostle each other, which causes some to fall out of line. This has a knock-on effect on sensitivity, and so image resolution. To increase sensitivity, we used a trick called hyperpolarization. We cooled carbon-13-labelled molecules together with stable radicals that had fully polarized electron spins to just above absolute zero; then transferred the polarization to the carbon-13 nuclei with microwave irradiation. We took advantage of the body's natural pH buffer, bicarbonate, and injected hyperpolarized carbon-13-labelled bicarbonate into mice. The labelled carbon dioxide produced from this in body tissues allowed us to calculate the pH.

Is hyperpolarization an established technique?

It was first described in 1953, but didn't become practical for imaging applications until 2003, when my industry-based co-authors figured out how to blast a sample with hot water to bring it from almost absolute zero to body temperature in a fraction of a second. Our collaboration led first to detecting labelled pyruvate as an indicator of treatment-induced tumour cell death. Being able to detect labelled bicarbonate may provide a generic method for imaging disease.

When might this technique make it to the clinic?

It's hard to say. If all goes well with a clinical trial GE Healthcare is planning for labelled pyruvate in 2009, one for bicarbonate could take place during the next few years.

What challenges does the technique face?

The polarization is very short lived, with a half-life of less than a minute. That means we'll have to polarize, inject and image very quickly. It's a challenge, but a solvable one. ■

MAKING THE PAPER

Arnon Lotem

Perception affects whether we play the odds or go for a sure thing.

Sometimes, people are no smarter in their decision-making than rats. At least, so it seemed from a paper shown to Arnon Lotem by his colleague and co-author Ido Erev. Lotem, a professor of zoology at Tel-Aviv University, wondered why this might be.

The paper reported on the 'certainty effect', whereby rats repeatedly faced with the option of receiving either a bigger reward infrequently or a lesser reward with certainty preferred the safer option, despite it being less profitable on average. In so doing, they behaved just as humans do when the pay-off odds of choosing two alternatives are described to them verbally.

However, Erev's group had found that if humans are faced with the same situation as the rats — that is, the pay-off probabilities are not explained to them — they behave differently. On a 'computerized money machine', they repeatedly gravitate towards the bigger pay-off, even though it is statistically less likely. This penchant is known as the 'reverse certainty effect'. Lotem and his colleagues set out to establish what lay behind this difference in behaviour. They discovered that both humans and other animals can exhibit certainty or reverse certainty, depending on the cues available to them.

Because humans can perceive the precise amount of a reward from reading numbers, whereas rats must rely on their senses to make estimates, Lotem and his team suspected that perceptual accuracy was the key to solving this paradox. They started by devising a series of experimental scenarios that manipulate the clarity of reward cues, then ran them in both honeybees and humans.

In one experiment, human subjects had to choose repeatedly between two unlabelled buttons on the money machine. One button always provided a small payout; the other supplied a larger one, but did not always pay out. No explanation was offered of the odds of the payout.

Watching people push buttons seemingly at random was enlightening, says Lotem. "In theory, people could have been very smart and pressed one button 20 times and pressed another button 20 times, and, like a scientist, figured out the average," Lotem says. "But people don't behave like statisticians." Instead, subjects tried both buttons and developed a preference for the button perceived as better 'most of the time' (see page 917).

However, when payouts were represented by a visual display of scattered dots rather than through clear numerical means — making it more difficult to tell which was better — people preferred the safer button. In other words, they exhibited the certainty effect, just like the rats in the study that first piqued Lotem's interest.

Meanwhile, honeybees rewarded with sugary solutions of varying concentration behaved remarkably similarly to humans, preferring the risky option when discrimination between rewards was easy, and the safe option when discrimination was difficult. "Honeybees can't count," says Lotem. "But, if you give them a high concentration of sugar, they remember. If they get zero, they remember." Like humans, the bees behaved as though they preferred the option perceived as better most of the time.

Lotem and his colleagues wondered how their findings might apply to real-world situations. "In the real world, rewards may frequently be ambiguous, and you never know when conditions are going to change," says Lotem. "So perhaps the tendency to explore both options and to prefer the one perceived as better most of the time is a good strategy." ■

FROM THE BLOGOSPHERE

Does research need new measuring sticks? The Nature Network group 'Citation in Science' (http://tinyurl.com/6afj8a) hopes to find common ground among researchers, funders, information providers and others concerning the measures of research output.

Allan Sudlow of the British Library lists common ways in which citations are manipulated or otherwise abused. 'The art of counting', a post by Nature product developer Ian Mulvany, is a useful account of how the impact factor and the H-index are calculated, and concludes that there are many growing areas of contribution such as blogs and open data sets that, at present, are ignored by such metrics. Another post explores whether the number of times an article is downloaded from the Internet could be more informative than its citation counts.

Biologist David Colquhoun of University College London argues that publication metrics are inappropriate for assessing people: "The pressure to produce cheap headline-grabbing work will be enormous. The long-term reputation of UK science will surely be damaged by this sort of bean-counting approach." ■

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