

to the inactivated viruses, but not more distantly related H1 or H3 viruses, much less viruses from other subtypes. When a new virus strain is introduced into humans, such as the H1N1 virus in 2009, an entirely new vaccine or vaccine component is required. This continual game of catch-up is a dangerous one because it takes time to produce a vaccine to a new circulating strain, and a particularly virulent strain might reach pandemic status before the process is complete. This has spurred the search for antibodies that can neutralize not only multiple strains within an influenza virus subtype, but viruses from different subtypes as well. Recently, a number of antibodies that fulfill these properties have been identified (3–6). Two of these have been crystallized while bound to HA, showing that these antibodies, unlike the vast majority of neutralizing antibodies elicited by infection or vaccination, bind to a highly conserved region in the stem region of HA rather than to epitopes in the globular head domain (5, 6). By binding to HA in this position, stem-targeting antibodies prevent HA from undergoing the conformational changes needed to catalyze the membrane fusion reaction needed for virus infection.

Identifying broadly cross-reactive, neutralizing antibodies to influenza virus reveals the potential for a more effective vaccine, but stimulating the production of such antibodies presents a challenge. A growing number of broadly neutralizing antibodies to HIV have been identified, for example, but

no vaccination strategy to date has elicited such antibodies efficiently (7–9). Strategies to achieve broad neutralization include generating novel immunogens that elicit broadly neutralizing antibodies, or using immunization procedures coupled with existing vaccine components to achieve the same end. Wei *et al.* took the second approach, using a prime-boost strategy in which mice, ferrets, and monkeys were primed with a DNA vaccine expressing an HA protein based on an existing seasonal flu vaccine. They were then boosted with the inactivated seasonal flu vaccine itself. Thus, the innovation was not the immunogen per se, but rather the DNA vaccine priming step. Strikingly, when HA from the 1999 seasonal H1 flu vaccine was used in this manner, the resulting sera efficiently neutralized H1 viruses dating as far back as 1934, as well as H1 viruses that emerged in 2006 and 2007—a span of more than 70 years. Some cross-neutralization of H3 and H5 viruses was also achieved, and animals were protected from a lethal challenge with virus. Neither the DNA vaccine nor the seasonal vaccine alone achieved these results. Viruses bearing mutations in the conserved stem epitope escaped neutralization elicited by this vaccination strategy. Therefore, DNA priming before the use of a standard seasonal flu vaccine broadened the humoral immune response to include antibodies to the stem of HA, perhaps by facilitating the T cell help needed to stimulate the development of antibody-producing B cells.

The findings of Wei *et al.* provide proof of concept that broadly neutralizing antibodies to influenza virus can be elicited through immunization, although similar prime-boost approaches have failed to produce broadly neutralizing antibodies to HIV (9). An important practical consideration is that the prime-boost technique used by Wei *et al.* will require at least two or more injections at different times, necessitating multiple visits to a care-giver. By contrast, the most commonly used seasonal flu vaccine requires only a single intramuscular injection. On the other hand, the broad neutralization seen in the prime-boost method may diminish the need for annual immunizations. Further work is needed to elucidate whether all influenza subtypes and strains will lend themselves to this immunization approach. The results of Wei *et al.* call for a renewed focus on vaccine development, with emphasis on immunization strategies as well as the immunogens themselves.

References

1. S. Salzberg, *Nature* **454**, 160 (2008).
2. C.-J. Wei *et al.*, *Science* **329**, 1060 (2010); published online 15 July 2010 (10.1126/science.1192517).
3. A. K. Kashyap *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **105**, 5986 (2008).
4. T. T. Wang *et al.*, *PLoS Pathog.* **6**, e1000796 (2010).
5. D. C. Ekiert *et al.*, *Science* **324**, 246 (2009).
6. J. Sui *et al.*, *Nat. Struct. Mol. Biol.* **16**, 265 (2009).
7. T. Zhou *et al.*, *Science* **329**, 811 (2010); published online 8 July 2010 (10.1126/science.1192819).
8. L. M. Walker *et al.*, *Science* **326**, 285 (2009).
9. P. D. Kwong, I. A. Wilson, *Nat. Immunol.* **10**, 573 (2009).
10.1126/science.1195116

BEHAVIOR

Decisions Made Better

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We constantly make decisions based on perceptual experiences. For example, a referee at a soccer match trusts his eyes to judge whether the ball crossed the goal line. Sometimes, the resulting decisions are false, with devastating consequences for one team. If two referees watching the same match made joint decisions, would the result overall be more precise? On page 1081 of this issue, Bahrami *et al.* (1) find that joint decisions are better than those made individually, but only under certain conditions.

For most joint decisions, the referees will not need to confer with one another about their observations, as their individual perceptions will agree—the ball crossed the goal line or it did not. No benefit in joint decision-making can result from such concurring observations. If during negotiation, however, it becomes apparent that their observations differ, what strategy can be used to resolve this conflict and come up with the best joint answer? That is, what decision strategy would result in a benefit for the group?

If the referees disagree in their individual judgments, the simplest way to resolve the conflict is to flip a coin. This strategy is less than optimal because it would be wrong half of the time, such that joint decision perfor-

Under certain circumstances, joint decisions of a group can be better than those of the individuals.

mance, taking all decisions together, will be in-between that of the two referees and not better than either one alone. To improve on this outcome, more information is needed. For example, if we knew from previous experience that Referee 1 usually makes more accurate decisions, we would ask that person to always make the final call. However, decision performance is just as good as having one referee present at the match, and there is still no improvement. So what is the best strategy to resolve the conflict and lead to a group benefit? The answer is simple. Every decision has a right and a wrong answer, so when there is a conflict, only one referee is correct. Which referee is correct, however, will differ from decision to decision. If in every case the

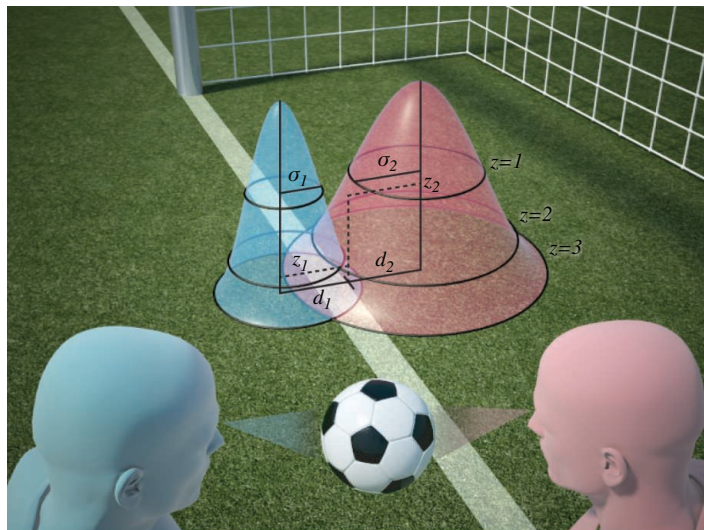
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referee who currently has the correct answer would make the joint decision, group performance (considering all decisions) would be better than that of each individual alone. The problem is, how do the referees know who currently makes the correct decision?

Decisions based on individual perceptions are inevitably uncertain because they rely on sensory evidence that is corrupted by noise. Such noise is always introduced when sensory information from the eyes, ears, or hands is processed by the nervous system (2). The amount of noise depends on the particular perceptual situation (viewing distance, lighting conditions, etc.) so that decisional uncertainty will vary from moment to moment. More noise

implies more uncertainty and a greater chance to get the answer wrong. Thus, an indication of who got the right answer can be the level of certainty with which a decision can be made. If so, an individual would need to communicate this certainty level to the other group members. If the more certain referee always provides the joint answer, because she or he is more likely to be correct, an overall group benefit can be achieved.

Bahrami *et al.* show that humans do indeed communicate some measure of certainty in their decision when they are free to discuss their perceptual experiences. This allowed pairs of individuals in their study to improve joint performance substantially under most of the conditions tested. To understand why performance on joint decisions did not always improve, the authors looked at the certainty measure that participants communicated to each other. To illustrate the decision process, consider the perceptual experiences of the two referees (see the figure). The peaks of the two normal distributions specify the percept where the ball apparently landed; the spread of the distributions indicates the noise associated with the individual perceptual estimates. According to Bahrami *et al.*, the certainty with which each referee decides whether the ball crossed the goal line is the distance (d_i) between the percept (peak) and decision-line (i.e., goal line), divided by the spread of the distribution (σ_i). This ratio, a z -score ($z_i = d_i/\sigma_i$), is the level of certainty that humans apparently communicate to each other when making a joint decision, as this model best fits the data of Bahrami *et al.* Given this certainty measure, there is a simple strategy for resolving disagreement over decisions: The



Joint decisions. Noisy estimates of the landing position of the ball for Referee 1 (blue) and Referee 2 (red). See the text for a description on how referees might make the best possible decision on where the ball landed.

referee who is currently more certain—that is, the one who has the higher z -score—gets to make the joint decision. Expressed as an equation, this decision rule is given by: $d_1/\sigma_1 + d_2/\sigma_2 = 0$. When this sum is positive, Referee 1 will make the joint decision; otherwise, Referee 2 will.

However, this is not the best possible way to combine information and come to a joint decision. Examples of how to combine information in the most optimal way, thereby guaranteeing the most precise final judgement, are provided by studies on the integration of information across the senses (3–6). For example, when judging the size of an object, visual and tactile information is integrated to improve the overall size estimation (5). These studies show that the best possible way to integrate information is to form a weighted average of the different information sources (7). Applied to the situation of judging whether the ball crossed the goal line, this weighted average is given by $d = (d_1/\sigma_1^2 + d_2/\sigma_2^2)/N$ with $N = 1/\sigma_1^2 + 1/\sigma_2^2$. According to this equation, the distance d is the optimal joint estimate of where the ball has landed. The sign of d , therefore, determines whether the ball apparently went over the goal line. Thus, the optimal decision rule can then easily be derived as $d_1/\sigma_1^2 + d_2/\sigma_2^2 = 0$. Comparing this optimal decision rule to the earlier one, it is clear that the referees (and humans generally) should use d_i/σ_i^2 , instead of the z -score d_i/σ_i , for communicating the level of certainty in their perceptual estimates. Such optimal joint decision-making would guarantee the group a benefit over its individuals, similar to the way in which multisensory integration incurs a benefit for sensory estimation.

Joint decision-making is generally worse when using d_i/σ_i instead of d_i/σ_i^2 . However, the difference in performance based on these measures vanishes when the noises are equal ($\sigma_1 = \sigma_2$), because then the two decision rules become equal ($d_1 + d_2 = 0$). When the noises are equal, the maximal benefit of joint decision-making can be achieved, which is an improvement of roughly 40% (factor of $\sqrt{2}$) over its individuals. As the difference between σ_1 and σ_2 increases, joint decision-making using a certainty measure based on the z -scores will become increasingly less beneficial, up to a point where joint decision-making even incurs a cost instead of providing a benefit.

This switch occurs when the difference between the noises of the individual judgments falls below $\sigma_1 \approx 0.4\sigma_2$ (1). Thus, referees using z -scores as their certainty measure can benefit from joint decision-making only if the noise levels of their perceptual estimates are similar; otherwise, they risk incurring a cost when deciding jointly.

Humans use d_i/σ_i instead of d_i/σ_i^2 when communicating their level of certainty and by doing so they risk a cost, but it is unclear why. One reason may be that the optimal certainty measure, other than the z -score, is not unit-free. This may cause problems when trying to communicate such measures, because all group members have to use the same units. Imagine an American and a European referee making joint decisions—one using inches, the other meters. It would be interesting to see whether, by providing feedback, people could be trained to use the better of the two certainty measures, so that joint decisions would always be better than that of individuals. Whether it is feasible to have two referees negotiating each decision during a soccer match is another matter entirely.

References and Notes

- B. Bahrami *et al.*, *Science* **329**, 1081 (2010).
- A. A. Faisal *et al.*, *Nat. Rev. Neurosci.* **9**, 292 (2008).
- M. S. Landy *et al.*, *Vision Res.* **35**, 389 (1995).
- Z. Ghahramani *et al.*, in *Self-Organization, Computational Maps and Motor Control*, P. G. Morasso, V. Sanguinetti, Eds. (Elsevier, Amsterdam, 1997), pp. 117–147.
- M. O. Ernst, M. S. Banks, *Nature* **415**, 429 (2002).
- D. Alais, D. Burr, *Curr. Biol.* **14**, 257 (2004).
- W. G. Cochran, *J.R. Stat. Soc.* **4** (suppl.), 102 (1937).
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