ical pathway in the regulation of IL-1 activity in myelomonocytic cells that can be subverted by pathogens and may provide a target for pharmacological intervention.

The existence of multiple pathways of regulation, including a polypeptide receptor antagonist (*1*) and the decoy target for IL-1 binding, emphasizes the need for tight regulation of IL-1 activity. We suggest that the term "receptor" may be an inappropriate designation, at least until evidence is obtained that IL-1R II binding protein is indeed a signaling receptor, and propose to refer to this acceptor molecule as a "decoy receptor."

REFERENCES AND NOTES

1. C. A. Dinarello, *Blood* **77**, 1627 (1991).
2. S. K. Dower *et al.*, *J. Exp. Med.* **162**, 501 (1985); S. K. Dower *et al.*, *Nature* **324**, 266 (1986); T. A. Bird and J. Saklatvala, *ibid.*, p. 263; P. L. Kilian *et al.*, *J. Immunol.* **136**, 4509 (1986); J. Chin, P. M. Cameron, E. A. Rupp, J. A. Schmidt, *J. Exp. Med.* **165**, 70 (1987); T. A. Bird, A. J. H. Gearing, J. Saklatvala, *J. Biol. Chem.* **263**, 12063 (1988); D. L. Urdal, S. M. Call, J. J. Jackson, S. K. Dower, *ibid.*, p. 2870; E. Stylianou *et al.*, *ibid.* **267**, 15836 (1992); J. E. Sims *et al.*, *Science* **241**, 585 (1988).
3. K. Matsushima *et al.*, *J. Immunol.* **136**, 4496 (1986); R. Horuk, J. J. Huang, M. Covington, R. C. Newton, *J. Biol. Chem.* **262**, 16275 (1987); C. Bensimon *et al.*, *J. Immunol.* **143**, 1168 (1989); K. Bomstyk *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **86**, 8034 (1989); R. Chizzonite *et al.*, *ibid.*, p. 8029; G. Scapigliati *et al.*, *FEBS Lett.* **243**, 394 (1989); D. Benjamin, S. Wormsley, S. K. Dower, *J. Biol. Chem.* **265**, 9943 (1990).
4. J. A. Rhyne *et al.*, *Clin. Immunol. Immunopathol.* **48**, 354 (1988); E. V. Granowitz, B. D. Clarck, J. Mancilla, C. A. Dinarello, *J. Biol. Chem.* **266**, 14147 (1991).
5. M. K. Spriggs *et al.*, *Cytokine* **4**, 90 (1992).
6. C. J. McMahan *et al.*, *EMBO J.* **10**, 2821 (1991).
7. F. Colotta, F. Re, N. Polentarutti, S. Sozzani, A. Mantovani, *Blood* **80**, 2012 (1992).
8. A. F. Lopez *et al.*, *J. Clin. Invest.* **78**, 1220 (1986); Y. Yamaguchi *et al.*, *Blood* **78**, 2542 (1991).
9. W. E. Paul, *Blood* **77**, 1859 (1991).
10. F. Colotta, F. Re, A. Mantovani, unpublished data.
11. K. Tiku, M. L. Tiku, J. L. Skoshey, *J. Immunol.* **136**, 3677 (1986); P. C. W. Lord, L. M. G. Wilmoth, S. B. Mizel, C. E. McCall, *J. Clin. Invest.* **87**, 1312 (1991).
12. J. A. Symons, J. A. Eastgate, G. W. Duff, *J. Exp. Med.* **174**, 1251 (1991); J. G. Giri, R. C. Newton, R. Horuk, *J. Biol. Chem.* **265**, 17416 (1990).
13. K.-C. Koch, K. Ye, B. D. Clark, C. A. Dinarello, *Eur. J. Immunol.* **22**, 153 (1992).
14. M. K. Spriggs *et al.*, *J. Biol. Chem.* **265**, 2249 (1990).
15. D. Boraschi *et al.*, *Blood* **78**, 1262 (1991); F. Colotta *et al.*, *ibid.* **81**, 1347 (1993).
16. T. Akahoshi, J. J. Oppenheim, K. Matsushima, *J. Exp. Med.* **167**, 924 (1988).
17. M. K. Spriggs *et al.*, *Cell* **71**, 145 (1992); A. Alcami and G. L. Smith, *ibid.*, p. 153.
18. F. Colotta, J. M. Wang, N. Polentarutti, A. Mantovani, *J. Exp. Med.* **165**, 122 (1987).
19. F. Colotta *et al.*, *J. Immunol.* **148**, 760 (1992); M. Sironi *et al.*, *ibid.* **142**, 549 (1989).

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Right Hemisphere Dominance for the Production of Facial Expression in Monkeys

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In humans, the left side of the face (right hemisphere of the brain) is dominant in emotional expression. In rhesus monkeys, the left side of the face begins to display facial expression earlier than the right side and is more expressive. Humans perceive rhesus chimeras created by pairing the left half of the face with its mirror-reversed duplicate as more expressive than chimeras created by right-right pairings. That the right hemisphere determines facial expression, and the left hemisphere processes species-typical vocal signals, suggests that human and nonhuman primates exhibit the same pattern of brain asymmetry for communication.

In humans, neuroanatomical differences between the right and left hemispheres of the brain are associated with differences in the production and perception of behavior (*1–3*). Although nonhuman animals show both neuroanatomical and behavioral asymmetries (*2, 4–6*), humans show stronger and more varied asymmetries (*1, 2*). In general, the left hemisphere dominates in linguistic function and manual control, whereas the right hemisphere dominates in spatial reasoning, emotional perception, and face recognition.

Studies of some nonhuman primate populations have provided evidence that hand preference is nonrandom during both unimanual and bimanual motor tasks (*4*). Evidence of lateralization for auditory and visual perception is, however, more ambiguous. In the Japanese macaque, the left hemisphere is dominant with regard to the perception of species-typical vocal signals (*7, 8*). Thus, both human and nonhuman primates exhibit left hemisphere dominance for referentially relevant stimuli. An assumption underlying this claim, however, is that the vocalizations used in these experiments provide referentially salient information rather than affective information. The relative contribution of referential and affective information to signal structure is currently unclear (*9, 10*). Experiments on face recognition in monkeys and apes sometimes show a strong right hemisphere bias (*11, 12*) but may also show more symmetric contributions of left and right hemispheres (*13*). To my knowledge, no study has examined hemispheric asymmetries in the production of vocal signals in nonhuman primates (*14*). However, a study demonstrated that, when split brain rhesus macaques were presented with videotaped sequences of human and nonhuman primate scenes to the right hemisphere, they showed significantly more facial expressions, both submissive and aggressive, than when sequences were presented to the left hemisphere (*15*).

Video records of free-ranging rhesus monkeys living on the island of Cayo Santiago, Puerto Rico, were analyzed to assess hemispheric asymmetries in the production of facial expressions (*16*). All data were collected from individually recognizable animals from one social group. Most individuals from the sample were genetically unrelated males. Frame-by-frame (one frame = 33 ms) analyses (*16*) were carried out for all expressions for which the subject's entire face was oriented toward the video camera.

Four facial expressions were evaluated, representing three different emotional states. The fear grimace (Fig. 1), which is produced by retracting the lips, is given by a subordinate individual being attacked or intimidated by a higher ranking group member. The copulation grimace, which is also produced by retracting the lips but which is not held in position as long as the fear grimace, is given by adult males during copulation. The open mouth threat, which is produced by slightly protruding the lips and placing them into an O-shaped configuration, is given by a dominant individual attacking or intimidating a subordinate. The ear flap threat, which is produced by retracting the ears back against the head, is also given by a dominant individual attacking or intimidating a subordinate.

I calculated asymmetries in the temporal emergence of an expression by comparing the onset of facial movement on the

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right and left sides. Timing was considered asymmetric if the gesture on one side of the face started moving into the expression at least one frame before the other side of the face. For fear and copulation grimaces, it was also possible to measure the asymmetry in the form of the expression. Two quantifiable aspects were the number of skin folds between eye and the cheekbone and the height of the corner of the mouth during lip retraction. Higher retraction of the corner of the mouth and greater number of skin folds were considered more expressive. In this context, expressiveness is considered from the human observer's perspective rather than from the monkey's. Statistical analyses were carried out on the proportion of individuals showing lateral asymmetries in expression.

The largest sample size was obtained for fear grimaces (Table 1); of the 19 individuals analyzed, one to seven fear grimaces were produced per individual. Frame-by-frame analysis (Fig. 1) of the onset and termination of an adult male's fear grimace reveals that the left side of the face begins moving into the retracted position (see frame 2 and especially frame 3) earlier than the right side. This pattern was robust within the sample of 19 individuals (Table 1). Over 75% of the individuals were asymmetric with regard to the timing of the expression. Of those showing such asymmetries, the left side started moving first in over 90% of the individuals. On average, the left side of the face started moving 1.4 frames (SD = 0.42 frame, range = 1 to 3 frames) before the right side.

The form of the expression was also asymmetric. For most of the 19 individuals, there were more folds on the left side of the face than on the right, and the left corner of the mouth attained a higher position than the right.

For all of the other expressions analyzed (Table 1), the proportion of subjects showing asymmetry in timing or form of expression ranged from 50 to 100%. In a majority of cases in which an individual exhibited an asymmetry in facial affect, however, the left side was consistently more expressive than the right. Thus, for example, during the let-down phase of the fear and copulation grimaces, the left side typically maintained the expression longer than the right. This timing bias was statistically significant only for the copulation grimace. For open mouth threats, the left side of the mouth opened up earlier than the right, and for the ear flap gesture the left ear moved before the right.

Visual chimeras of human faces formed by pairing each side of the face with a mirror-reversed duplicate show that humans perceive left-left chimeras as more expressive than right-right chimeras (Fig. 2) (*17*). Chimeras of three different rhesus monkey faces were created (*18*). Human adults (28 females, 15 males; age range, 19 to 38 years) were then asked to report which chimera appeared to express a more intense state of fear. All human subjects were naïve with regard to research on hemispheric specialization. Out of 43 subjects, 41 reported that the left-left chimera appeared to be in a relatively heightened state of fear compared with the right-right chimera.

These results reveal that in rhesus monkeys, as in humans, rats, and chickens (*2*), the right hemisphere of the brain is dominant with regard to emotional expression. However, in some electroencephalogram studies of humans (*19*), the right hemisphere appears dominant for negative-withdrawal emotion whereas the left hemisphere is dominant for positive-approach emotion. Although current observations limit our ability to dichotomize the emotions of nonhuman primates, most of the facial expressions in these rhesus monkeys are associated with agonistic interactions and thus are likely to represent negative emotion; one possible exception is the copulation grimace. Of the nonhuman primates, only chimpanzees and bonobos appear to use facial expressions that are clearly associated with positive emotions and a tendency to approach (*20, 21*).

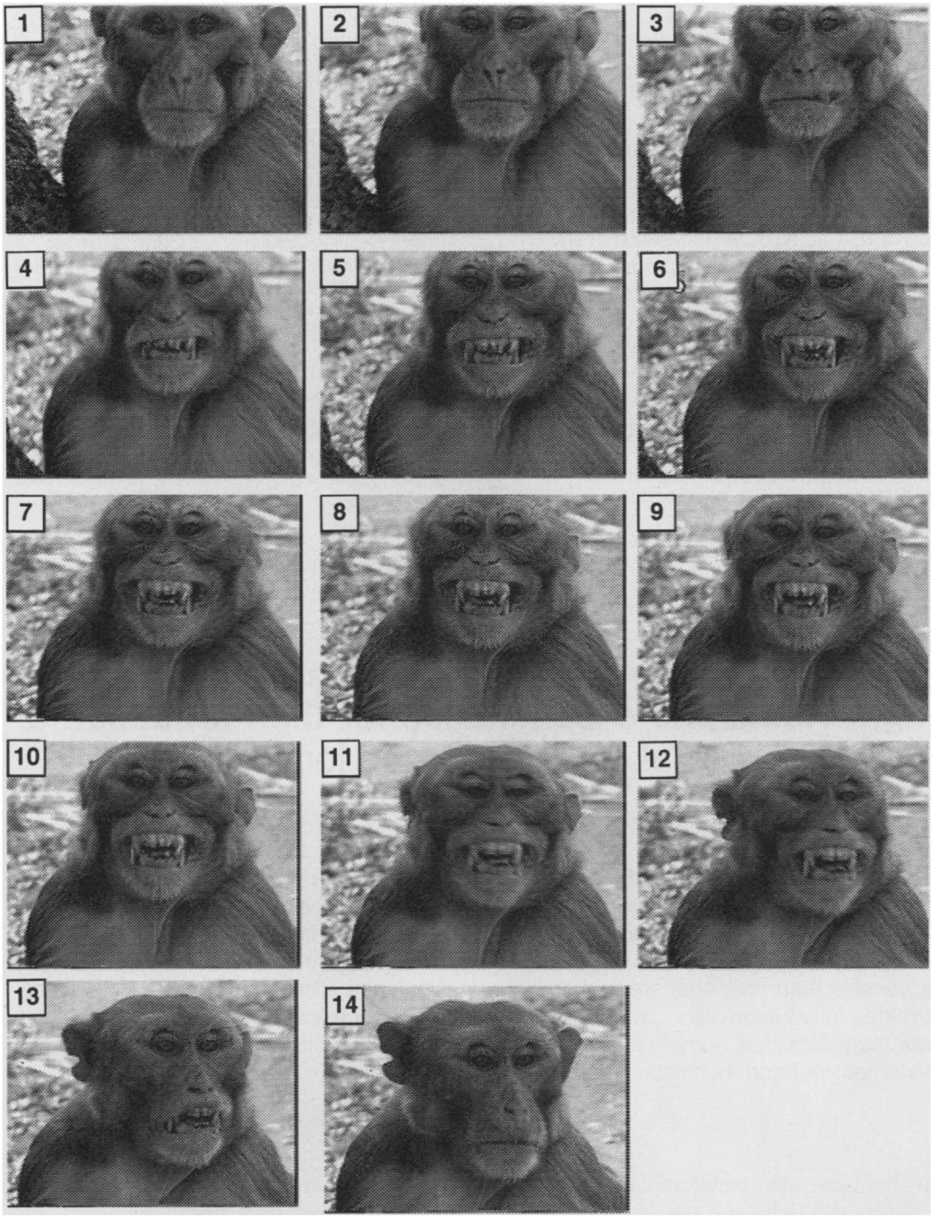

Fig. 1. Frame-by-frame illustration of the fear grimace of a rhesus monkey, produced in the context of submission. In frame 2 the left side of the face has begun moving into the fear grimace position whereas the right side only begins moving in frame 4.

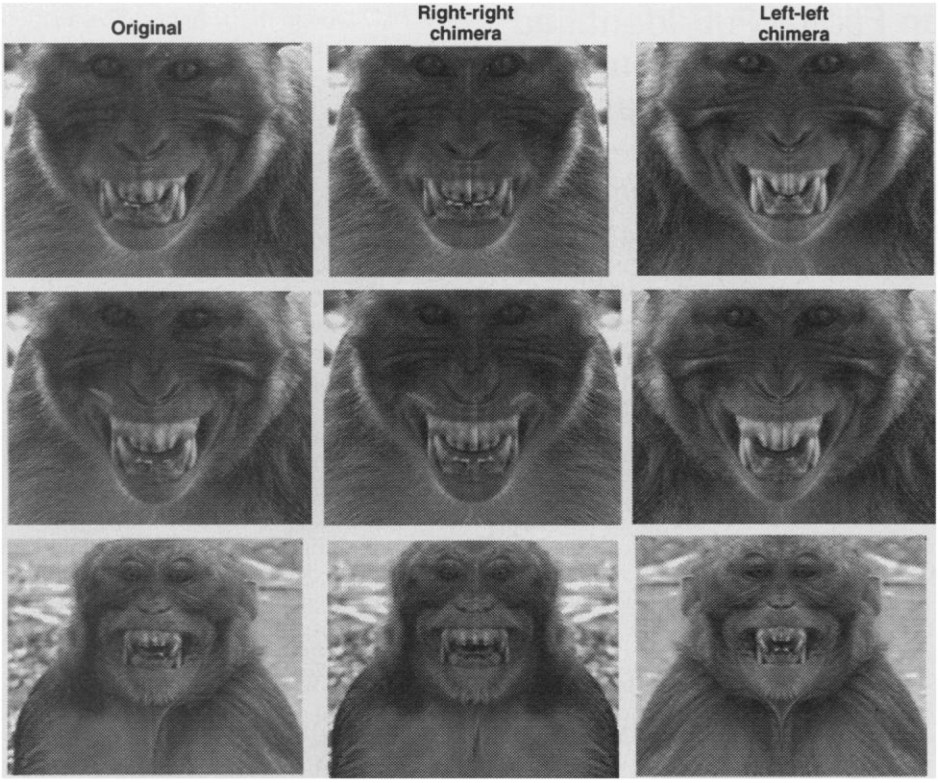

Fig. 2. Three examples of an original fear grimace and two chimeras produced by pairing one-half of the face with its mirror-reversed duplicate. Each example is from a different adult male.

Table 1. Asymmetries in rhesus facial expression. Sign tests were conducted on the proportion of individuals exhibiting asymmetries.

Expression	Variable	Number of Individuals	Number of Expressions	Asymmetric expressions (%)	Left-biased expressions (%)
Fear grimace	Timing	17	60	76.5*	92.3**
Fear grimace	Number of folds	19	63	78.9**	86.7**
Fear grimace	Lip retraction	12	36	91.7**	90.9**
Fear grimace to resting position	Timing	4	8	75.0	66.7
Copulation grimace	Timing	8	35	50.0	50.0
Copulation grimace	Number of folds	7	30	85.7	83.3
Copulation grimace	Lip retraction	4	21	100.0	75.0
Copulation grimace to resting position	Timing	8	17	100.0*	87.5*
Open mouth threat	Timing	10	21	60.0	100.0*
Ear flap threat	Timing	4	9	100.0	100.0

*$P < 0.05$. **$P < 0.01$.

Evidence in monkeys of a right hemisphere bias for the production of facial emotion, together with observations of a left hemisphere bias for the perception of species-typical vocal signals (*7, 8*), suggests that human and nonhuman primates show the same patterns of hemispheric differentiation for communication (*2, 3*). Two points must be borne in mind, however, in evaluating this conclusion. First, other nonprimate species such as rats and chicks evidence similar patterns of asymmetry for communication (*2*). At present, it is unclear whether such similarities are due to convergent evolution or whether the hemispheric differentiation of the brain is an evolutionarily ancient trait, common to most vertebrates. Second, the left hemisphere bias for the perception of vocalizations in nonhuman primates only supports the human pattern if the signals tested convey referential information. The signals may, however, convey relatively more information about the individual's emotional state (*22*), in which case the bias is opposite that observed in humans.

REFERENCES AND NOTES

1. M. C. Corballis, *The Lopsided Ape* (Oxford Univ. Press, Oxford, 1991).
2. J. L. Bradshaw and L. Rogers, *The Evolution of Lateral Asymmetries, Language, Tool Use, and Intellect* (Academic Press, San Diego, CA, 1993).
3. J. B. Hellige, *Hemispheric Asymmetry: What's Right and What's Left* (Harvard Univ. Press, Cambridge, MA, 1993).
4. P. MacNeilage, in *Biological Foundations of Language Development*, N. Krasnegor, D. Rumbaugh, M. Studdert-Kennedy, R. Schiefelbusch, Eds. (Erlbaum, Hillsdale, NJ, 1991), pp. 165–188.
5. D. Falk, J. Cheverud, M. W. Vannier, C. G. Conroy, *Folia Primatol.* **46**, 98 (1986).
6. P. L. Heilbroner and R. L. Holloway, *Am. J. Phys. Anthropol.* **76**, 39 (1988).
7. M. R. Petersen, M. D. Beecher, S. R. Zoloth, D. B. Moody, W. C. Stebbins, *Science* **202**, 324 (1978).
8. H. E. Heffner and R. S. Heffner, *ibid.* **226**, 75 (1984).
9. D. L. Cheney and R. M. Seyfarth, *How Monkeys See the World* (Univ. of Chicago Press, Chicago, 1990).
10. P. Marler, C. S. Evans, M. D. Hauser, in *Human and Nonhuman Animal Vocal Communication: Comparative and Developmental Approaches*, H. Papoucek, U. Jurgens, M. Papoucek, Eds. (Cambridge Univ. Press, Cambridge, 1992), pp. 66–86.
11. S. Dimond and R. Harries, *Neuropsychologia* **26**, 445 (1984).
12. C. R. Hamilton and B. A. Vermeire, in *Cerebral Laterality*, F. L. Kitterle, Ed. (Cambridge Univ. Press, Cambridge, 1991), pp. 19–34.
13. W. H. Overman and R. W. Doty, *Neuropsychologia* **20**, 113 (1982).
14. Studies of asymmetry in the production of vocalizations have been reported for songbirds [F. Nottebohm *et al.*, *Philos. Trans. R. Soc. London Ser. B* **292**, 205 (1990)].
15. C. K. Ifune, B. A. Vermeire, C. R. Hamilton, *Behav. Neural Biol.* **41**, 231 (1985).
16. M. D. Hauser, C. S. Evans, P. Marler, *Anim. Behav.* **45**, 423 (1993).
17. J. Levy, W. Heller, M. T. Banich, L. A. Burton, *Brain Cognition* **2**, 404 (1983).
18. Digitized frames of three adult male rhesus monkey faces were used to create chimeras. Images from these particular individuals were selected because they provided the most direct shots of the front of the face; visual artifacts result if chimeras are produced from faces that are even slightly turned to one side. The original image was first split down the center. Each half was then paired with its mirror-reversed duplicate to produce a left-left chimera and a right-right chimera. For one male, inter-eye distance was greater for the left-left chimera than for the right-right chimera (see bottom row of Fig. 2). For the other two males, there was no measurable asymmetry in inter-eye distance. Human subjects were asked to compare only one set of chimeras with the original.
19. R. J. Davidson, *Psychol. Sci.* **3** (no. 1), 39 (1992).
20. J. Goodall, *The Chimpanzees of Gombe* (Belknap, Cambridge, MA, 1986).
21. F. B. M. de Waal, *Behaviour* **106**, 183 (1988).
22. M. D. Hauser, *Ethology* **89**, 29 (1991).

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