will take several years to complete carcinogenicity studies of EMPD in vivo and to enact any appropriate regulations.

The close structural similarity of EMPD to the carcinogenic and mutagenic chemicals TDA and MMPD, as well as the results reported here, imply that EMPD should have been subjected to thorough evaluation for skin absorption, carcinogenicity, and mutagenicity in a variety of test systems before it was used in hair dyes. The use of the then-untested MMPD after the removal of the carcinogen TDA from hair dyes, and the recent introduction of untested EMPD after the carcinogen MMPD was removed from these products, underscore the importance of considering possible relationships between chemical structure and biological effects before exposing consumers to new chemicals.

MICHAEL J. PRIVAL
VALERIE D. MITCHELL
YOLANDA P. GOMEZ
Genetic Toxicology Branch,
Food and Drug Administration,
Washington, D.C. 20204

References and Notes

1. J. F. Corbett, *Cosmet. Toiletries* **91**, 21 (December 1976).
2. N. Ito, Y. Hiasa, Y. Konishi, M. Marugami, *Cancer Res.* **29**, 1137 (1969).
3. National Cancer Institute, *Bioassay of 2,4-Diaminoanisole Sulfate for Possible Carcinogenecity* (Carcinogenesis Technical Report No. 84) (Report PB279940/LLC, National Technical Information Service, Springfield, Va., 1978); J. M. Ward, S. F. Stinson, J. F. Hardisty, B. Y. Cockrell, D. W. Hayden, *J. Natl. Cancer Inst.* **62**, 1067 (1979).
4. *Fed. Regis.* **44**, 59509 (1979).
5. In the United States, ingredients of hair dyes are listed on the boxes containing these products.
6. B. N. Ames, J. McCann, E. Yamasaki, *Mutat. Res.* **31**, 347 (1975).
7. Studies on the correlation between mutagenicity in *S. typhimurium* and carcinogenicity in mammals include: J. McCann, E. Choi, E. Yamasaki, B. N. Ames, *Proc. Natl. Acad. Sci. U.S.A.* **72**, 5135 (1975); J. McCann and B. N. Ames, *ibid.* **73**, 950 (1976); B. Commoner, A. J. Vithayathil, J. I. Henry, J. C. Gold, M. J. Reding, *Reliability of Bacterial Mutagenesis Techniques to Distinguish Carcinogenic and Noncarcinogenic Chemicals* (Environmental Protection Agency Report EPA-600/1-76-022) (Report PB259934/LLC, National Technical Information Service, Springfield, Va., 1976); T. Sugimura, S. Sato, M. Nagao, T. Yahagi, T. Matsushima, Y. Seino, M. Takeuchi, T. Kawachi, in *Fundamentals in Cancer Prevention*, P. N. Magee *et al.*, Eds. (University Park Press, Baltimore, 1976), p. 191; I. F. H. Purchase, E. Longstaff, J. Ashby, J. A Styles, D. Anderson, P. A. Lefevre, F. R. Westwood, *Br. J. Cancer* **37**, 873 (1978); and V. F. Simmon, *J. Natl. Cancer Inst.* **62**, 893 (1979).
8. B. N. Ames, H. O. Kammen, E. Yamasaki, *Proc. Natl. Acad. Sci. U.S.A.* **72**, 2423 (1975).
9. M. Meselson and K. Russell, in *Origins of Human Cancer*, H. H. Hiatt, J. D. Watson, J. A. Winsten, Eds. (Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y., 1977), p. 1473.
10. W. G. H. Blijleven, *Mutat. Res.* **48**, 181 (1977).
11. An exception is the Ministry of Health of Italy, which has banned several ingredients of hair dyes, including MMPD, on the basis of their mutagenicity to *S. typhimurium* [*Gazz. Uffic. Repub. Ital.* (No. 166, 25 June 1976), p. 5025].
12. We thank the Revlon Research Center, Inc., for their generous gifts of MMPD sulfate and EMPD sulfate; Dr. B. N. Ames for the *S. typhimurium* strains used in this work; and L. Katzenstein of *Consumer Reports* for bringing the use of EMPD in hair dyes to the attention of the Food and Drug Administration.

10 September 1979; revised 5 November 1979

Adapting to Two Orientations: Disinhibition in a Visual Aftereffect

Abstract. *The tilt aftereffect of adapting to two different orientations simultaneously is weaker than the aftereffect of adapting to the more effective of the two orientations alone. This finding is consistent with explanations of orientational aftereffects in terms of lateral inhibition between cortical orientation detectors, but not with explanations in terms of neural "fatigue" from excitation.*

Visual contours that differ in retinal orientation may interact and produce distortions in their apparent orientation. For example, a line tilted 10° clockwise from the vertical induces an approximate 2° to 4° apparent counterclockwise tilt in a vertical test line when it is presented simultaneously with and adjacent to the test line (tilt illusion, orientation contrast), or when it is inspected prior to the test line (tilt aftereffect); the magnitude of the perceived orientation shifts varies with the angle between the interacting lines (*1*). Such contour interactions have been suggested to be manifestations of lateral inhibition between orientation detectors in the human visual cortex (*2-5*), a form of inhibition for which there is good neurophysiological evidence in the visual cortex of the cat (*6*). The hypothesis of orientation-specific inhibition seems uncontroversial when applied to simultaneous psychophysical contour interactions, but the hypothesis that aftereffects of spatial adaptation are the result of inhibition rather than of neural "fatigue" following prolonged excitation (*7*) is debated (*8, 9*). We have obtained evidence for the role of inhibition in the tilt aftereffect by adopting Carpenter and Blakemore's (*4*) disinhibition paradigm. They showed that the orientation contrast induced by, for example, a 10° clockwise inducing line may be canceled (rather than increased) by a second clockwise inducing line. In our experiment, the subject adapted to two orientations simultaneously.

The stimuli (inset in Fig. 1) were black lines, 0.03° wide and 1.3° long, viewed binocularly in a modified tachistoscope (Scientific Prototype N-1000). The background luminance was approximately 40 cd/m^2, and the contrast between the line and the background, defined as $(L_{\max} - L_{\min})/(L_{\max} + L_{\min})$, where L is luminance, was about 0.3. The adapting pattern consisted (except for the control condition) of two lines: A_1 was fixed at 12° clockwise tilt, the orientation of A_2 was varied between 6° and 60° clockwise tilt (*10*). The test pattern consisted of a vertical test line (T) and a variable micrometer-controlled comparison line (C). The subject's task was to set C parallel to the apparent orientation of T. The orientation of C was read to the nearest 0.07°.

To generate an aftereffect, the subject viewed the adapting pattern for 2 minutes, moving his eyes along a horizontal fixation bar to avoid confounding with afterimages. This initial adaptation period was followed by a sequence of 1.5-second presentations of the test pattern and 10-second readaptation periods; this sequence was continued until five settings were made. The experimental sessions opened with five parallel settings of C and T without previous adaptation; this null position was rechecked before each new adapting condition.

Figure 1 shows results for two subjects adjusted to a common baseline. Except when A_1 and A_2 were superimposed (actually a second run of the control condition), the aftereffects of adapting to two orientations were weaker than the aftereffect of adapting to A_1 alone. The reduction was most pronounced when A_1 and A_2 formed an angle of 10° to 15°; as the angle between the two adapting lines grew, the aftereffect gradually returned to the baseline, but it did not fully regain its strength at the largest angle tested. Thus, the angular function of the reduction effect was similar to the angular function of the aftereffect itself (*1, 10*).

These results follow directly from the hypothesis that the tilt aftereffect is an aftereffect of lateral inhibition between orientation detectors (*3*). During the adaptation phase the inhibitory signals from neurons optimally excited by orientation A_1 to the vertical and near-vertical detecting neurons are reduced by themselves being inhibited by neurons optimally excited by orientation A_2; consequently the aftereffect decreases, since it depends on the amount of inhibition received by the vertical and near-vertical detecting neurons during adaptation.

The results are, on the other hand, difficult to reconcile with explanations in terms of neural fatigue from prolonged excitation. According to this view, the angular function of the tilt aftereffect reflects the excitatory bandwidth of orientation channels. If orientation channels were independent, as implied by the early models (*7*), the excitatory effects of A_1 and A_2 on neurons with optimal orientations along the vertical and near-vertical meridians should simply sum and produce stronger aftereffects. But the same prediction follows from a fatigue-from-excitation model that recognizes inhibitory pathways between channels (*11*). Since, in our experiment, the second adapting orientation A_2 was in the range where, by itself, it induced a tilt aftereffect (*10*), it would mean that its excitatory influence must be stronger than its inhibitory effect (otherwise, it could not induce an aftereffect). In fact, the introduction of A_2 should, according to such a model, increase the level of activity in neurons with optimal orientation along the vertical meridian both by its direct excitatory influence and by its disinhibitory effect on A_1 and should lead to stronger aftereffects. Our experiment demonstrates weaker aftereffects under these conditions, results consistent with the inhibition hypothesis. By implication, our results also support the view that the orientation specificity of visual aftereffects reflects the broad tuning properties of inhibition in the domain of orientation rather than of the excitatory bandwidth of the channels (*12*).

The hypothesis of interchannel inhibition, proposed on psychophysical grounds for spatial frequency, movement, and retinal disparity (*13*), offers a unitary explanation for many, if not all, simultaneous and successive psychophysical interactions within the domains, but the evidence that aftereffects are results of inhibition is not quite conclusive (*14*). Our results provide a strong case for the role of orientation-specific lateral inhibition in the tilt aftereffect and add considerable circumstantial evidence to the more general hypothesis. How inhibition persists to produce aftereffects we do not know (*15*).

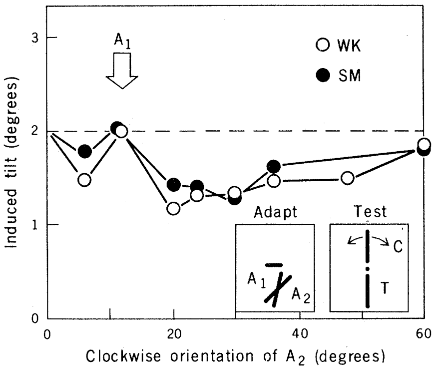

Fig. 1. Tilt aftereffect from adapting to two orientations simultaneously. The adapting and test patterns are shown in insets; A_1 and A_2 are adapting lines, T is the test line and C is a comparison line. The figure plots strength of the aftereffect (difference between pre- and postadaptation settings of C) as a function of the orientation of A_2, with A_1 fixed at 12° of clockwise tilt (indicated by arrow). The dashed line indicates the aftereffect produced by adapting to A_1 alone; the results for the two subjects have been slightly adjusted along the ordinate to a common baseline. Standard deviations of the settings were in the order of 0.12°.

SVEIN MAGNUSSEN*
WOLFGANG KURTENBACH
Neurologische Universitätsklinik mit Abteilung für Neurophysiologie,
D-7800 Freiburg im Breisgau,
West Germany

References and Notes

1. J. J. Gibson, *J. Exp. Psychol.* **20**, 553 (1937); _____ and M. Radner, *ibid.*, p. 453; F. W. Campbell and L. Maffei, *Vision Res.* **11**, 833 (1971); C. Blakemore, R. H. S. Carpenter, M. A. Georgeson, *Nature (London)* **228** 37 (1970).
2. G. K. Wallace, *Percept. Psychophys.* **5**, 261 (1969).
3. C. Blakemore, R. H. S. Carpenter, M. A. Georgeson, *Nature (London)* **234**, 418 (1971).
4. R. H. S. Carpenter and C. Blakemore, *Exp. Brain Res.* **18**, 287 (1973).
5. D. J. Tolhurst and P. G. Thompson, *Vision Res.* **15**, 967 (1975).
6. C. Blakemore and E. Tobin, *Exp. Brain Res.* **15**, 439 (1972); J. I. Nelson and B. J. Frost, *Brain Res.* **139**, 359 (1978); A. M. Sillito, *J. Physiol. (London)* **289**, 33 (1979).
7. N. S. Sutherland, *Q. J. Exp. Psychol.* **13**, 222 (1961); M. Coltheart, *Psychol. Rev.* **78**, 114 (1971).
8. S. Klein, C. F. Stromeyer III, L. Ganz, *Vision Res.* **14**, 1421 (1974).
9. C. F. Stromeyer III, S. Klein, C. E. Sternheim, *ibid.* **17**, 603 (1977).
10. The values of A_1 and A_2 were selected from control measurements of the angular function of the tilt aftereffect with one adapting line. Under the conditions we used, the optimal angle between the adapting and test lines was 12°; as the adapting angle grew, the aftereffect gradually decreased to 0 at about 60°. This result is consistent with previous ones (*1*).
11. In the spatial-frequency domain Klein *et al.* (*8*) have proposed a two-stage model that recognizes lateral inhibition between channels but still attributes aftereffects to neural fatigue from excitation.
12. C. Blakemore, J. P. J. Muncey, R. M. Ridley, *Vision Res.* **13**, 1915 (1973).
13. See recent reviews by O. Braddick, F. W. Campbell, J. Atkinson, in *Handbook of Sensory Physiology*, R. Held, H. W. Leibowitz, H.-L. Teuber, Eds. (Springer, Berlin, 1978), vol. 8, pp. 3-38; R. Sekuler, A. Pantle, E. Levinson, *ibid.*, pp. 67-96; J. I. Nelson, *J. Theor. Biol.* **66**, 303 (1977).
14. A spatial-frequency experiment by S. Stecher, C. Siegel, and R. V. Lange [*Vision Res.* 13, 2527 (1973)] appears analogous to our experiment; they observed that adapting to a pair of spatial frequencies that were both within the adaptable range of the test frequency may cause less threshold elevation than adapting to one member of the pair. Evidence for the role of inhibition in aftereffects was also reported by R. S. Dealy and D. J. Tolhurst [*J. Physiol. (London)* **241**, 261 (1974)] and C. R. Sharpe [*Vision Res.* **14**, 41 (1974)], who found that an adapting grating may elevate the threshold for a different test grating even when the contrast of the adapting grating was below the unadapted threshold of the test grating; Stromeyer *et al.* (*9*) failed to replicate this finding. However, L. Maffei [in *Handbook of Sensory Physiology*, R. Held, H. W. Leibowitz, H.-L. Teuber, Eds. (Springer, Berlin, 1978), vol. 8] found adaptation effects on single units in the cat's visual cortex after exposing the cat to prolonged grating stimulation outside the classically defined receptive field (that is, stimuli that did not excite the neuron).
15. We have elsewhere (S. Magnussen and W. Kurtenbach, *Vision Res.*, in press) suggested that aftereffects may be due to enhanced inhibitory "noise."
16. S. M. thanks the Alexander von Humboldt Foundation (Bonn-Bad Godesberg, West Germany) and Norwegian Research Council for Science and the Humanities for support during a sabbatical leave in Freiburg. W.K. was supported through Deutsche Forschungsgemeinschaft Sonderforschungsbereich 70, Teilprojekt A6 (to L. Spillmann). We thank L. Spillmann for providing laboratory facilities and for comments on the manuscript. The data reported here were part of papers presented at the 50th meeting of the German Physiological Society, Göttingen, 3 to 6 October 1978, and at the annual meeting of the Association for Research in Vision and Ophthalmology, Sarasota, Fla., 30 April to 5 May 1979.

* Present address: Institute of Psychology, University of Oslo, Box 1094, Blindern, Oslo 3, Norway.

8 August 1979; revised 27 November 1979