concentration EC_{50} = 6 mM; P. S. McPherson *et al.*, *Neuron* **7**, 17 (1991); K. Kuba, *J. Physiol.* **298**, 547 (1980); I. R. Neering and R. N. McBurney, *Nature* **309**, 158 (1984); D. D. Freil and R. W. Tsien, *J. Physiol.* **450**, 217 (1992)].
2. A. A. Borbély, *Hum. Neurobiol.* **1**, 195 (1982); I. Feinberg *et al.*, *Electroencephalogr. Clin. Neurophysiol.* **61**, 134 (1985).
3. J. Horne, *Experientia* **48**, 941 (1992).
4. D. McGinty and R. Szymusiak, *Trends Neurosci.* **13**, 480 (1990).
5. G. Yanik, S. Glaum, M. Radulovacki, *Brain Res.* **403**, 177 (1987); R. B. Virus *et al.*, *Neuropsychopharmacology* **3**, 243 (1990).
6. M. Steriade, D. A. McCormick, T. J. Sejnowski, *Science* **262**, 679 (1993).
7. M. Steriade, S. Datta, D. Paré, G. Oakson, R. Curró Dossi, *J. Neurosci.* **10**, 2541 (1990); M. Steriade, D. Paré, S. Datta, G. Oakson, R. Curró Dossi, *ibid.*, p. 2560.
8. M. Steriade, D. Paré, A. Parent, Y. Smith, *Neuroscience* **25**, 47 (1988); K. Semba and H. C. Fibiger, *Prog. Brain Res.* **79**, 37 (1989).
9. I. Pull and H. McIlwain, *Biochem. J.* **130**, 975 (1972); H. R. Winn, J. E. Welsh, R. Rubio, R. M. Berne, *Circ. Res.* **47**, 568 (1980); J. Schrader *et al.*, *Pflugers Arch.* **387**, 245 (1980); R. M. Berne *et al.*, in *Cerebral Hypoxia in the Pathogenesis of Migraine*, F. C. Rose and W. K. Amery, Eds. (Pitman, London, 1982), pp. 89–91; D. G. L. Van Wylen *et al.*, *J. Cereb. Blood Flow Metab.* **6**, 522 (1986); H. McIlwain and J. D. Poll, *J. Neurobiol.* **17**, 39 (1986).
10. In humans, a 44% reduction in the cerebral metabolic rate (CMR) of glucose during delta-wave sleep, compared with that during wakefulness, was determined by P. Maquet *et al.* [*Brain Res.* **571**, 149 (1992)], and a 25% reduction in the CMR of O_2 was determined by P. L. Madsen *et al.* [*J. Appl. Physiol.* **70**, 2597 (1991)]. Horne (*3*) has reviewed metabolism and hyperthermia.
11. T. V. Dunwiddie, B. J. Hoffer, B. B. Fredholm, *Naunyn Schmiedebergs Arch. Pharmacol.* **316**, 326 (1981); R. W. Greene, H. L. Haas, A. Hermann, *Br. J. Pharmacol.* **85**, 163 (1985).
12. For reviews, see T. V. Dunwiddie, *Int. Rev. Neurobiol.* **27**, 63 (1985); R. W. Greene and H. L. Haas, *Prog. Neurobiol.* **36**, 329 (1991).
13. Slices were obtained from anesthetized 14- to 21-day-old male and female Long-Evans rat pups and were prepared with standard procedures (*23*). Extracellular single units were recorded (electrode filled with modified Ringer solution had resistances from 12 to 15 megohms) with ac filtering, and spike rates were analyzed with a computer-generated window and spike-rate integration. Whole-cell recordings were obtained with the technique of M. G. Blanton, J. J. LoTurco, and A. R. Kriegstein [*J. Neurosci. Methods* **30**, 203 (1989)]. Briefly, borosilicate glass electrodes (resistance, 4 to 6 megohms) were filled with 100 mM potassium citrate, 20 mM KCl, 1 mM $CaCl_2$, 3 mM $MgCl_2$, 2 mM MgATP, 2 mM NaGTP, 3 mM EGTA, 40 mM Hepes, and biocytin (0.25%). Recordings were made with an Axoclamp 2A amplifier (Axon Instruments, Burlingame, CA) and Basic Fastlab software (Indec Systems, Sunnyvale, CA). Voltage-clamp records were obtained in discontinuous voltage-clamp mode at a switching frequency of 2.5 to 4.0 kHz. Head-stage output was continuously monitored to ensure adequate settling in each duty cycle. Neurons filled with 0.25% biocytin were visualized with standard procedures and processed for reduced nicotinamide adenine dinucleotide phosphate (NADPH)–diaphorase histochemistry (*30*). Data are expressed as mean ± SD, and significance was determined by Wilcoxon signed-rank test.
14. The CPT K_i = 10.9 nM at A_1 receptors, and at A_2 receptors, K_i = 1440 nM; R. F. Bruns, *J. Biochem. Pharmacol.* **30**, 325 (1981).
15. The 8-*p*-ST K_i = 2630 nM at A_1 receptors, and at A_2 receptors, K_i = 15,300 nM; R. F. Bruns, J. W. Daly, S. H. Snyder, *Proc. Nat. Acad. Sci. U.S.A.* **77**, 5547 (1980).
16. J. V. Halliwell and P. R. Adams, *Brain Res.* **250**, 71 (1983); M. L. Mayer and G. L. Westbrook, *J. Physiol.* **340**, 19 (1983). In LDT neurons, I_h was also blocked by extracellular application of cesium (2 mM; n = 3). In the presence of cesium, which itself increased firing rates (n = 4), the increase in firing rate evoked by CPT was reduced by 87 ± 23%.
17. H. C. Pape, *J. Physiol.* **447**, 729 (1992).
18. For examination of the effect of AD on I_h, neurons were required to show an appreciable inward relaxation ≥10 pA after a −40-mV step command from V_h = −60 mV.
19. Although a direct effect resulting from an increase in the low-threshold Ca^{2+} current cannot be excluded, the increase is consistent with a reduced shunt caused by a decreased I_h [(*30*); A. Kamondi *et al.*, *J. Neurophysiol.* **68**, 1359 (1992)].
20. The inhibitory response was usually (>90%) triphasic, consisting of a hyperpolarization followed by a depolarization (but not a complete return to E_m) and then a subsequent hyperpolarization that persisted until removal of the AD. In many neurons, after washout of AD, the membrane potential returned to a point more depolarized than E_m. The triphasic composition could result from (i) A_1 receptor activation and subsequent activation of a non-A_1 receptor, (ii) deamination and subsequent saturation of the AD deaminase, (iii) delayed activation and saturation of an uptake pump, or (iv) a combination of these effects.
21. The CHA IC_{50} = 1 to 2 nM at A_1 receptors, and at A_2 receptors, IC_{50} = 450 to 1000 nM; R. F. Bruns *et al.*, *Mol. Pharmacol.* **29**, 331 (1986).
22. S. R. Vincent *et al.*, *Neurosci. Lett.* **43**, 31 (1983).
23. J. Leubke *et al.*, *J. Neurophysiol.* **70**, 2128 (1993).
24. D. G. Rainnie, H. C. R. Grunze, R. W. McCarley, R. W. Greene, unpublished data.
25. The observation that endogenous AD blocks primarily I_h is consistent with the notion that this pathway is most sensitive to AD receptor activation and that the most efficacious AD effect is activation of the inward rectifier.
26. D. A. McCormick and H. Pape, *J. Physiol. London* **431**, 291 (1990).
27. J. G. Gu and J. D. Geiger, *J. Neurochem.* **58**, 1699 (1992); P. H. Wu and J. W. Phyllis, *Neurochem. Int.* **6**, 613 (1984); J. D. Geiger and J. I. Nagy, in *Adenosine and Adenosine Receptors*, M. Williams, Ed. (Humana Press, Clifton, NJ, 1990). Other mechanisms that would similarly influence extracellular AD levels include modulation of AD anabolic and catabolic enzyme activity and AD transport rate constants or activities.
28. V. Chagoya de Sánchez *et al.*, *Brain Res.* **612**, 115 (1993).
29. This metabolic-dependent AD buildup and decay is consistent with a phenomenologically accurate mathematical model of delta-sleep buildup and decay (*2*), including the very subtle point that delta-wave propensity increases during rapid eye movement sleep, when brain metabolic activity is similar to that during wakefulness.
30. J. I. Luebke *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **89**, 743 (1992).

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Associative Odor Learning in *Drosophila* Abolished by Chemical Ablation of Mushroom Bodies

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The corpora pedunculata, or mushroom bodies (MBs), in the brain of *Drosophila melanogaster* adults consist of ~2500 parallel Kenyon cell fibers derived from four MB neuroblasts. Hydroxyurea fed to newly hatched larvae selectively deletes these cells, resulting in complete, precise MB ablation. Adult flies developing without MBs behave normally in most respects, but are unable to perform in a classical conditioning paradigm that tests associative learning of odor cues and electric shock. This deficit cannot be attributed to reductions in olfactory sensitivity, shock reactivity, or locomotor behavior. The results demonstrate that MBs mediate associative odor learning in flies.

Common cellular processes underlie both associative and nonassociative learning in both invertebrate and vertebrate species (*1*). Beyond the realm of single cells, specialized neuronal assemblies have been implicated in the learning and storage of sensory information. In mammals, the hippocampus is important for the initial formation of declarative memory (*2*). In insects, MBs are assumed to play a role in the processing and storage of chemosensory information (*3*, *4*).

The relative simplicity and unusual shape of the MB neuropil (*5*) suggests that it has a specialized function. The primary input to the MBs is the antennal-glomerular tract (AGT), which extends from the antennal lobe (AL) to the lateral horn (LH) of the lateral protocerebrum (LPR) and sends a network of fibers into the MB calyx (*5*, *6*). At least in some insect species, the calyx also receives fibers from visual and other sensory systems (*5*, *6*) and, therefore, likely processes multimodal information. MB outputs extend from the lobes to many areas in the brain including the LPR. Some fibers provide feedback connections between the calyx, peduncle, and lobes, whereas other fibers connect the MBs to each other across the sagittal midplane (*5*).

In honeybees, local cooling of the MBs interrupts olfactory memory (*7*). Depolarization of a ventral unpaired medial neuron (VUMmx1) innervating the calyces of bees can supplant the unconditioned stimulus

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(US) during the course of olfactory conditioning (*8*). Recordings of another neuron, PE1, which projects from the MB β exit (junction of the α and β lobes) to the LPR in bees, suggest that MBs participate in short-term memory formation (*9*). In *Drosophila*, genetic dissection of learning and memory (*4*, *10*) has shown that the mutants *dunce* (*dnc*) and *rutabaga* (*rut*) have biochemical deficits affecting adenosine 3′,5′-monophosphate (cAMP) metabolism (*11*). Defects in cAMP-dependent protein kinase (PKA), protein phosphatase–1 (PP1), and calcium-calmodulin–dependent protein kinase II (CaM kinase) impair various forms of learning (*12*). These results point to a model of neuronal plasticity in which cellular signals converge on PKA (*1*, *13*). At the network level, MB structural mutants have impaired olfactory learning and memory (*14*, *15*). Furthermore, gene products of *dnc* and *rut* are preferentially expressed in the MBs (*16*).

Structural changes in neurons and neuronal assemblies are known to accompany memory storage (*17*). The MBs of *Drosophila* show a remarkable degree of plasticity, both during the course of development and as a response to environmental stimuli in adult flies. MBs in *dnc* and *rut* mutants do not show this experience-related structural plasticity (*18*). Volumetric differences between MBs of nurse and forager worker honeybees are also attributed to differences in experience (*19*).

Taken together, the above evidence implies that MBs are specialized structures mediating learning and memory processes. However, both surgical interference and genetic dissection have their drawbacks. Cooling, for instance, cannot be confined to the MBs. Widespread defects (*20*), and general expression patterns associated with the biochemical learning and memory genes (*16*) as well as the unknown etiology and specificity of defects in the MB structural mutants (*4*, *14*, *15*) prohibit definitive conclusions. To gain a more precise understanding of MB function in olfactory learning, we used an ablation procedure (*21*) that owes its specificity to the unique pattern of development of the MBs (*22*, *23*). In *Drosophila*, MB Kenyon cells are derived from four neuroblasts (MBNbs) that divide continuously from embryogenesis until the end of metamorphosis (*21–23*). MBNbs and one lateral neuroblast (LNb) are the only proliferating cells from 0 through 8 to 12 hours after larval hatching (ALH) (*21–24*). We fed hydroxyurea (HU) to newly hatched wild-type *D. melanogaster* larvae (*25*). This treatment should kill MBNbs and delete all MB Kenyon cell lineages (*21*) with the exception of the 40 to 300 cells per hemisphere that arise during the course of embryonic development (*23*, *26*).

Complete MB ablation at the level of the light microscope was observed in 93.5% of HU-treated flies (Fig. 1). A total of 17 very reduced calyces were observed (only in males) in 246 sectioned heads. The mean calyx volume for treated flies was 0.7% of the control value (equivalent to 19 ± 6 Kenyon cells and their connections) (Figs. 1, A and B, and 2A). Reduced ALs were also observed in HU-treated flies (Fig. 1, G and H). The mean AL volume was 68% of the control value (Fig. 2B), which we attribute to ablation of one LNb (*22*, *23*). We noted a fiber bundle posterior to the MB knee area in all MB-ablated flies (Fig. 1, E and F) that could represent embryonic Kenyon cell fibers (*23*, *26*) or extrinsic MB tracts (*5*, *9*). HU treatment and the subsequent absence of the MB neuropil did not appear to affect other brain regions, including the central complex (Fig. 1, A through F). The optic lobes (OL) are derived from neuroblasts that begin proliferating at 8 to 12 hours ALH (*24*); these structures also showed no significant volume differences (Fig. 2C). The size and external anatomy of treated and control flies were indistinguishable.

On initial observation, the general behavior of MB-less flies seemed entirely normal. They appeared active, exhibited vigorous courtship, and reproduced abundant-

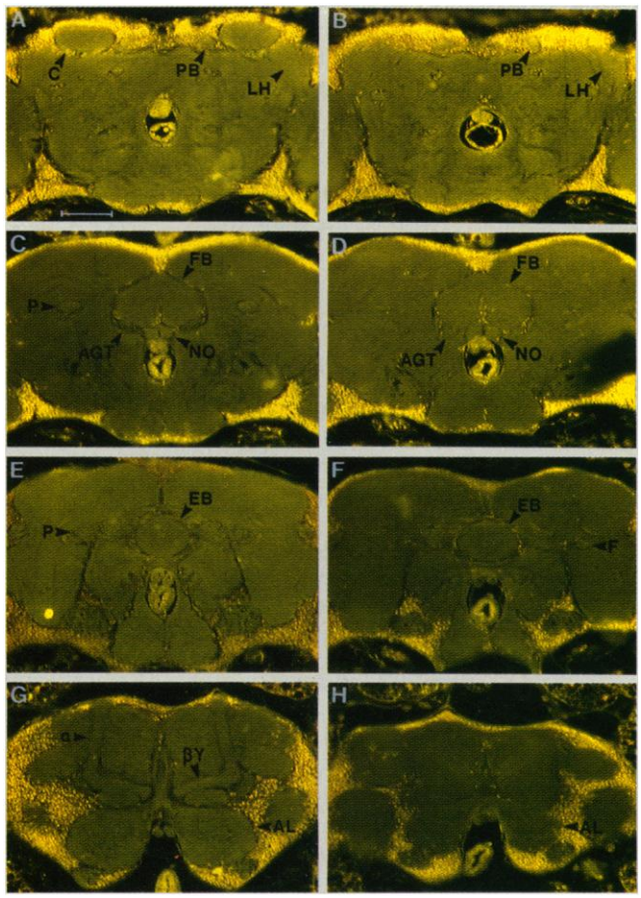

Fig. 1. Brains of control (left) and HU-treated (right) flies. Frontal paraffin sections (7 μm, posterior to anterior) were photographed under a fluorescence microscope (*29*); bar, 50 μm. Perikarya and neuropil appear yellow and green, respectively. (**A** and **B**) C, calyx; LH, lateral horn; PB, protocerebral bridge. (**C** and **D**) P, peduncle; AGT, antennal-glomerular tract; FB, fan-shaped body; NO, noduli. (**E** and **F**) Peduncle; F, fiber bundle; EB, ellipsoid body. (**G** and **H**) α, α lobe; βγ, βγ lobe; AL, antennal lobe.

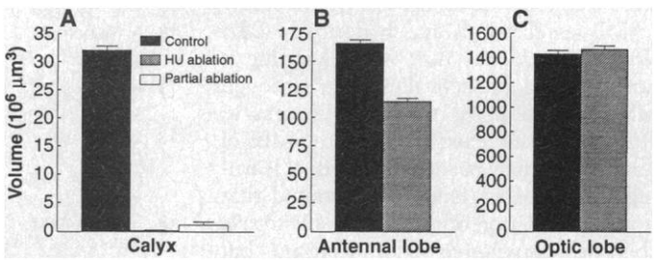

Fig. 2. Brain substructure volumes derived from planimetric measurements of 7-μm serial sections (*29*) of flies sampled from those tested in behavior experiments (Fig. 3). Bars represent mean ± SE of mean brain hemisphere values; n = 20 flies per bar except in (A). (**A**) Calyx volumes of all groups were significantly different [analysis of variance (ANOVA), $F_{[2,296]} = 2963.47$, $P < 0.0001$; Student–Newman-Keuls multiple range test (SNK), $P \leq 0.05$; n = 20, 246, and 33; (*30*)]. (**B**) AL volumes were significantly different (t test, $t_{[19,19]} = 12.48$, $P < 0.0001$). (**C**) OL (medulla + lobula + lobula plate) volumes were not significantly different (t test, $t_{[19,19]} = 0.91$, $P = 0.3667$).

ly. To address the hypothesis that MBs mediate associative learning of olfactory signals, populations of MB-ablated and control flies were trained to avoid odors [4-methylcyclohexanol (MCH) and benzaldehyde (BAL)] when paired with electric shock (120 V dc) in a discriminative classical conditioning paradigm (*27*) (Fig. 3). Control flies performed well (PI = 83 ± 2), whereas MB-less flies were almost completely unable to learn odor-shock associations (PI = 7 ± 2) (Fig. 3A). Residual learning in these flies can be attributed to embryonic (*23*, *26*) or the few remaining postembryonic Kenyon cells, or both (Fig. 2A). In one experiment, adult flies were found to have partial MB ablation. Calyces were observed in 15% of these animals; both mean calyx volume (4% of the control value, Fig. 2A) and learning (PI = 20 ± 6, Fig. 3A) were significantly higher than in the total ablation group. Our results confirm previous studies suggesting a correlation between odor learning and calyx volume (*14*, *15*). In preliminary experiments, HU-treated flies could not learn odor-shock associations when MCH versus 3-octanol (OCT) or BAL versus propionic acid (PRA) were used (*15*), indicating that olfactory conditioning defects in these flies are not odor specific.

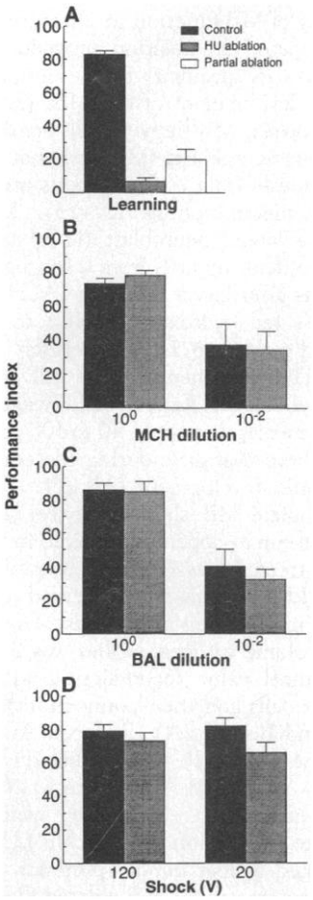

Fig. 3. Classical conditioning and sensory acuity (*27*). Bars represent mean ± SE of PIs, n = 8 per bar except in (A). (**A**) Learning. All groups were significantly different (ANOVA, $F_{[2,20]}$ = 142.28, $P < 0.0001$; SNK, $P \leq 0.05$; n = 8, 8, and 7). Learning in MB-less flies was significantly different from 0 (t test, $t_{[7]}$ = 3.53, P = 0.0095). (**B** and **C**) Odor avoidance. Responses of naïve flies to pure and 10^{-2} dilutions (in mineral oil) of MCH (B) or BAL (C) versus air. A three-way ANOVA detected a significant effect of dilution only ($F_{[1,56]}$ = 71.66, $P < 0.0001$). Effects of HU treatment, different odorants, and interactions were not significant. (**D**) Shock avoidance. Responses of naïve flies to 120- and 20-V dc shock. A two-way ANOVA testing the effects of HU treatment, voltage, and interactions was not significant ($F_{[3,28]}$ = 2.52, P = 0.0782).

Low performance of MB-less flies in conditioning experiments might have been a secondary result of reduced olfactory ability because of AL reduction (Figs. 1, G and H, and 2B). We tested responses of naïve flies to MCH and BAL (*27*) (Fig. 3, B and C). HU treatment had no significant effect on the ability of flies to avoid either pure or diluted odorants. These results show that MBs are not required for simple odor detection and that AL reduction did not result in anosmias to MCH and BAL.

Reduced shock reactivity also might have contributed to the low performance of MB-less flies in conditioning. HU-treated flies responded normally to 120 V, the shock intensity used in conditioning (*27*) (Fig. 3D). Avoidance of 20-V shock tended to be slightly (although not significantly) reduced.

Preliminary odor avoidance tests with alternative odorants revealed specific olfactory deficits in HU-treated flies (*15*). For example, treated flies were anosmic to isoamyl acetate and displayed reduced aversion to both OCT and PRA. Acetone elicited a normal response comparable to those of MCH (Fig. 3B) and BAL (Fig. 3C). This pattern of selective anosmia and reduced AL volume (Figs. 1, G and H, and 2B) implies the deletion of either a subset of AL glomeruli or local interneurons providing connections among glomeruli (*6*). We did not attempt to identify individual deleted elements within the AL in this study.

MB-less flies walk and fly normally (*28*). We have evidence that visual learning is not disturbed in these flies (*28*), although MB connections to the visual system in *Drosophila* likely exist (*26*) and the MBs of some insects may participate in visual learning (*3*). Here we have demonstrated that restricted deletion of the MBs in *Drosophila* abolishes associative odor learning but leaves other aspects of olfaction intact. We therefore propose that signal convergence in the MBs (*4*) accounts for the associative processes contributing to odor learning in flies. However, we have not shown that MBs are the storage sites of learned odor evaluation. Structures downstream from the MBs must still be considered. It is unknown if the MBs are specific for learning. An alternative hypothesis is that MBs also might serve to discriminate odor qualities, leaving the most basic good or bad decisions to other elements of the brain. Distinguishing between these possibilities will further elucidate MB function.

REFERENCES AND NOTES

1. R. D. Hawkins, E. R. Kandel, S. A. Siegelbaum, *Annu. Rev. Neurosci.* **16**, 625 (1993).
2. R. L. Squire, *Psychol. Rev.* **99**, 195 (1992).
3. J. Erber, U. Homberg, W. Gronenberg, in *Arthropod Brain: Its Evolution, Development, Structure, and Functions*, A. P. Gupta, Ed. (Wiley, New York, 1987), chap. 21; R. Menzel *et al.*, in *The Behaviour and Physiology of Bees*, L. J. Goodman and R. C. Fisher, Eds. (CAB, London, 1991), pp. 323–353.
4. M. Heisenberg, in *Fundamentals of Memory Formation: Neuronal Plasticity and Brain Function*, H. Rahmann, Ed. (Fischer, Stuttgart, 1989), pp. 3–45.
5. N. J. Strausfeld, *Atlas of an Insect Brain* (Springer-Verlag, Berlin, 1976), chaps. 3, 6, and 7; M. Heisenberg, in *Development and Neurobiology of* Drosophila, O. Siddiqi, P. Babu, L. M. Hall, J. C. Hall, Eds. (Plenum, New York, 1980), pp. 373–390; P. G. Mobbs, *Philos. Trans. R. Soc. London B* **298**, 309 (1982); F.-W. Schürmann, in *Arthropod Brain: Its Evolution, Development, Structure, and Functions*, A. P. Gupta, Ed. (Wiley, New York, 1987), chap. 11.
6. R. F. Stocker, M. C. Lienhard, A. Borst, K.-F. Fischbach, *Cell Tissue Res.* **262**, 9 (1990); AGT synonym, inner antennocerebral tract (iACT).
7. J. Erber, T. Masuhr, R. Menzel, *Physiol. Entomol.* **5**, 343 (1980).
8. M. Hammer, *Nature* **366**, 59 (1993).
9. J. Mauelshagen, *J. Neurophysiol.* **69**, 609 (1993).
10. T. Tully, in *Perspectives in Cognitive Neuroscience*, R. G. Lister and H. J. Weingartner, Eds. (Oxford Univ. Press, Oxford, 1991), pp. 46–64.
11. D. Byers, R. L. Davis, J. A. Kiger Jr., *Nature* **289**, 79 (1981); Y. Qui *et al.*, *J. Mol. Biol.* **222**, 553 (1991); M. S. Livingstone, P. P. Sziber, W. G. Quinn, *Cell* **37**, 205 (1984); L. R. Levin *et al.*, *ibid.* **68**, 479 (1992); Y. Dudai, *Annu. Rev. Neurosci.* **11**, 537 (1988).
12. P. Drain, E. Folkers, W. G. Quinn, *Neuron* **6**, 71 (1991); S. F. Goodwin, M. Del Vecchio, T. Tully, K. Kaiser, *J. Neurogenet.* **8**, 232 (1993); Z. Asztalos *et al.*, *J. Neurosci.* **13**, 924 (1993); L. C. Griffith *et al.*, *Neuron* **10**, 501 (1993).
13. U. Müller and H.-C. Spatz, *J. Neurogenet.* **6**, 95 (1989); A. Aszodi, U. Müller, P. Friedrich, H.-C. Spatz, *Proc. Natl. Acad. Sci. U.S.A.* **88**, 5832 (1991).
14. M. Heisenberg, A. Borst, S. Wagner, D. Byers, *J. Neurogenet.* **2**, 1 (1985); J. S. de Belle and M. Heisenberg, *ibid.* **8**, 225 (1993).
15. J. S. de Belle, unpublished data.
16. A. Nighorn, M. J. Healy, R. L. Davis, *Neuron* **6**, 455 (1991); P.-L. Han, L. R. Levin, R. R. Reed, R. L. Davis, *ibid.* **9**, 619 (1992).
17. C. H. Bailey and E. R. Kandel, *Annu. Rev. Physiol.* **55**, 397 (1993).
18. G. Technau and M. Heisenberg, *Nature* **295**, 405 (1982); G. M. Technau, *J. Neurogenet.* **1**, 113 (1984); A. Balling, G. M. Technau, M. Heisenberg, *ibid.* **4**, 65 (1987).
19. G. S. Withers, S. E. Fahrbach, G. E. Robinson, *Nature* **364**, 238 (1993); C. Durst, S. Eichmüller, R. Menzel, in *Gene—Brain—Behaviour, Proceedings of the 21st Göttingen Neurobiology Conference*, N. Elsner and M. Heisenberg, Eds. (Thieme, Stuttgart, 1993), abstr. 777.
20. H. J. Bellen and J. A. Kiger, *Genetics* **115**, 153 (1987); G. Corfas and Y. Dudai, *Proc. Natl. Acad. Sci. U.S.A.* **88**, 7252 (1991); T. Tully, *Trends*

Neurosci. **14**, 163 (1991); Y. Zhong, V. Budnik, C.-F. Wu, *J. Neurosci.* **12**, 644 (1992).
21. A. Prokop and G. M. Technau, *Dev. Biol.*, in press.
22. ———, *Development* **111**, 79 (1991).
23. K. Ito and Y. Hotta, *Dev. Biol.* **149**, 134 (1992).
24. J. W. Truman and M. Bate, *ibid.* **125**, 145 (1988).
25. HU inhibits ribonucleotide reductase, blocks DNA synthesis, and kills dividing cells [J. Timson, *Mutat. Res.* **32**, 115 (1975)]. Groups of 500 *Canton S* larvae ± 1 hour ALH [M. B. Sokolowski, C. Kent, J. Wong, *Anim. Behav.* **32**, 645 (1984)] were fed a heat-killed yeast suspension containing HU (50 mg/ml) for 4 hours (*20*). Control larvae were fed yeast only. Larvae were then washed in distilled water and allowed to develop in plastic bottles containing 40 ml of fresh medium at 25°C, 60% relative humidity with a 16L:8D light regime.
26. G. M. Technau, thesis, Universität Würzburg (1983).
27. Groups of ~100 2- to 5-day-old flies were aspirated into an electrifiable training tube through which air currents delivered MCH or BAL [conditioned stimuli (CS+ and CS−)]. The CS+ was paired temporally with 120-V dc shock pulses (US), followed by the unpaired CS−. Flies were then permitted to choose between CS+ and CS− odors delivered by converging air currents in a T-maze. A second group of flies was trained to avoid the previous CS− and tested [T. Tully and W. G. Quinn, *J. Comp. Physiol. A* **157**, 263 (1985)]. A performance index (PI) represents the average normalized percent avoidance of the CS+ in both half experiments (0, no learning, 100, perfect learning). In odor and shock avoidance, naïve flies were aspirated into the T-maze and permitted to choose between odor and air or shock and no shock, respectively. The PIs in these tests were calculated from single groups of flies (half PIs) [S. Boynton and T. Tully, *Genetics* **131**, 655 (1992)]. Surface areas of pure odorants exposed to air currents were adjusted so that naïve flies distributed themselves 50:50 in the T-maze (MCH, 90 mm^2; BAL, 20 mm^2). All behavior experiments were performed blind under 665-nm red light at 25°C and >80% relative humidity.
28. Walking behavior in Buridan's paradigm [R. Strauss and M. Heisenberg, *J. Neurosci.* **13**, 1852 (1993)], basic visual flight control, and operant color or light intensity learning at the torque compensator [R. Wolf and M. Heisenberg, *J. Comp. Physiol. A* **169**, 699 (1991)] were unaffected by HU treatment (R. Strauss and R. Wolf, personal communication).
29. M. Heisenberg and K. Böhl, *Z. Naturforsch. Sect. C* **34**, 143 (1979).
30. J. H. Zar, *Biostatistical Analysis* (Prentice-Hall, Englewood Cliffs, NJ, ed. 2, 1984), chaps. 8–13; *SAS User's Guide: Statistics, Version 5* (SAS Institute Inc., Cary, NC, 1985).
31. We thank B. Forbes and T. Wanke for assisting with collection of larvae; K. Ito and A. Prokop for introducing us to HU and sharing unpublished results; R. Wolf for providing a computer program for planimetric measurements; T. Préat and T. Tully for advice concerning the classical conditioning paradigm; R. Strauss and R. Wolf for testing HU flies in Buridan's paradigm and at the torque compensator; the Würzburg "Verhaltens Gruppe" for stimulating discussion; and M. Dill, B. Forbes, T. Préat, and A. Prokop for commenting on preliminary versions of the manuscript. Supported by grants from the Deutsche Forschungsgemeinschaft (HE986) and Human Frontier Science Program to M.H. J.S. de B. is a National Sciences and Engineering Research Council of Canada Postdoctoral Research Fellow.

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TECHNICAL COMMENT

Envisioning a Quantum Supercomputer

Since the publication of my report (*1*), several readers have written to discuss issues that I originally treated peripherally. In addition, I have become aware of additional references that supply useful information about aspects of quantum computation. A full treatment of physical effects that would arise in the complicated quantum-optical device proposed will be given elsewhere. The following questions have been asked.

1) Wouldn't the localized excitations by means of which information is registered rapidly delocalize as excitations "hopped" or tunneled along the polymer chain?

The excitations would eventually hop and delocalize, but the rate at which they would do so would be suppressed because they would have to tunnel through several units with significantly different excitation energies. For relatively weak interactions between units, the characteristic hopping time would generally be longer than the spontaneous emission time.

2) Wouldn't imperfections in the polymer or lattice of spins cause errors?

Indeed they would. The problems of "reflection" of the computation (in which repeated scattering off of multiple defects causes the computation to reverse itself) and of error generation in quantum computers in general have been investigated extensively by Landauer (*2–4*), who has noted that eventually error correction would be required in quantum computers and that it would cause a loss of coherence. This loss of coherence would be evident in the proposed device because error correction is accomplished by spontaneous emission, with accompanied phase randomization; but because the computation would be moved forward from state to state by a sequence of externally applied pulses, reflection would not be a problem. If an imperfection were large enough to throw a unit completely off resonance, however, then the whole computation would grind to a halt.

3) Wouldn't the scattered light depend on the logical state of the computer, thereby causing dissipation and inducing decoherence [for example (*3*)]?

How the light of π pulses is scattered would depend on the logical state, but in general the computer could be constructed and programmed so that this dependence would be too weak to induce decoherence. Because the lifetimes of the excited states are long, inelastic scattering would be minimal, and the entropy of the light would increase by considerably less than k_BT per bit flipped, where k_B is Boltzmann's constant and T is the ambient temperature. Dissipation may be greater than this in whatever mechanisms produce and absorb the light, but the logical updating process itself would be essentially free of dissipation except for error correction.

The main evidence that pulses do not destroy coherence is experimental: If decoherence were at all substantial, then the spin-echo effect and its various incarnations (in nuclear magnetic resonance and optical technologies), in which hundreds of pulses can be delivered without destroying coherence, would never have been experimentally verified.

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REFERENCES

1. S. Lloyd, *Science* **261**, 1569 (1993).
2. R. Landauer, *Phys. Today* **44**, 23 (May 1991).
3. ———, *Physica A* **168**, 75 (1990); *Proceedings of the 3rd International Symposium on the Foundations of Quantum Mechanics*, Tokyo, 28 to 31 August 1989, p. 407.
4. ———, *Found. Phys.* **16**, 551 (1986); *Int. J. Th. Phys.* **21**, 283 (1982).

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