Cholesterol's Role in Synapse Formation

A FACTOR RELEASED FROM GLIAL CELLS IN the central nervous system had been known to promote the formation of synapses. That factor, Daniela H. Mauch and colleagues have discovered, is cholesterol (Reports, 9 Nov., p. 1354). In their Perspective accompanying the report by Mauch *et al.*, Ben A. Barres and Stephen J. Smith begin the final paragraph by asking the question, "Could the cholesterol supply also regulate synaptic plasticity in the adult brain?" (*Science*'s Compass, "Cholesterol—making or breaking the synapse," 9 Nov., p. 1296). In fact, we addressed this issue in a recent paper (*1*).

We experimentally modeled neuronal cholesterol disbalance by biochemically increasing the turnover of cholesterol in rat hippocampal slices. Such an experimental setup impairs the redistribution of cholesterol from one cell to another via lipoprotein transport. While increasing cholesterol removal, or immediately thereafter, we evoked and recorded two brain waveforms, paired pulse facilitation (PPF) or long-term potentiation (LTP), which are indicative of neurotransmission and synaptic plasticity, respectively. We found that the lack of cholesterol supply to neurons by means of lipoprotein transport impaired PPF and LTP and caused the failure of the neurotransmission and synaptic plasticity.

From additional immunofluorescent analysis of the slices, we discovered that cholesterol disbalance also caused neurodegeneration of hippocampal neuronal cell processes and the appearance of tau protein pathology (one of the key features of Alzheimer's disease) in axon fibers of the hippocampus (also called "mossy fibers"). This finding is in accord with other data on cholesterol and tau phosphorylation obtained in neuronal cell culture experiments (*2*).

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References and Notes
1. A. R. Koudinov, N. V. Koudinova, *FASEB J.* **15**, 1858 (2001).
2. Q. W. Fan, W. Yu, T. Senda, K. Yanagisawa, M. Michikawa, *J. Neurochem.* **76**, 391 (2001).

CORRECTIONS AND CLARIFICATIONS

VIEWPOINT: "Will retina implants restore vision?" by E. Zrenner (8 Feb., p.1022). Reference number 37 was incompletely cited. The full citation is M. Clements *et al.*, *IEEE Intl. Solid-State Circuits Conference TP* **12.7**, 216 (1999).

NEWS FOCUS: "Homeland defense in the wild" by D. Normile (8 Feb., p. 957). The pictures on page 959 that accompanied the two meeting summaries "Set out another plate, Ma" and "A conservation success story" were reversed. The picture in the third column of the 1998 forest fires in East Kalimantan should have accompanied the former summary with the caption labeled "Fireproof friendships." The picture in the first column of Brazilian muriquis should have appeared with the latter summary with the caption labeled "Fast friends."

NEWS OF THE WEEK: "Livestock feed ban preserves drugs' power" by D. Ferber (4 Jan., p. 27). Contrary to the statement in the last paragraph, the U.S. Food and Drug Administration had not proposed banning on the farm antibiotic virginiamycin from livestock feed.