velopment. Although the research that Barinaga discusses (E. Knudsen, "Capacity for plasticity in the adult owl auditory system expanded by juvenile experience," Reports, 6 Mar., p. 1531) may well add support to the idea of plasticity in the young brain in general, it says little about what the brain should learn.

Barinaga concludes by stating, "It all reinforces what Hillary Clinton and the news magazines have been telling us: that exposing our kids to more experiences at a young age may make them smarter adults. Indeed, it may physically lay down the pathways for achievement later in life." This conclusion could be read as supporting any and all kinds of stimulation aimed at infants and young children.

The owls appear to have learned at an early age because they were motivated to do so in order to survive. A young child may well have the capacity to learn a foreign language, but likely has no motivation to do so if the language is not spoken in his or her home or by the parents. The fallacy in leaping from brain to behavior is that behavior is determined by many factors other than brain capacity. A natural athlete may never realize his or her potential because of lack of motivation, whereas a less-gifted athlete may win medals thanks to sheer energy and drive.

Not all stimulation is necessarily good for young children—witness the newly imported British television program "Teletubbies," aimed at 1-year-olds, and computer programs for 6-month-olds. Brain and behavior are at such different levels of analysis and measurement that we need to be cautious in leaping from one to the other. Overstimulation of infants and young children can endanger healthy development.

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In her article about the splendid report by Knudsen, Barinaga states that the owl's eyes are "fixed in their sockets." An owl's eyes do in fact move—not a great deal, just enough for two papers (*1*). The phrase "nearly immobile" would be more accurate.

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Natron Trade, 2000 B.C.

In her article "Yemen's Stonehenge suggests Bronze Age Red Sea culture" (Research News, 6 Mar., p. 1452), Heather Pringle states that the al-Midaman culture of 4000 years ago may have acquired wealth by trading in natron because it is a key ingredient in soap. Natron was also used in large quantities in the mummification process in order to remove water from the body before it was wrapped. This would be another use for natron in trade with the Egyptians.

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Kaposi's Sarcoma and Protection from HIV Dementia

In their report "Angiogenic and HIV-inhibitory functions of KSHV-encoded chemokines" (10 Oct., p. 290), C. Boshoff *et al.* found that Kaposi's sarcoma (KS)–associated herpesvirus (KSHV) encodes chemokine-like proteins (vMIPs) that block infection of human immunodeficiency virus–type 1 (HIV-1) on the surface of cells from a CD4-positive cell line that expresses the chemokine receptor CCR3. Because CCR3 is a receptor for HIV-1 entry into microglia, Boshoff *et al.* suggest that patients with KS or high loads of KSHV might be less prone to HIV infection of microglia cells and thus less likely to develop HIV-related dementia.

We examined the relation between KS and HIV dementia in 229 deceased AIDS patients from Oslo, Norway, treated at Ullevål hospital (*1*). The sample corresponds to 91% of registered dead AIDS victims in Oslo from 1983 to 1996. The autopsy rate was 73%, and in this group the occurrence of HIV encephalitis could be studied.

HIV dementia develops gradually. The clinical diagnosis of definite and possible dementia was based on the staging described by Price and Brew, their stage 2 or more corresponding to definite dementia (*2*). The diagnosis of HIV encephalitis at autopsy was based on the presence of multinucleated giant cells (MGCs) in the brain tissue, while diffuse damage of white matter may indicate a less advanced stage of brain infection.

Among the 22 KS cases, one case of definite clinical dementia (4.5%) and three with possible dementia (13.6%) had been diagnosed. Among 207 non-KS cases, 52 had definite dementia (25.1%) and 51 had possible dementia (24.6%). Treating the numbers as a 2 × 3 table with ordered categories (definite dementia, possible dementia, and no

dementia) provides a statistical significance ($P < 0.01$, Kendall rank test). In the group that was autopsied, there was one person with MGCs out of 18 patients with KS (5.6%), as compared with 36 people with MGCs out of 149 patients without KS (24.5%; $P = 0.06$ if a one-sided exact test is used; $P < 0.05$ if one uses the grading MGC, diffuse damage of white matter, and no signs).

Factors such as survival length in the immunodeficient stage, timing of disease events, and treatment with the neuroprotective drug Zidovudine were considered as possible confounding factors. Differences in survival and drug use were small, and these factors appear not to explain the observations. There may, however, be differences between patients with KS and those without KS (such as viral subtype and host factors) that are difficult to examine.

Thus, our results from a sample of patients from Oslo conform to the expected outcome—there is a blocking effect of KSHV-encoded chemokines where HIV binds to CCR3 on microglia that can protect a patient from the development of HIV dementia. There are, however, several open questions, and it will be a challenge to further test this interesting hypothesis with more direct methods.

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Response: Like Liestœl *et al.*, we have examined whether KS/KSHV can protect against HIV-1 dementia, as we suggested in our earlier report. We measured the probability that HIV-1 dementia and opportunistic central nervous system (CNS) disease would appear in patients who developed KS as compared with the probability for those in whom KS did not develop. These data were gathered during the follow-up of a retrospective study of a cohort of patients with AIDS (*1*).

A total of 1109 patients with an AIDS-defining illness between 1 January 1990 and 31 December 1994 who attended a specialized center of HIV medicine in London were identified from a central database. Three diagnostic groups were defined: (i) no CNS impairment ($n = 914$), (ii) HIV-1 dementia ($n = 88$), and (iii) opportunistic brain disease ($n = 107$), including progressive multifocal leukoencephalopathy (PML), cerebral toxoplasmosis, and primary CNS B-cell lymphoma. Patients with HIV-1 dementia were identified after review of medical notes to establish whether or not they met the World Health Organization criteria for HIV-1 dementia (*2*). A Cox regression analysis was applied to the survival times from AIDS diagnosis until the onset of brain disease. For patients without brain impairment (censored cases), the time until death or last observation was entered into the calculation. The following independent variables were included in the model: age, Zidovudine treatment, CD4 counts at AIDS diagnosis, and presence of confirmed KS. There were 158 cases where the CD4 count was missing at time of AIDS diagnosis (14% of the total), but there was no difference between the CNS groups (this information was missing in 13.3% of those with KS and in 14.4% of those without CNS disease). We included a variable to indicate the missing CD4 counts in the analysis. Relative risk (*RR*) was computed with reference to the group of patients without KS.

A total of 401 out of 1109 patients (36%) were diagnosed with KS, 41 of whom (10%) had suffered a CNS disease, as compared with 154 out of 708 patients (22%) without KS [$RR = 0.410$, $P < 0.00001$, with a 95% confidence interval (CI) = 0.283 to 0.593]. Unadjusted *RR* across diagnostic groups were as follows: HIV-1 dementia, 0.42 (CI = 0.25 to 0.72), PML, 0.15 (CI = 0.02 to 1.21), cerebral toxoplasmosis, 0.44 (CI = 0.25 to 0.77), and lymphoma 0.38 (CI = 0.13 to 1.16).

Although the mean CD4 count at the time of AIDS diagnosis was higher in patients with KS (129 cells per microliter, CI = 114 to 145) as compared with that for patients without KS (104 cells per microliter, CI = 94 to 115), the mean survival time (159 weeks, CI = 147 to 171) was not different in those with KS and in those without KS if one adjusts for CD4 count at the time of AIDS diagnosis (*RR* = 0.924, $P = 0.394$, CI = 0.770 to 1.11). In particular, there was no difference between the groups (those with and those without KS) in survival time from first positive HIV test, or when the CD4 count was less than 200 cells per microliter, until death or the last observation.

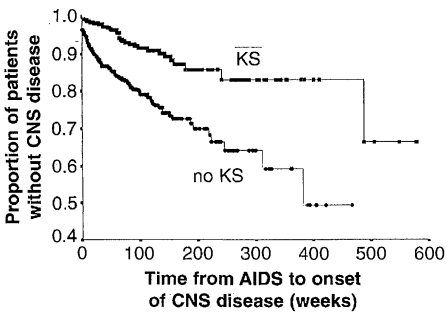

Fig. 1. Time from AIDS to onset of CNS disease in a sample of 1109 patients.

This finding suggests that KS/KSHV (or the chemokines encoded by KSHV) do not protect significantly against systemic HIV-1 progression. In contrast, the risk of developing any CNS disease (Fig. 1) was markedly lower in patients with KS as compared with those without KS (*RR* 0.385, $P < 0.0001$, CI = 0.247 to 0.601). Similar results were obtained in separate analyses for HIV-1 dementia ($P = 0.006$) and opportunistic brain disease ($P = 0.0021$). Furthermore, the immunologic status, as measured by CD4 count at onset of CNS involvement, was markedly lower in patients with KS (28 cells per microliter, CI = 16 to 40) as compared with those without KS (67 cells per microliter, $P = 0.008$, CI = 52 to 81).

Questions for further research include whether the vMIPs actually block infection of microglial cells, whether vMIPs (or cellular chemokines, or both) concentrate in large amounts in the CNS, or whether other viral or cellular cytokines in patients with KS have neuroprotective effects (*3*).

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Oliver Update

A Random Samples item of 1 November 1996 "'Mutant' chimp gets gene check" (p. 727) correctly described some of the fantastic rumors that have surrounded Oliver, an