In this issue ...

Chaco Canyon timbers imported from distant mountains

The monumental great houses of Chaco Canyon in New Mexico, built between 850 and 1140 CE, include hundreds of thousands of construction timbers. However, the Chaco Canyon landscape is nearly treeless, sparking decades of curiosity and investigation into the origins of the construction timbers. Christopher Guiterman et al. (pp. 1186–1190) used methods of tree-ring-based sourcing developed in Europe and applied in the southwestern United States to determine the timber origins. The authors compared tree-ring growth patterns between 170 great house timbers and tree-ring chronologies from eight potential timber harvesting areas. The authors found that 70% of timbers most likely originated from the Zuni and Chuska Mountains, more than 75 kilometers from Chaco. In addition, the authors determined that prior to 1020 CE, nearly all timbers originated from the Zuni Mountains south of Chaco Canyon, a previously unrecognized timber source. By 1060 CE, most of the beam imports had shifted west to the Chuska Mountains. This shift coincided with substantial expansion of Chaco Canyon society, including enlargement of existing great houses and the addition of seven new great houses. These findings independently corroborate other lines of evidence that suggest vast quantities of Chacoan materials, including timbers, were procured from the Chuska Mountains, according to the authors. — B.A.

Chetro Ketl, one of the largest great houses in Chaco Canyon. Image courtesy of Adriel Heisey (photographer).

How cocaine kills neurons

Cocaine is one of the most widely abused drugs in the United States, resulting in thousands of overdose deaths every year. However, relatively little is known about the molecular mechanisms underlying the drug's toxic effects. Prasun Guha et al. (pp. 1417–1422) used biochemical and microscopy techniques to assess how cocaine kills neurons in the brain. Compared with exposure to a control substance, cocaine exposure increased and depleted levels of the proteins LC3-II and p62, respectively, stimulated the formation of double-membrane vesicles, caused the border of the cell nucleus to curve inward, and triggered cell death. These observations demonstrate that the toxic effects of cocaine are mediated by autophagy—a process that degrades cellular components and can kill cells. Moreover, treatment of neurons with the drug CGP3466B, which prevents nitrosylation of the GAPDH enzyme, abolished cocaine-induced autophagy. The findings demonstrate that cocaine activates the nitric oxide-GAPDH signaling pathway to trigger autophagy in neurons. Because CGP3466B strongly suppresses nitric oxide-GAPDH signaling at low doses and has not produced serious side effects in past clinical trials for neurodegenerative disorders, this drug or other autophagy-inhibiting agents may prove safe and effective for treatment of cocaine abuse, according to the authors. — J.W.

Adolescent marijuana use and intelligence

Marijuana use during adolescence has been associated with reduced intelligence, memory, attention, and verbal ability. However, whether marijuana use

causes reduced cognitive ability or if the association results from confounding factors remains unclear. Nicholas Jackson et al. (pp. E500–E508) examined the relationship between marijuana use and various standard measures of intelligence in two longitudinal twin studies comprising more than 3,000 individuals. Study participants who had used marijuana showed significantly greater decreases in measures of crystallized intelligence between preadolescence

Intelligence and marijuana use during adolescence.

(ages 9–12) and late adolescence (ages 17–20) than nonusers. However, among users there was no association between the level of marijuana use and the decline in intelligence. To control for potentially confounding genetic and familial factors, the authors compared intelligence scores within twin pairs in which only one twin used marijuana. No significant differences in intelligence were observed between the marijuana-using twin and the nonusing twin in both fraternal and identical twin pairs. The results suggest that the cognitive decline observed in marijuana users may not be directly caused by marijuana use. Instead, both marijuana use and cognitive ability might be influenced by aspects of the family environment, according to the authors. — B.D.

Reducing side effects of dopamine treatment

Neurons that produce dopamine are degraded in Parkinson's disease. Although replacing dopamine can improve the resulting loss of motor function, such treatments can also produce involuntary movements, or dyskinesia. Roberta Marongiu et al. (pp. 1423–1428) investigated the molecular pathways that lead to this dyskinesia in an effort to ameliorate the condition. Because upregulating serotonin can reduce dyskinesia, the authors focused on p11, a cellular scaffold protein that increases the presence of certain serotonin receptors in the brain. Using mice with brain lesions similar to those found in Parkinson's disease, the authors injected small viral

vectors encoding an RNA molecule that blocks p11 production in the dorsal striatum, a brain region that responds to dopamine. Despite predictions that blocking p11 would worsen dyskinesia, the treatment improved motor function. When the mice were treated with dopamine, they showed reduced indicators of dyskinesia. Because p11 is found throughout the brain, the authors note that systemic p11 blockade could produce side effects such as depression, but suggest that blocking p11 in the dorsal striatum alone may offer a potentially viable therapeutic strategy for Parkinson's disease. — B.D.

Mortality and socioeconomic status in the United States and Costa Rica

Costa Rica's life expectancy exceeds that of the United States by about 1 year, despite Costa Rica having a per capita gross domestic product less than one quarter of that of the United States. Luis Rosero-Bixby and William Dow (pp. 1130–1137) compared mortality rates and health risk factors between the United States and Costa Rica to uncover reasons for the difference in life expectancy between the two countries. The most striking difference was a stronger correlation between mortality rate and socioeconomic status (SES) in the United States than in Costa Rica. When the populations of both countries were separated into SES quartiles, the highest quartile in the United States had lower mortality than the highest quartile in Costa Rica, but the lowest quartile in the United States had higher mortality than the lowest quartile in Costa Rica. The steep inequality in mortality with SES in the United States was observed across nine cause-of-death categories. The authors also observed correlations between SES and several health risk factors, such as lack of health insurance, smoking, obesity, uncontrolled high blood sugar, and hypertension. These correlations were much stronger in the United States than in Costa Rica, potentially explaining the steep variation in mortality with SES in the United States, according to the authors. — B.D.
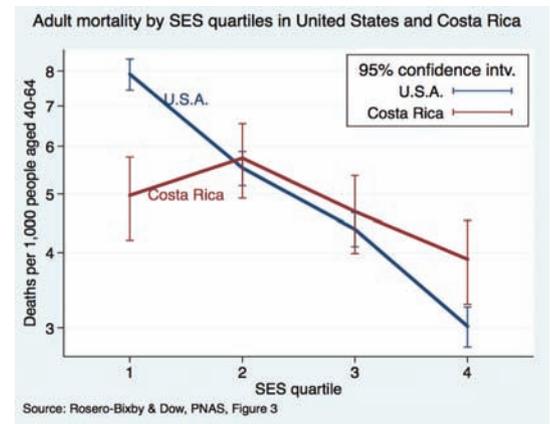
Adult mortality is lower in the United States than in Costa Rica for people with high socioeconomic status, but higher for people with low socioeconomic status.