

tions and feelings of depersonalization. In Gabon, the Bwiti religion revolves around “visits to the ancestors” induced by eating root bark from the shrub *Tabernanthe iboga*, the source of ibogaine. Many patients in the West also report emotionally intense, sometimes frightening visions: scenes from childhood, or past mistakes and regrets replayed and somehow released. Debate rages over whether these experiences are key to ibogaine’s antiaddictive potential or simply a psychedelic side effect.

Not every patient experiences visions, but animal and human pharmacokinetic data reveal a common physiological response: The liver converts ibogaine into its primary metabolite, noribogaine, which fills opiate receptors hungry for heroin or morphine. Mash believes that this dramatically reduces or eliminates withdrawal symptoms, and “that’s why [addicts] don’t feel dope sick anymore.” Ibogaine also stimulates nicotinic receptors in the cerebellum, an action that, according to Glick, contributes to ibogaine’s long-lasting antiaddictive properties by modulating the dopamine reward circuit in the midbrain.

Besides tweaking neurotransmitters, rodent studies suggest that ibogaine increases quantities of a protein in the brain called glial cell line–derived neurotrophic factor (GDNF). Researchers at the University of California, San Francisco, recently observed this effect in the brain’s dopamine-producing areas. Dorit Ron and colleagues reported in the January issue of the *Journal of Neuroscience* that addicted rodents lose interest in opiates when given either ibogaine or GDNF. But after injecting an anti-GDNF antibody that scoops the growth factor out of play, the team found that the animals go dope-crazy again.

Ron goes further, suggesting that GDNF maintains and possibly even repairs frazzled dopamine receptors. She reported last year in the *Journal of Neuroscience* that genetically modified mice producing excess GDNF grow up to have denser dopamine connections in the ventral tegmental area, where the dopamine reward pathway begins.

Mash and others suggest that the effects of the St. Kitt’s therapy lasted up to 3 months because unmetabolized ibogaine deposits in fat, creating a slow-release reservoir, and because metabolized ibogaine can stay in circulation for weeks. But government agencies are wary of ibogaine, in part because of its myriad effects. It slows the heart and, at very high doses, can destroy neurons in the cerebellum. FDA and NIDA cited these toxicity risks repeatedly in the 1990s.

Glick has been trying to develop cleaner-acting derivatives. The best-studied, 18-methoxycoronaridine (18-MC), exhibits strong action at nicotinic receptors but “seems to lack all of the actions that make ibogaine undesirable,” said Glick. Mash and other ibo-

gaine supporters claim that the neurotoxicity risks have been hyped. But the St. Kitt’s team closely monitors heart activity of volunteers, excluding any with irregular rhythms.

While Glick tries to line up funding for clinical studies of 18-MC, Mash is betting on a formulation of the metabolite noribogaine. She and the University of Miami won patent rights to noribogaine in 2002 after a long-running dispute with Lotsof, who holds a patent claim on ibogaine. Mash hopes that, like 18-MC, noribogaine may offer antiaddictive effects without the scary trip.

Meanwhile, Vocci is disappointed that

Mash has not published her data from St. Kitt’s. “This big case series, no one knows what to make of it,” he said. “I would expect to see a spectrum of responses. Even though it’s not a controlled study, it would still give us some idea whether or not she has anything worth looking at.” If Mash’s new trial does produce promising data, ibogaine advocates will have a token of legitimacy to point to. But the circle of true believers seems to be expanding, Wachtel says, because users insist that ibogaine works.

—BRIAN VASTAG

Brian Vastag, a writer in Washington, D.C., is working on a book about ibogaine.

## Ecology

# Experimental Drought Predicts Grim Future for Rainforest

An extraordinary research effort in the Amazon starved a tropical forest of rain and provides a glimpse of the potential effects of climate change

For 5 years, Daniel Nepstad has been slowly killing trees throughout a hectare of his beloved Amazonian rainforest. In an elaborate experiment akin to an installation by the artist Christo, Nepstad’s team set up a 1-hectare array of 5600 large plastic panels that diverted the rain and created an artificial drought. The point of the \$1.4 million experiment is to provide the most detailed look ever at how tropical forests respond to such stress.

The good news, as Nepstad, an ecologist at the Woods Hole Research Center (WHRC) in Massachusetts, and colleagues have reported in recent papers, is that the forest is quite tough. Although that’s no great

surprise—forests in the eastern Amazon have long experienced regular droughts from El Niño events—the team is discovering clever tricks that the trees use to survive when the soil becomes parched.

What’s worrisome is that when drought lasts more than a year or two, the all-important canopy trees are decimated. Everyone knows that a lack of water eventually kills plants. But by pushing the tropical forest to its breaking point, researchers now have a better idea of exactly how much punishment these forests can withstand.

These kinds of data will be indispensable for predicting how future droughts might change the ecological structure of the forest, the risk of fire, and how the forest functions as a carbon sink, experts say. Given that droughts in the Amazon are projected to increase in several climate models, the implications for these rich ecosystems is grim, says ecologist Deborah Clark of the University of Missouri, St. Louis, who works at La Selva Biological Station in Costa Rica. The forests are “headed in a terrible direction,” she says. What’s more, the picture includes a loss of carbon storage that might exacerbate global warming.

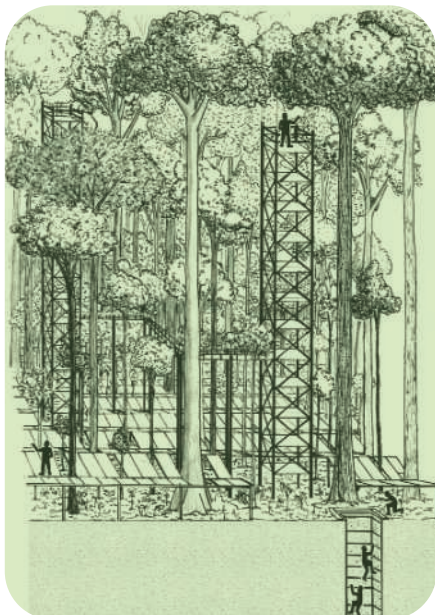
## Basement to attic

Nepstad got the idea for the experiment while working in the eastern Amazon in 1992 during



**Parched.** Thousands of panels prevented most rain from reaching the forest floor.

CREDIT: WOODS HOLE RESEARCH CENTER



**Extreme instrumentation.** Towers and trenches revealed the inner workings of the forest.

an El Niño drought. Some forests there had dried out so much that they burned, apparently, for the first time. To find out more, Nepstad teamed up with Paulo Moutinho of the Institute for Environmental Research in the Amazon in Belém and Eric Davidson of WHRC. They chose a field site in the Tapajós National Forest, 67 km south of Santarém, Brazil, in the lowlands that are predicted to be especially vulnerable to climate change. It's not as wet as true rainforest and has an annual dry season that lasts for up to 6 months.

The setup required a year's worth of effort in hot, muggy conditions. With a crew of up to 15 local workers, the team outfitted two sites with four 30-meter-high towers, linked by catwalks to study the canopy. Working with hand tools to avoid disturbing the forest, the crew also dug five pits down to 11 meters in each site to enable researchers to regularly examine roots and soil water. "You can look from the basement to the attic of the forest," says Nepstad. Even more earth was moved as workers dug a 1.5-meter-deep trench around the hectare-sized experimental site to prevent rainwater from seeping in from the surrounding forest. To control for the impact of digging on tree roots, they excavated a similar trench around the comparison plot.

As has been done in similar but smaller experiments elsewhere, they then assembled a system of wooden rafters 1 to 4 meters above the forest floor. Some 5600 plastic panels, each 0.6 m by 3 m, rested on these rafters. "It's like the whole understory of the forest is wrapped in plastic," says team member Rafael Oliveira, a plant ecophysiologicalist now at the National Institute for Space Research in São Paulo. The panels caught about 80% of the rain that fell through the canopy and diverted it to wooden gutters that

drain to the trench. To mimic natural conditions, workers flipped each panel three times a week to allow leaves and other material to reach the forest floor.

The forest was remarkably resilient—at first. As expected, photosynthesis slowed down to conserve water, and the roots drew water from ever deeper in the soil—ultimately as far down as 13 meters. These deep roots help irrigate the topsoil, the researchers found: At night, water flows from the tap roots and dribbles out of the larger network of shallow roots to be used after daybreak, as Oliveira and Todd Dawson of the University of California, Berkeley, will report in a paper accepted at *Oecologia*. This phenomenon, called hydraulic redistribution, had been seen in temperate forests but wasn't known to occur in the tropics.

The canopy also had tricks up its sleeve. No one would have expected leaves to absorb rainwater, says Gina Cardinot, a grad student at the Federal University of Rio de Janeiro, because of their adaptations to prevent water loss. But unpublished research by Cardinot and Leonel Sternberg of the University of Miami in Coral Gables, Florida, suggests otherwise. Stable isotope tracers applied during the drought experiment indicate that two of three common species take up some water through their leaves. "All of this adds up to a forest with enormous drought tolerance," says Nepstad.

That's not to say there weren't changes. Trees in the experimental plot slowed their growth, and many of the smaller trees stopped growing entirely. And then, 4 years after the drought began, they began to die. The mortality rate was especially high in tall, canopy trees—up to 9% per year—as Nepstad's team describes in a paper submitted to *Ecology*. "These are astonishing effects," says Clark, who says no one ever really knew exactly how much death was specifically due to drought.

The loss of large, centuries-old trees has big implications. Gaps in the canopy allowed more light to reach the forest floor, drying out the leaf litter and increasing the risk of fire. According to a model of fire risk that Nepstad has devised, in press at *Ecological Applications*, the control plot is highly flammable for about 10 days a year. The experimental plot, by contrast, is now highly vulnerable for 8 to 10 weeks each year. Intense fires not only convert tropical forest to savanna, they also release a lot of carbon and generate smoke that can further dry out remaining forest. Even without fires, dead trees release large amounts of carbon when the wood and roots decompose.

Severe drought also brought dramatic

changes in the ability of the forest to store carbon, because of the slower plant growth. By the third year of drought, the experimental plot was storing only 2 tons of carbon as wood, whereas the control plot still tucked away 7 tons. "That's a profound reduction," says John Grace of the University of Edinburgh, U.K.

By putting hard numbers on these kinds of processes, the drought experiment will help refine climate models, says David Lawrence of the National Center for Atmospheric Research (NCAR) in Boulder, Colorado. Already, Jung-Eun Lee and Inez Fung of the University of California, Berkeley, have shown in unpublished research that incorporating the hydraulic redistribution of water into the NCAR climate model makes it more accurate.

One important question is how broadly Nepstad's results can be extrapolated. In contrast to the Tapajós forest, large swaths of tropical forest further west don't experience regular dry seasons. That could mean these forests haven't evolved coping strategies and



**Diversion.** Panels and gutters caught rain, enabling Daniel Nepstad and his team to mimic a drought.

might suffer even more dramatically when drought-stricken, Nepstad warns. On the other hand, wetter environments are more buffered. Nepstad deliberately picked a site with a water table so low that roots couldn't reach it. In contrast, Grace and Brazilian colleagues have finished a smaller scale experiment farther east where the water table was higher; they found less tree mortality.

Another factor is the time scale. Five years is just a blink of an eye for a forest. Ariel Lugo, director of the U.S. Forest Service's International Institute of Tropical Forestry in Puerto Rico, suggests that climate change will be more gradual than the onset of this experiment, perhaps allowing forests to adapt: "You have to be aware those are worst-case scenarios."

The next step is to observe what happens after the end of a severe drought. Nepstad's team has removed the plastic panels and will study the two plots for another 2 years to see how—or whether—the forest recovers.

—ERIK STOKSTAD