EVOLUTIONARY MEDICINE

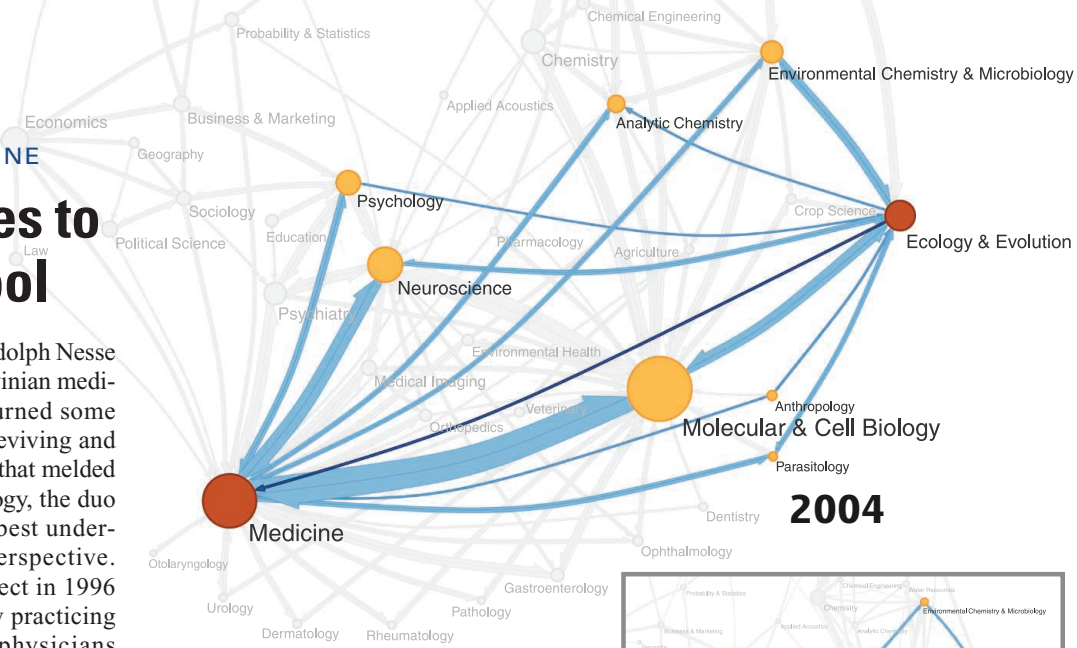
Darwin Applies to Medical School

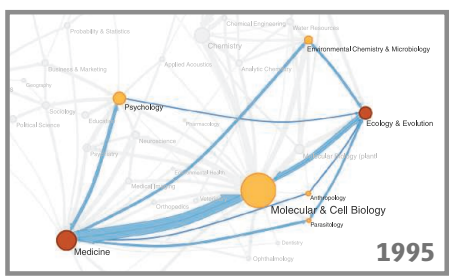
When George Williams and Randolph Nesse made their first pitches for Darwinian medicine in the early 1990s, they turned some heads, but not the right ones. Reviving and building on European traditions that melded medicine and evolutionary biology, the duo argued that diseases could be best understood from an evolutionary perspective. Their first meeting on the subject in 1996 attracted 60 enthusiasts but few practicing clinicians, probably because physicians couldn't envision practical applications. "The folks who were excited about it weren't in a position to do anything about it," recalls anthropologist Peter Ellison of Harvard University. Although a better understanding of the evolution of drug resistance has helped shape the use of antibiotics, when it comes to evolution, "medical schools are mostly oblivious," says Nesse, a psychiatrist at the University of Michigan, Ann Arbor.

But times may be changing. Last week, a similar meeting* in Washington, D.C., attracted dozens of physicians, including the dean of Harvard Medical School and the president of the Institute of Medicine (IOM). Several participants described new medical school programs at the University of Auckland, New Zealand, and at Johns Hopkins University in Baltimore, Maryland, involving evolutionary medicine, as well as a pending textbook. "A thoughtful strategy for the future education for health professionals would incorporate a strong evolutionary perspective," says IOM President Harvey Feinberg.

At the meeting, researchers reported headway in understanding drug resistance through the lens of evolution. Others described progress linking past evolutionary adaptations with current health problems. For instance, anthropologist Kathleen Barnes of Johns Hopkins University has evidence that for some asthmatics, this overly energetic inflammatory response may be a holdover from the body's successes in coping with parasitic disease.

*Evolution in Health and Medicine was held at the National Academy of Sciences in Washington, D.C., 2–3 April 2009.





Connections. Citation maps from 1995 and 2004 (*above*) reveal a sevenfold increase in direct interactions between evolutionary biology and medicine.

Despite the intellectual appeal of adding evolution to the medical school curriculum, medical schools are already straining from an explosion in information and technology, and clamors for change come from many directions. "Medical schools have a lot on their plate," says James Lupski of Baylor College of Medicine in Houston, Texas. And, notes Harvard evolutionary biologist David Haig, "Evolutionary thinking is not going to give cheap medical solutions."

Proponents counter that evolutionary thinking can provide a fresh way of looking at the human body and a framework for organiz-

CREDIT: M. ROSVALL AND C. T. BERGSTROM, *PNAS* **105**, 1118-1123 (2008); EIGENFACTOR PROJECT; (DATA SOURCE) THOMSON-REUTERS' JOURNAL CITATION REPORTS

Two Sides of the Same Coin?

Scientists have long puzzled over the persistence of schizophrenia—a deleterious condition that by rights should have been pretty much bred out of the human gene pool.

At the Sackler Colloquium on Evolution in Health and Medicine held last week at the National Academy of Sciences (NAS) in Washington, D.C., evolutionary geneticist Bernard Crespi of Simon Fraser University in Burnaby, Canada, threw some evolutionary firepower at the question. He proposes that both schizophrenia and autism are disorders of the "social brain"—but at opposite ends of the same spectrum. Psychiatrist Ezra Susser of Columbia University calls it an "imaginative proposal, … although I don't think it's supported yet by the data."

Last year Crespi, with Christopher Badcock of the London School of Economics, presented the hypothesis in a lengthy article in *Behavioral and Brain Sciences*. At the NAS meeting, Crespi claimed that recent research on copy number variations (CNV), segments of DNA containing duplications or deletions, further bolster his case. These new studies suggest that schizophrenia may be the result of multiple rare mutations that occur spontaneously. A number of studies have shown some overlap in genomic "hot spots" for CNVs in schizophrenia and autism, with, in some cases, deletions in one condition just where there are duplications for the other. Some scientists suspect some overlap between the two conditions. Crespi and Badcock think, rather, that they are diametric opposites, occupying the same continuum and thus affecting the same pathways.

That would fit with their theory that psychotic disorders—including not only schizophrenia but also bipolar disorder and some major depression—result from "overdevelopment" of the social brain, and autism spectrum disorders reflect underdevelopment of that brain. Many scientists believe socialization is the main force behind the rapid expansion of human brains, said Crespi, pointing out that in primates the size of the cortex increases with size of social groups. The components of the social brain, according to Crespi, include language, self-awareness, "social emotions" such as pride and guilt, logical thinking, pursuit of goals, and awareness of the mental states of others.

In autism, he pointed out, these functions are deficient. In schizophrenia, on the other hand, they are out of control—the language function leads to auditory hallucinations; awareness of

ing a deluge of new genomic information. Those new data are driving home how tightly disease is linked to evolution, says David Valle, a geneticist at Johns Hopkins University School of Medicine. He and others want to move away from viewing the human body as a generic, one-size-fits-all machine. Individuals vary not just in their genetic makeup but in their connections to the microbes in their gut and their environmental exposures. "All this must somehow be understood" to manage disease, says Diddahally R. Govindaraju, a Boston University geneticist who co-organized the meeting. With genomic data in hand, "medical students are much more equipped to understand the connections between all organisms," he adds.

During her talk, Barnes presented several examples that suggest that how humans evolved to cope with past parasitic diseases has predisposed some of us to contemporary health problems. The malaria parasite *Plasmodium vivax*, for instance, depends on a surface protein called Duffy to gain entry into human red blood cells. In certain malaria-endemic areas, a mutation in the gene for Duffy, called *DARC*, leads to the loss of this surface protein, and malaria can't gain a foothold. But Duffy also acts as a sponge to keep immune system messengers in check; otherwise excess immunoglobulin E (IgE), which underlies allergic asthma and other allergic reactions, may be produced. Barnes and her colleagues have found that asthma is associated with the defective Duffy gene in populations in Brazil, Columbia, and the Caribbean whose recent African ancestors lived where malaria was endemic.

Similarly, others have found asthma associated with high IgE in areas such as Egypt where schistosomiasis is common. Today, cockroach and dust mite allergens are well-established triggers for asthma, and those proteins are quite similar to the schistosomiasis worm protein tropomyosin, which sets off the IgE response. People with high IgE are most able to curb parasite infection, but there can be a downside. "Individuals who are most resistant in these [worm-ridden] environments are the ones who produce the most IgE, and they are primed to respond to the common household allergens," says Barnes. She has traced this sensitivity to some variants of the gene for the immune system messenger interleukin 13.

"She has sophisticated evolutionary thinking that she's applied to two different medical problems, and she has not just clinical and epidemiological data, she has the genetic underpinnings. She has the complete story," says Nesse.

Knowing these evolutionary connections could help physicians recognize who might be at increased risk for asthma and who should take precautions to limit exposure to allergens, says Barnes.

At the beginning of the meeting, Harvard Medical School Dean Jeffrey Flier called himself agnostic about the need to incorporate evolution into medical education. But now, "I want to start to influence the medical curriculum toward that," he announced as the meeting wrapped up. "Evolutionary biology needs to get in the queue."

At last, says meeting co-organizer Stephen Stearns of Yale University, "we've gotten the attention of the medical community."

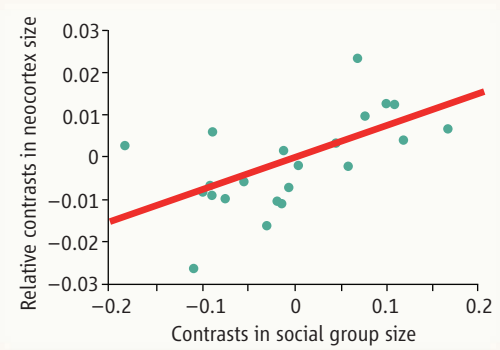
–ELIZABETH PENNISI

others' mental states becomes paranoia; and logic is distorted by uninhibited associations.

Although the data are admittedly preliminary, Crespi maintains they support the notion that autism and schizophrenia are "cognitive, neurodevelopmental, and genomic opposites." He pointed out that some existing theories about the disorders complement this view—for example, some have proposed that glutamate, the brain's main neurotransmitter, is deficient in schizophrenia and overactive in autism.

To evolutionary biologist Randolph Nesse of the University of Michigan, Ann Arbor, who organized the talks on evolution and mental health, the hypothesis shows "the heuristic value of an evolutionary approach in medicine." If correct, "it will fundamentally change our understanding of schizophrenia and autism, … [and] even if it is not, the research is deepening our understanding."

–CONSTANCE HOLDEN



Social brain. In existing primate species, the size of the neocortex in relation to total brain increases with group size.

CREDITS (TOP TO BOTTOM): C. R. JOHNSON AND S. MCBREARTY/UNIVERSITY OF CONNECTICUT; ADAPTED FROM R. A. BARTON, *PROC. BIOL. SCI.* **263**, 1367 (22 FEBRUARY 1996) THE ROYAL SOCIETY

ScienceNOW.org

From *Science*'s Online Daily News Site

Bugs build batteries. Green technology just went viral. Researchers have used viruses to create rechargeable batteries similar to those found in hybrid cars and laptops. Until now, batteries like these were made in chemically intensive, high-heat processes. The results could herald a low-energy, environmentally friendly alternative. http://tinyurl.com/csuebz

Oldest stone blades uncovered. Paleoanthropologists working in Africa have discovered stone blades more than a half-million years old. That pushes the date of the earliest known blades back a remarkable 150,000 years and raises a question: Which human ancestor made them? http://tinyurl.com/dajyf7

Tropical parents more likely to hear, "It's a girl!" Wondering about the gender of your future offspring? Check your GPS. Girls are more likely to be born at tropical latitudes than in temperate or subarctic climes, according to new research. The study provides the first global look at human sex ratios and could shed light on how temperature and day length influence human reproduction. http://tinyurl.com/dfbxag

Heat and acidity ganging up on coral. Human-caused emissions of carbon dioxide are starting to harm marine life with a one-two punch of rising temperatures and stronger ocean acidity. Now a study of a reef in the Red Sea confirms the impact of rising acidity and suggests that it could eventually make reefs across the globe dissolve. "This is a very significant and important result," says Ben McNeil of the University of New South Wales in Sydney, Australia. "We are finally moving towards a more complete picture of how coral reefs will respond to a high CO_2 and warmer ocean." http://tinyurl.com/chn9ej

Read the full postings, comments, and more at **sciencenow.sciencemag.org**.

Published by AAAS