Are Human Brains Still Evolving?
Brain Genes Show Signs of Selection

We humans are proud of our big brains, and rightly so. Averaging 1350 cubic centimeters (cc), the human brain is proportionally larger than that of any other animal. Its highly advanced cognitive powers have spurred us to create art, build cities, and send representatives of our species into space. Just why natural selection blessed us with these talents is poorly understood. But the fossil record and genetic studies clearly show that the evolution of higher cognition began sometime after the chimp and human lines split, some 5 million to 6 million years ago, and continued at least until the rise of modern humans, roughly 200,000 years ago.

Now two new reports on pages 1717 and 1720 of this issue suggest that the evolution of the human brain may not have stopped when *Homo sapiens* first came on the scene. The studies, both led by human geneticist Bruce Lahn of the University of Chicago, conclude that two genes thought to regulate brain growth have continued to evolve under natural selection until very recently—and perhaps are doing so today.

The possibility that our brains are continuing to adapt is fascinating and important,” says Huntington Willard, director of the Institute for Genome Sciences and Policy at Duke University in Durham, North Carolina. “Most laypeople tend to assume that humans are the pinnacle of evolution and that we have stopped evolving.”

But researchers caution that although these genetic variants, or alleles, do seem to have been the target of natural selection, there’s as yet little solid evidence that the advantage they confer was brain-related. “The case for selection acting on [the genes] is reasonably strong,” says anthropologist Mark Stoneking of the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany. “However, there is absolutely nothing in either paper to relate the signature of selection to any brain-related phenotype.”

Lahn’s group focused on two genes, called *microcephalin* and *ASPM*, that cause primary microcephaly, a condition in which the brain is severely reduced in size. Earlier work by Lahn’s group and others had shown that the human versions of *microcephalin* and *ASPM* have come under strong natural selection since the chimp-human split, implicating both genes in our ancestors’ dramatic brain expansion.

Several other genes have also been identified as potential contributors to our early ancestors’ evolution (*Science*, 8 July, p. 234). On page 1693 of this issue, Ajit Varki of the University of California, San Diego, and his colleagues add another to the list: They report that a gene expressed in microglia, immune cells of the nervous system, produces a protein found only in humans. This suggests that it too has been the target of selection during human evolution, and that human microglia are specialized compared to those of chimps.

In their new research, Lahn and his co-workers looked for evidence that selection had operated on *microcephalin* and *ASPM* much more recently—since the rise of modern humans. The team sequenced the DNA of about 90 human cells housed at the Coriell Institute for Medical Research in Camden, New Jersey, whose cell collection is broadly representative of global human diversity. For each gene, they found an allele with a surprisingly high frequency in human populations. Statistical tests showed that these frequencies are unlikely to be due to random genetic drift or population migration, suggesting that the alleles were instead favored by natural selection. Making assumptions about past mutation rates, the team then estimated when each allele arose. The favored *microcephalin* allele clocked in at 37,000 years ago (with confidence intervals ranging from 14,000 to 60,000 years)—about the time of the explosion of symbolic behavior in Europe. The *ASPM* allele arose 5800 years ago (with a possible range of 500 to 14,100 years), just before cities arose in the Near East.

Lahn’s team argues that in the case of *ASPM* in particular, the young age of the selected allele and its worldwide distribution suggest that it was subject to a strong “selective sweep” in the very recent past. Lahn says these alleles may have provided an adaptive advantage in some brain-related function, possibly although not necessarily cognition. His group is now collaborating with others to see if living people with the alleles have some sort of cognitive advantage. The team has also taken out patents on both genes, which will cover tests to see whether an individual carries the favored alleles.

Despite these potentially dramatic findings, many researchers who spoke to *Science* were unwilling to immediately accept all of the Lahn team’s conclusions. The data do bear the fingerprints of natural selection, says geneticist Chris Tyler-Smith of the Sanger Institute near Cambridge, U.K. But he questions whether that selection was acting upon the brain or some other function. Both genes are expressed in tissues other than the brain, although previous studies have shown that their expression is strongest in the developing brain of mice and humans.

Even if the favored alleles did provide some sort of cognitive or cultural advantage, some researchers say that it was unlikely to have been a dramatic one. All normal modern humans are capable of language and symbolic expression, regardless of which alleles they have. “This suggests that the new alleles don’t have a big effect.”
on these abilities,” says Tyler-Smith, who calls the possible links to events in human prehistory “highly speculative.”

Lahn and colleagues also found a pronounced pattern in the distribution of the favored alleles in populations around the world: The microcephalin allele, for example, is much more common in Europe, Asia, and the Americas than in sub-Saharan Africa. Using a larger sample from 1184 individuals, the team found this allele in roughly 75% or more of Italians, Russians, and Han Chinese, and in nearly 100% of Colombians. In contrast, the allele had frequencies of less than 10% in the Chornobyl area do not trust government officials, he notes, because “there was a tradition of lying” in Soviet times. Mettler hopes the Chernobyl Forum report will reassure residents. “It’s a start,” he says.

—Michael Balter

NUCLEAR MEDICINE

Panel Puts Eventual Chornobyl Death Toll in Thousands

VIENNA, AUSTRIA—A study released this week predicts that 4000 people or even more will die from cancers caused by the 1986 Chornobyl nuclear accident, a figure that dwarfs the 50 known deaths linked to the disaster so far. The report, compiled by the Chernobyl Forum, a joint effort of eight United Nations agencies and the governments of Ukraine, Belarus, and Russia, also highlights the thousands who are suffering a variety of mental health problems since the accident.

The meltdowns of one of the reactors at the Chornobyl power plant in Ukraine on 26 April 1986 released approximately 50 tons of radioactive material into the atmosphere, contaminating an area inhabited by 5 million people. Because the most pernicious contamination was radioactive iodine-131, which lodges in the thyroid, most of the casualties are expected to succumb to thyroid cancer, which typically takes 25 years or more to show up.

Over the 19 years since the accident, estimates of the final death toll from radiation-induced cancer have ranged from zero to tens of thousands. The panel of 100 scientists involved in the Chernobyl Forum reduced that uncertainty by reviewing all available data and discounting studies that were not sufficiently rigorous. “But that only considers the 600,000 people living in the most exposed areas. [The total] could double to 8000 if you also consider people around that area,” says forum member Fred Mettler, a radiologist at the University of New Mexico in Albuquerque.

Radiation biologist Mikhail Balonov was part of the Soviet team rushed in to assess Chornobyl in 1986, and he says his team “also predicted 4000 deaths. But our conclusions were classified.” The forum’s 600-page report, released by the International Atomic Energy Agency (IAEA) here on 5 September, also echoes initial predictions that the radiation will have no effect on fertility or the frequency of birth defects in the second generation. “Luckily, the exposure was too low for that,” says Balonov, who now heads IAEA’s Radioactive Discharges Unit. Other effects of the radiation are either too subtle or have not yet been detected.

The outlook for the environment around Chornobyl appears somewhat better. According to the report, 90% of the radioactive contamination was cleaned up through a massive removal of surface soils. Researchers are developing special salts and fertilizers to inhibit the remaining radioactive material in soil from getting into crop plants. But on the whole, the forum concludes, most of the originally exposed area is close to background levels of radiation.

The report’s most surprising conclusion is that mental health problems appear to be more common than any radiation-linked disease. The incidence of high anxiety is twice normal levels, and unexplained pain or debilitation is three to four times that in similar unexposed populations. One possible cause is the trauma experienced by the 350,000 residents who were forcibly relocated.

Mettler, a member of the international scientific team that first visited the Chornobyl site in 1990, says another factor “is the psychological impact on people of not knowing the extent of contamination or the real health risks it poses.” That uncertainty, according to the report, seems to have translated into unhealthy lifestyle choices such as heavy smoking, drinking, drug use, and poor diet.

Removing anxiety won’t be easy, says Balonov. People in the Chornobyl area do not trust government officials, he notes, because “there was a tradition of lying” in Soviet times. Mettler hopes the Chernobyl Forum report will reassure residents. “It’s a start,” he says.

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John Bohannon is a writer in Berlin, Germany.

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*Chornobyl’s Legacy: Health, Environmental, and Socio-economic Impacts*, www.iaea.org/NewsCenter/Focus/Chornobyl

**Sleeping giant**. A guard walks past the remains of Chernobyl’s reactor #4, which is encased in a now-crumbling sarcophagus.