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Brain gene activity changes through life

Studies track biochemical patterns from just after conception to old age

By [Laura Sanders](#)

Web edition : Friday, October 28th, 2011

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Human brains all work pretty much the same and use roughly the same genes in the same way to build and maintain the infrastructure that makes people who they are, two new studies show. And by charting the brain's genetic activity from before birth to old age, the studies reveal that the brain continually remodels itself in predictable ways throughout life.

In addition to uncovering details of how the brain grows and ages, the results may help scientists better understand what goes awry in brain disorders such as schizophrenia and autism.

"The complexity is mind-numbing," says neuroscientist Stephen Ginsberg of the Nathan Kline Institute and New York University Langone Medical Center, who wasn't involved in the studies. "It puts the brain in rarefied air."

In the studies, published in the Oct. 27 *Nature*, researchers focused not on DNA — virtually every cell's raw genetic material is identical — but on when, where and for how long each gene is turned on over the course of a person's life. To do this, the researchers measured levels of mRNA, a molecule whose appearance marks one of the first steps in executing the orders contained in a gene, in postmortem samples of donated brains that ranged in age from weeks after conception to old age.

These different patterns of mRNA levels distinguish the brain from a heart, for instance, and a human from a mouse, too, says Nenad Šestan of Yale University School of Medicine and coauthor of one of the studies. "Essentially, we carry the same genes as mice," he says. "However, in us, these genes are up to something quite different."

To see what those genes were up to, Šestan's study examined mRNA levels of different genes in 57 brain samples. The team divided the brain tissue up by region, so they were also able to get an idea of genes' behavior in different parts of the brain. A parallel study, headed by Joel Kleinman of the National Institute of Mental Health in Bethesda, looked at gene behavior in 269 brain samples from a single region called the prefrontal cortex that also spanned the lifetime.

This approach allowed the researchers to get access to the brain that had previously been impossible.

"One of the limitations in studying human brain development is that you cannot do experiments," Šestan says. "It's very hard to understand when things happen."

Both studies found lots of variation in gene behavior at different life stages, but one particular period stood out: The prenatal brain had massive changes in gene activity. Many genes there were pumping out big quantities of mRNA, and this production abruptly slowed after birth. "Prenatally, things are changing faster than they change at any other time," says Carlo Colantuoni of the Lieber Institute for Brain Development at Johns Hopkins University Medical Center, and coauthor on one paper. "Things are happening fast in there."

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- ▶ C. Colantuoni et al. Temporal dynamics and genetic control of transcription in the human prefrontal cortex. *Nature*, Vol. 478, October 27, 2011. doi: 10.1038/nature10524. Available online: [\[Go to\]](#)
- ▶ H. J. Kang et al. Spatio-temporal transcriptome of the human brain. *Nature*, Vol. 478, October 27, 2011. doi: 10.1038/nature10523. Available online: [\[Go to\]](#)

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Kleinman and his colleagues turned up a curious finding: Many of the genes that slow down right after birth show a surge of activity as a person gets older. "The biggest changes that are going on occur fetally," he says. "And then they drop off until mid-life, and then in the 50s to 70s, expression changes pick up again and become quite dramatic."

Researchers don't yet know what to make of this reversal, says Colantuoni. "We have just scratched the surface of what it means."

Genes involved with building new brain cells were highly active early on, and then this activity quickly fell after birth. As these genes grew less active, genes involved in linking up nerve cells took on a greater role and became busier.

What's more, the differences in gene behavior between male and female brains were greatest at early stages of development. Some of the genes found to be busier in male brains have been linked to schizophrenia, autism and other disorders that are known to be more prevalent among males, the researchers report. These disease-associated genes are very active early on in development and less so as a person ages, the researchers found, suggesting that something goes wrong very early in these conditions.

The scientists don't know exactly which cells are responsible for these gene behavior differences. Figuring out whether gene behavior changes in all kinds of cells in the brain — neurons and glia, for instance — is the next step, says Ginsberg. "That's going to be really important, especially for neuropsychiatric disorders."

Although gene behavior is incredibly dynamic, the results suggest that brains are more alike than different. Despite millions of differences in DNA, brains have a common biochemical shape, Kleinman says. Two people who have very different DNA make-up don't necessarily have very different gene behavior in the brain. "These individual genetic variations, they do matter — no question," he says. But overall, genes behave similarly from person to person. "And that's a really cool thing. It means that we're much more alike than we are different."

Many more studies are needed before scientists fully understand how the brain is built. Both teams plan on boosting the number of brain samples and studying the brains of people with disorders such as schizophrenia and autism. But the work is a major step forward, says geneticist Christopher Mason of Weill Cornell Medical College of Cornell University in New York City. "This is extraordinary work," he says. "This is the beginning of telling us what the whole brain looks like."

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I think I would be remiss if I did not, in keeping with the season, say... BRAINS!!!

 Johnay

Oct. 31, 2011 at 9:59am

.....
This article shows just how amazing God is and truly glorifies Him.

 zetty

Oct. 31, 2011 at 1:29pm

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 kathleen sisco

Oct. 31, 2011 at 2:40pm

.....
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 LookingForAnswers

Oct. 31, 2011 at 3:31pm

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