David Amaral wanted to watch the young brain take shape. He thought that studying post-mortem brains under the microscope would help him to work out why children with autism often have abnormalities in the key structures that drive emotion and behaviour. But he soon found that existing brain banks couldn’t give him what he needed. “It’s just too hard to get high-quality tissue,” he says. The banks may contain hundreds or even thousands of brains — but not from children, and not necessarily in the best condition.

Amaral, who is director of research at the MIND (Medical Investigation of Neurodevelopmental Disorders) Institute at the University of California, Davis, is not the only scientist eager for access to brains from children. The crucial stages of brain development span early fetal life through to the end of the teenage years; and destructive neurodevelopmental disorders such as autism and schizophrenia are thought to arise partly because of faulty connections laid down during this time. Many researchers want to apply new technologies, including increasingly sensitive molecular analyses and ever smarter microscopy, to developing brains to create a dynamic picture of what goes wrong.

When they succeed, the results can be breathtaking, says neuropathologist Joel Kleinman at the National Institute of Mental Health (NIMH) in Bethesda, Maryland. In work reported in this week’s *Nature*, he and his colleagues applied genomic technologies to 269 brains spanning the human lifetime and revealed an extraordinary wave of changes in gene expression that occur as the human brain develops. “It’s like I witnessed the poetry of birth,” he says.

But experiences such as Kleinman’s are rare, owing to the challenges of collecting and storing children’s brains. Parents must give permission shortly after their child has died, a time of inconsolable grief, and fetal brains are available only after an abortion — an incendiary political issue as well as an emotionally painful one for the women involved. Biomedical organizations have been tiptoeing around the delicacies for a decade or more.

The solution, according to Amaral, is not complicated. Outreach programmes could be aimed at the coroners who conduct autopsies as well as at the families of children with brain disorders. They could explain the research value of donated brains and encourage families to sign up to a donor registry. A network of brain-collection centres around the United States could ensure that brains are preserved quickly. And centralized governance of the banks could direct tissue from each donated brain towards as much high-quality research as possible. “All it needs is for someone to take ownership of the issue,” Amaral says.

That ownership may now be emerging from advocacy groups for neurodevelopmental disorders. “I know there has been a lot of talk and no action till now,” says neuroscientist Robert Ring, vice-president of translational research at Autism Speaks, a research and advocacy organization based in New York. So Ring is pushing forward plans for a bank along the lines Amaral suggests. “Give us one year and we’ll have developed a collaborative model with the scientific community,” he says.

Only two major brain banks store brains from children or fetuses and distribute them to the research community at large. One is run by the National Institute of Child Health and Human Development (NICHD) and held at the University of Maryland School of Medicine in Baltimore; the other, called the Autism Tissue Program, is run by Autism Speaks and is hosted at the Harvard Brain Tissue Resource Center in Belmont, Massachusetts.

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**Brain child**

Asking parents to donate a child’s brain to research is emotionally fraught. Some researchers say that it is time to put aside the taboos.

**BY ALISON ABBOTT**
At most brain banks, including the NICHD’s, personnel typically call the local coroner’s office each morning. If a child is to be autopsied, they ask the office’s permission to contact the family and request the brain for research. But the few coroner’s offices involved can collect only a small amount of tissue. The Autism Tissue Program depends more on families that get in touch when they experience such a bereavement. Experts then go out to retrieve and prepare the brain. As the programme collects brains from across the United States, this often means a long journey. Ideally, though, the brain should be acquired quickly after death to minimize the breakdown of proteins and other molecules that researchers might wish to study. Other factors also influence tissue integrity, such as how soon after death a body is refrigerated and whether the person died slowly and painfully, as scientists have shown that this alters gene expression in the brain, making it less useful for research.

Collecting fetal brains is also hard. Brains from spontaneous abortions can’t be used for research because the fetus has generally been dead for many hours before it is expelled. In fact, brains can be collected from abortions only when labour has been induced medically, because surgical procedures tend to damage the tissue.

Neither the NICHD bank nor the Autism Tissue Program bank — which together hold nearly 1,300 brains from people aged 19 and under — can meet the demand from researchers. Neuroscientist H. Ronald Zielke, director of the NICHD bank, says that he turns down 20% of requests for tissue because of a lack of material. In particular, this and other brain banks are running critically short — or have run out — of the brain areas that are the most interesting for research into developmental disorders, says Zielke. That includes the amygdala, which processes emotion, and the prefrontal cortex, which processes other cognitive and social behaviours. A brain bank, like any tissue repository, is also very expensive to run — the annual direct costs for the NICHD bank come to US$900,000.

To get around the shortage, some researchers have built up collections for their own use. Kleinman’s research on gene expression drew on a collection that he heads at the NIMH. A similar study in this week’s Nature, led by Nenad Šestan from the Yale University School of Medicine in New Haven, Connecticut, and with Kleinman as a co-author, drew in part on a collection that Šestan has generated at Yale. Their study showed the dramatic changes in gene expression that occur before and shortly after birth (see ‘Brain waves’). Neonatologist David Rowitch at the University of California, San Francisco, began a collection of brains at his hospital, which led to a paper published in last week’s Nature showing that the migration of ‘progenitor’ cells between two brain structures seen in infants slows down after the age of 18 months and has almost disappeared by adulthood. He began collecting brains in 2008 with the support of the Howard Hughes Medical Institute in Chevy Chase, Maryland, and now has more than 100, most of which are from very young babies.

These studies show how valuable such collections can be, but both Rowitch and Šestan describe the process of creating and running their own banks as “a big headache” because of the bureaucracy associated with handling human material. Šestan says that he would feel “much more comfortable” if the National Institutes of Health (NIH) were to run his collection. “It’s a huge effort for a small group and the NIH could do something on a larger scale,” he says.

PUTTING BRAINS TOGETHER

In fact, neuroscientists have been proposing for years that the NIH take a leading role in establishing a network of collection centres and standardizing methods for brain collection and preservation.

In July last year, Autism Speaks and the other major US foundation that funds autism work, the Simons Foundation in New York, made a formal proposal to the NIMH for a public–private partnership to collect brains from children with and without autism. The idea is that the advocacy groups would engage in intensive outreach efforts to potential donors, particularly families who have a child with autism, and the NIH would fund and manage the bank.

The NIH, though, has been slow to commit. Ring, who moved from the drug giant Pfizer to Autism Speaks in June this year and has the candor of someone used to industry deadlines, sees “a unique opportunity for the foundations to take on a leadership role”. His organization and the Simons Foundation are now in discussions with scientists to get agreement on scientific standards for the bank. He says that multiple collection centres will help to overcome geographical logistics, shortening the time from death to collection, for example.

Thomas Insel, director of the NIMH, says that the NIH already supports 11 brain banks related to different neurological disorders, and would like to adopt “a rational overall strategy rather than simply adding another boutique brain bank to the list”. He says that the NIH has now agreed in principle, at least, to create a ‘neurobiobank’ that would include both adult and children’s brains. Although no firm plans have been released, the bank would probably have multiple collection points (the agency’s existing tissue banks would become ‘nodes’), but centralized oversight and tissue distribution. That is essentially what the advocacy groups want.

However the banks are organized, the agonizing task of approaching bereaved families will remain. Yet autism researcher Cynthia Schumann, who earlier this year became director of an effort by the MIND Institute to start a bank of its own, says that her first encounters with families who choose to donate were eye-opening. “I have been blown away by how parents have thanked us for helping them to handle grief.”

“I have been blown away by how parents have thanked us for helping them to handle grief.”

Alison Abbott is Nature’s senior European correspondent.


**Figuire 2.** The activity of genes linked to neural development changes most dramatically during prenatal development and infancy.

**Brain waves**

The activity of genes linked to neural development changes most dramatically during prenatal development and infancy. **SOURCE:** REF. 2