

## Biology

Julie Ann Miller reports from Anaheim, Calif., at the annual meeting of the Society for Neuroscience

### Fetuses watch the clock

Why do newborn babies doze and eat round-the-clock rather than sleep by night and eat by day as their parents would prefer? New findings seem to rule out one reason: The absence of a night-day cycle isn't for lack of an active timekeeping system in the infant's brain. William J. Schwartz of Harvard Medical School in Boston, Mass., reports evidence from animal studies indicating that the brain center that controls daily activity rhythms is in operation well before birth. This finding adds to a growing series of observations of extensive nervous system activity in utero (SN: 10/20/84, p. 247).

The timekeeping center of the brain is active in rat fetuses at least three days before birth, Schwartz finds. He has demonstrated this activity by moving a pregnant rat into constant darkness and then injecting radioactive 2-deoxyglucose, which labels active brain areas. If the injection occurs during the "day" period of the mother's accustomed light-dark cycle, then in both mother and fetuses the 2-deoxyglucose labels the timekeeping center, in the brain area called the suprachiasmatic nucleus. However, if the marker substance is injected at "night," the area is not labeled. Further experiments using blind dams have demonstrated that the fetuses somehow get their timekeeping information from their mother, rather than by sensing the light-dark cycle with their own eyes.

### Growth hormone active in brain

The big mice resulting from the transfer of a rat growth hormone gene into a fertilized mouse egg (SN: 12/18 & 25/82, p. 389) are posing an unexpected puzzle to biologists. In those mice the transferred gene is repeatedly active in an unusual location — nerve cells of the brain. The native growth hormone of a mouse, rat or human is expressed in only one organ, the anterior pituitary gland.

The composition of the transferred gene has given no clue to its surprising activity. "The brain does not normally express either of this gene's parents," says Ronald M. Evans of the Salk Institute in La Jolla, Calif. The gene that is actually inserted into fertilized mouse eggs is a hybrid, a rat growth hormone gene that has been fused to a regulatory segment that comes from a mouse gene called metallothionein. Normally, metallothionein expression is very low in the brain. And recent research demonstrates that even this low metallothionein activity in the brain occurs solely in one type of cell, called an astrocyte, and never in nerve cells.

Closer analysis of the brains of mice containing the hybrid mouse metallothionein/rat growth hormone genes revealed that growth hormone is produced by nerve cells only in a few very specific regions of the brain. This particular set of regions has no other recognized common characteristics.

The scientists at first thought the unusual pattern of expression might be due to the chromosome locations where the transplanted genes had taken up residence. These sites are thought to be randomly selected. However, analysis of eight additional animals, which were the products of separate gene transfers and thus are assumed to have the gene in different chromosomal locations, gave identical patterns of growth hormone production in the brain, Evans reports. In addition, mice receiving a hybrid gene of mouse metallothionein and human growth hormone also show the same distribution of growth hormone production in the brain.

Evans suggests that the gene for growth hormone may contain some as-yet-unidentified sequence of nucleotide subunits that signals hormone production in these specific brain areas. Such a sequence has been proposed for genes of natural brain components (SN: 10/1/83, p. 212). The studies, Evans says, "might reveal unique aspects of what is necessary to generate tissue specificity [of gene expression]."

## Behavior

### Autism: A step toward better treatment

Haloperidol, a powerful drug that is commonly used to treat schizophrenia, may also hold promise for autistic children. Lowell T. Anderson and colleagues of New York University Medical Center in New York City report that 40 autistic children given both haloperidol and placebo tablets showed a decrease in hyperactivity and repeated mechanical movements and received higher scores on a simple learning task while on the active drug. The children alternated from haloperidol to placebo treatment several times over a four-week period. They were observed by psychiatrists and nursery teachers who did not know which tablet was being administered.

"Optimal doses" of haloperidol were established for each child, say the researchers. At these levels, the drug enhanced learning and improved behavior without causing sedation or other undesirable effects. They explain that haloperidol may work by reducing excess levels of dopamine — a chemical messenger in the brain — that have been linked to autistic children with hyperactivity and other movement disorders. The drug could prove to be a valuable addition to language training with these youngsters, conclude the investigators in the October AMERICAN JOURNAL OF PSYCHIATRY.

### Teen suicide and 'masked' depression

Across the United States, state and local officials are beginning to organize suicide "awareness" programs to educate parents, teenagers and high school teachers about the suicide warning signs displayed by adolescents. A similar effort is being mounted by the National Institute of Mental Health (NIMH). This flurry of activity has been set in motion by some tragic statistics. Every day, 13 people between the ages of 15 and 24 kill themselves in the United States. The suicide rate among young adults in this age bracket has tripled in the past 30 years. Suicide is the third leading cause of death for this age group. Females are the most frequent suicide attempters, but the increase in completed suicides has occurred mainly among adolescent males, most noticeably in affluent suburbs. NIMH statistics, which provide a conservative estimate, show that 5,200 adolescents killed themselves last year.

There are no surefire signs of the potential for suicide among teenagers. A number of risk factors are known, such as displaying impulsive behavior, being the victim of child abuse, having decreased levels of serotonin, a chemical messenger in the brain, and having a family history of suicide.

But completed suicides are most strongly associated with psychiatric disorders, especially severe depression, says Susan Blumenthal, head of the NIMH suicide research unit. Unfortunately, teenage depression is often hard to recognize and may differ greatly from adult depression.

"Instead of feeling hopeless, helpless and empty, the teenager may mask his or her depression in boredom, listlessness, hyperactivity, risk taking or physical complaints," says Eva Deykin of the Harvard School of Public Health. Deykin is now attempting to determine conclusively whether adult depression significantly differs from adolescent depression; she also hopes to distinguish normal teenage turmoil from severe depression. Standard depression scales, with added items that may indicate teenage suicide risk, are being used to evaluate three groups: 480 normal college students, 50 adolescents hospitalized for psychological problems including depression and 40 adults hospitalized for depression. Depression measures will be compared in the hospitalized groups and contrasted with the normal group.

Whether or not significant differences turn up, public education programs on depression and other suicide risks encourage adults to get professional help for seriously troubled teenagers, says Deykin.