News
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******Technology developing for prevention of manic-depressive illness and Huntington's disease

DALLAS--For years Jack, age 36, suffered from stretches of stark depression going beyond sadness--void of emotional response. Then times of soaring euphoria blazed into money-making and matrimonial schemes and finally into talk of extraterrestrial beings.

Jack's family says he has an uncle with the same bizarre behavior.

Months of roaring mania ended when Jack held some reptiles at gunpoint. After his gun misfired, he waited patiently outside the herpetorium for police to carry him away. Peace at last! A few nights in jail, then doctors in a psychiatric hospital got his disease, manic-depressive illness, under control.

Scientific research has shown that Jack and others with manic-depressive illness have cell membrane abnormalities that are inherited. And new research approaches to identify these cellular defects are being tested at The University of Texas Health Science Center at Dallas. Already showing capabilities in differentiating manic-depressive patients from normal subjects, the technology offers the chance of detecting the illness long before symptoms reach the breaking point, indeed even before they begin. Two of the research tools are "fluorescence spectroscopy" and "nuclear magnetic resonance."

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Sara's ever-gesturing mouth barked as she tried to speak. Jerking and flailing, the limber 50-year-old walked on tiptoe as she pushed her wheelchair down the halls of the nursing home. Her mind was less than child-like. Parts of her brain were dying away from the disease she inherited from her mother, Huntington's disease.

Sara had a 50-50 chance of inheriting the abnormal Huntington's gene. Now the course of her illness is sure. Still in the "mild to moderate" phase, Huntington's will continue to deny her of a personality until it takes her life. There is no cure. There is no effective treatment.

Huntington's destructive symptoms usually don't surface until the person is between 30 and 50, often after the childbearing years and after the affliction has been tragically and unwittingly perpetuated.

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In Huntington's disease also, fluorescence and magnetic resonance are being used to identify the inherited abnormality. The cell membrane in those who have the gene is again abnormal. Further studies may prove these techniques useful in identifying Huntington's victims before symptoms occur, perhaps for "in utero" analysis to tell whether a fetus has inherited the disease.

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Developing methods for detecting these two neuro-psychiatric diseases is Dr. Jay Pettegrew in the UTHSCD Department of Neurology. Together with Drs. John Nichols, Nancy Minshew, John Rush and Malcolm Stewart, Pettegrew is announcing the findings on manic-depressive illness in the Journal of Affective Disorders. Results on this psychiatric disease evolved from three years of work on Huntington's.

Manic-depressive illness, affecting about one percent of the population, is the form of depression most often fatal. Suicide results in 15 percent of the cases. The prevalence of manic-depressive illness is about 100 times greater than that of Huntington's disease.

Since both diseases are genetic, cells outside the brain carry the abnormal gene. Therefore, easily accessible blood or skin cells are being used to study the presence of the brain disorders.

In blind studies using coded samples, Pettegrew has been able to distinguish cells containing the molecular defects relating to the two diseases. Of 40 persons tested in the manic-depressive illness study--with 20 patients known to have the disease and 20 normal subjects--the methods picked out the exact 20 who had previously been diagnosed as having manic-depressive illness. Likewise, with approximately 100 persons as test subjects for the Huntington's study, the methods determined the known Huntington's cases from the same number of normal control subjects.

Pettegrew made his identifications by monitoring the motion of molecules within the cell membranes. Abnormal movement showed the presence of a defect. Findings indicated that neither medication, severity of symptoms nor age had an effect on the membrane defects.

Pettegrew has also segregated an "at risk" group of 23 young adults for long-term Huntington's studies. If indeed his findings are linked to the defect, these people will begin to show symptoms in 10 to 20 years.

The unique aspect of Pettegrew's studies, allowing him success where others have failed, is that he is using intact living cells. Cells are analyzed less than an hour after being taken from the patient. By monitoring molecular motion in the living cells, an abnormality of molecular movement can be detected. For a cell to function normally, the dynamic qualities must be kept under control, by the body or artificially. In the studies,temperature and chemical environment are designed to avoid disturbing the molecular motion of the cells so that abnormal dynamic properties become evident.

In the fluorescence spectroscopy studies, fluorescent chemicals are applied to the cells and penetrate layers to certain depths. Polarized beams of light strike the membrane molecules and their emitted light allows measurement of excitation and emission energies and rotational rates of the molecules. Sensitive instruments monitor this movement and produce graphs of the dynamics on paper.

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Abnormalities in cells can also be detected by superconducting magnets. Placing a blood or tissue sample within a magnetic field, radio frequency energy can be applied to identify the kinds and amounts of molecules and their dynamic properties.

"With these two research techniques, it's possible to elegantly and accurately measure the dynamic properties of intact, living cellular membranes and the dynamic properties of their metabolism," explains Pettegrew.

Depression experts Drs. John Rush and Michael Schlesser collaborate with Pettegrew by providing carefully evaluated psychiatric patients, patients' family members and normal controls for study. Says Rush, "If we succeed in finding a molecular marker for this disease, psychiatry will be in a position for the first time ever to prevent an illness before it is clinically apparent. For example, in some children and adolescents who may have inherited this illness, we find dysfunctional behavior. The molecular marker may help us distinguish those whose behavior can be explained by manic-depressive disease from those who are troubled for other reasons."

Concerning Huntington's Pettegrew says, "It is not at all unreasonable that if we can understand the molecular defect we can use preventive measures and delay the brain degeneration indefinitely. This could allow people with the Huntington's gene the chance to live a long, normal life."

Part of the equipment used in Pettegrew's research was provided by the Southwestern Medical Foundation.

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