UNIVERSITY OF MIAMI
SCHOOL OF MEDICINE

# BRAINTrust

*Published to Promote Awareness of the UM Brain Endowment Bank*

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## Study of New Schizophrenia Drugs Seeks Participants

***Richard M. Steinbook, M.D.***
*Professor of Psychiatry,*
*UM School of Medicine*

The pharmaceutical industry has recently unearthed some very promising alternatives to Clozapine in treatment of schizophrenia. Dr. Richard Steinbook reported that the University of Miami will be studying two of the most interesting drugs that would provide the benefits of Clozapine, with hopefully, less risk. Two new neuroleptic medications are available to out-patients at no cost, on an FDA- approved trial basis in double-blind studies. In preliminary work, these medications appear to be effective and have fewer side effects than standard medications. If the medication works well for you, it will be continued for a year or more at no charge.

As this is a medication trial, you will continue your relationship with your own doctor for follow-up and counseling. You will also continue to get all additional psychosocial support services. The risk of side effects is to some extent unknown in this case, but appears to be minimal.

**Call the Study Coordinator, Jill Spera or Dr. Steinbook at 585-6335.**

To participate in the FDA approved double-blind study of two schizophrenic drugs, you must answer yes to the following questions:

1. Do you continue to have symptoms or side effects while taking your current medication, or wish to have better results?
2. Are you able to come to the Jackson Memorial/ University of Miami Medical Center or the Veteran's Administration Hospital weekly for 6-8 weeks and then monthly?
3. Will you agree to eye exams, chest x-ray, physical exams, blood tests and interviews provided by the program as required?
4. Are you willing to initially take one of these new medications or a standard medication until your response can be evaluated? (You will be provided the new medication, if you do not do well in double blind study.)
5. Are you able to understand and sign an informed consent form, which details the risks and benefits in detail?

**The Schizophrenia Interest Group meets monthly during the lunch hour. If interested, call 585-6335.**

# Brain Endowment Bank Holds Key To Research Advances

As scientists strive to unlock the mysteries surrounding disorders such as Alzheimer's and Parkinson's diseases, schizophrenia and depression, the critical need for a Brain Endowment Bank continues to rise.

At the University of Miami School of Medicine's Brain Bank, neurological tissues play an important role in understanding these devastating diseases/disorders that exact such a heavy toll on society.

Both normal elderly individuals and those with a history of neurological or neuropsychiatric disorders should consider a bequest to the Brain Bank. Post-mortum examination of the brain not only gives definitive answers as to whether an individual suffered from a disease, but it also provides data for comparative studies.

Our efforts to obtain brain donors for reserach studies involve a multicenter operation, including doctors, scientists and staff at the University of Miami School of Medicine, the National Parkinson Foundation and other pathologists throughout Florida. The Brain Bank staff are on-call 24 hours a day to perform this service.

Like the donation of other organs, a brain bequest does not interfere with a family's plans for funeral, burial or cremation, and absolutely no additional costs are incurred by the family.

***Deborah C. Mash, Ph.D.***
*Associate Professor of Neurology and Pharmacology, UM School of Medicine*

An individual or family should make a brain bequest well in advance. This allows the endowment to proceed with dignity and discretion, not interfering with the grieving associated with a loved one's death.

Your endowment could be a final gift, responsible for preventing the suffering of hundreds of thousands of people with neurodegenerative and neuropsychiatric disorders.

Help us as we strive to find the causes and ultimately the cure for these debilitating disorders. **Please call 1-800-UM BRAIN.**

156604

UM Brain Endowment Bank
Department of Neurology (D4-5)
P.O. Box 016960
Miami, FL 33101

# Aging and Cognition

**M.C. Brown, Pys.D.**
*Assistant Professor Neurology, Division of Neuropsychology*
*UM School of Medicine*

Discussions of aging often overlook the obvious: The aged are as varied as any other group, and perhaps even more. Some people change a lot with age, some change a little. If all we know about a person is his or her age, we cannot make meaningful predictions about cognitive abilities. Therefore, findings from research on cognitive changes with age should not be regarded as predictions of what will happen later in life to any one individual.

Age related changes in memory function have been studied extensively. Research suggests that some aspects of memory function decline with age and some do not. One of the questions asked of memory changes in aging is whether memory decline is due to problems with storage or retrieval.

When new information is acquired, it is placed in storage, to be retrieved when needed. If a person knows something, but cannot recall it, the difficulty is in retrieval only. A retrieval deficit can be evaluated by assessing whether the individual is able to recognize information which could not be recalled spontanously. For example, someone may not be able to answer the question, "Who was president during the Watergate period?," but can respond correctly when asked, "Was it Kennedy, Nixon or Johnson?"

In this case we can say that the information was present in storage, but was not accessible due to retrieval difficulties. Studies which compared recall and recognition suggest that, while recall memory tends to decline with age, recognition memory does not, or declines much less. This observation lead researchers to conclude that storage mechanism remain intact with aging, but retrieval mechanism do not.

Learning and memory are hard to differentiate. Learning has to do with getting information in, and memory deals with keeping the information retained for future retrieval and use. The traditional procedure for studying learning and memory involves presenting information (for example, a list of words, a story, a drawing) and asking the person to recall the same information after an interval time. These studies have shown that the elderly, as a group, do less well than younger people. The disadvantage of age is evident especially when the information that has to be learned is presented at a fast rate and the time to respond is limited. It is apparent from the study that the time alloted to learn new information is equally as important as the information itself. Therefore, presenting information at a slow rate, and having ample time to respond are especially desirable for older people and may enhance memory.

A broad range of possibilities exist as to how an individual's cognitive abilities may change over time. Just as each individual is unique in their physical attributes, cognitive skills should also be examined with an emphasis on the individual, rather than the group. Factors which must be considered include environmental conditions, level of education, and current state of health. All have an impact on cognitive function. As a result, what may be considered "normal" for one person, may be an underestimate of the cognitive potential of an individual that same age.

# Important New Find Research Reported

A team of investigators (Drs. Allen Roses, Warren Strittmatter, Donald Schmechel, Ann Saunders, Margaret Pericak-Vance) of the Joseph and Kathleen Bryan Alzheimer's Disease Research Center at Duke University Medical Center report that the B-amyloid (beta amyloid) protein may be deposited in the brain by normal cholesterol-carrying protein, apolipoprotein E or apoE. Beta amyloid, a main component of senile plaques in the Alzheimer's brain, is found in its soluble form in the blood and spinal fluid of healthy individuals. Individuals who develop Alzheimer's disease in late life have an increased rate of inheritance of one of the three common genetic forms of apoE. ApoE4, the form associated with late-onset Alzheimer's disease, binds more quickly with amyloid. This interaction with amyloid is separate from its normal role of carrying cholesterol, and may be related to the disease process. Intense study is now directed at the interaction of the apoE protein isoforms with amyloid and other proteins found in the nervous system.

## Leading Scientists Predict Advances in Alzheimer's Research

New York, NY, June 10, 1993 -- Close on the heels of their stunning discoveries -- dubbed by some science writers as the October and January surprises -- Drs. Dennis Selkoe and Allen Roses today predicted new directions and treatments for Alzheimer's at a briefing organized by the Dana Alliance for Brain Initiatives.

Dennis Selkoe, M.D. Professor of Neu-

## In Memory

***Their spirits live on through Brain Research.***

Arnold Andresen
Elwyn Archibald
Eugenio Batista
Richard Butler
Joseph Cadegan
Samuel Carroll
Betty Colchamiro
Charles Durrance
Leonard Eldridge
Agnus Engebretson
Kenneth Felton
Mildred Ford
Raphael Guanci
Seymour Horowitz
Anne Hughes
Raymond Lamas
Mable Land
Cecil Porter
Geraldine Press
Ronald Prickett
Socorro Rojas
Warren Slater
Robert Smith
Mary Thomas
William Van Houten
Dora Wirth
Emil Yde

# ings in Alzheimer's

*(Excerpted from the Caregiver, Summer 1993, Duke University Family Support Program)*

rology and Neuroscience at Harvard Medical School, recently established that Alzheimer's may be caused by abnormally high concentrations of beta amyloid, a protein that occurs naturally in cells throughout the body.

"We now know that excess amyloid build-up is common in 100 percent of all Alzheimer's cases, even those that are not genetic," says Dr. Selkoe. "That puts us within reach of designing treatments to block the earliest stages of the disease years or even decades before a patient's first memory failure -- much as cholesterol-lowering drugs can be used to stem heart attacks."

Allen D. Roses, M.D., Chief of Neurology and Professor of Neurobiology at Duke University Medical Center, thinks an explanation of the beta-amyloid build-up may be in his recent discovery that apolipoprotein E4 (APOE4), a gene on chromosome 19, is a cause of late-onset Alzheimer's. Prior to this discovery, researchers had identified two sites of early-onset Alzheimer's -- on chromosomes 14 and 21 -- and Roses' lab identified chromosomes 19 for late-onset cases, which affect 95 percent of all Alzheimer's patients.

"Five years ago, it was not accepted by most laboratories that late-onset Alzheimer's was genetic," says Dr. Roses. "We can now estimate the risk of people to get the late-onset disease and the average age of onset based on their APOE4 inheritance. We believe that the amyloid deposition is a by-product and not involved in causing the disease."

These two divergent views, which have important ramifications for the direction and funding of Alzheimer's research, were propounded by Drs. Selkoe and Roses at a discussion, "Closing In On Alzheimer's: A Progress Report From the Lab." at the New York Academy of Science.

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**UM BRAIN ENDOWMENT BANK**

University of Miami School of Medicine
Post Office box 016960 Miami, Fl 33101
1-800 UM BRAIN
Deborah C. Mash, Ph.D.
*Director of Research*
Trudy L. Skoke, B.A.
*Program Coordinator*

# New Experimental Agents in the Treatment of Parkinson's Disease

***Dr. William Weiner, Professor of Neurology, Director of the Movement Disorder Center, UM School of Medicine***

Although many powerful and useful drug treatments are available for Parkinson's disease, there is still much work that needs to be done in perfecting the treatment of this disorder. The drugs that are now available are very useful for controlling the symptoms of Parkinson's disease and work extremely well for many patients for years on end.

Unfortunately, often there comes a time in the drug therapy of Parkinson's disease when additional drugs are needed to control some of the symptoms which develop. Some of the troubling symptoms that develop in the course of Parkinson's Diseaseinclude the development of motor fluctuations, dyskinesias and the seeming loss of effect of the drugs on the basic symptoms of Parkinsons's disease. The motor fluctuations that patients often experience during the day include being "on" (near normal) or being "off" (very Parkinsonian). Many patients observe that after several years of therapy, the medication seems to only last from 2.5 - 3.5 hours. They then begin to develop increasing symptoms of Parkinson's until they take their next dose of medication.

Another problem that develops in the course of therapy is the development of dyskinesias. Dyskinesias are unusual involuntary movements that appear as restlessness or fidgetiness. Many patients also report that after years of therapy, the drugs that they are taking no longer seem to give them the same results achieved earlier. Whether this is because the drug is losing effect or because the disease has progressed is somewhat unclear at this time. In any event, these are some of the reasons that the members of the Parkinson's Disease Research Group and the Movement Disorders Center at the University of Miami continue to participate in the clinical testing of new agents to treat Parkinson's disease.

We are currently testing two new drugs in different situations, tolcapone and pramipexole.

Tolcapone is an exciting drug representing an entirely new approach to altering the affected biochemistry that exists in the brain of a Parkinson patient. We are currently enrolling patients in this study who are taking Sinemet but who are experiencing motor fluctuations, on-off or wearing off during the day. This study is for patients with moderate to advanced Parkinson's disease who are experiencing these specific problems.

The second new drug, pramipexole, is a unique dopamine receptor agonist. We have conducted previous tests with this agent and have been favorably impressed in its ability to help patients with moderate to advanced Parkinson's disease. We are currently enrolling patients in two types of experimental trials. The first is related to patients with moderate to advanced Parkinson's disease who, despite therapy, are having difficulty with their motor symptoms. This trial is termed the pramipexole trial in moderate to advanced Parkinson's disease.

The second way in which we are using pramipexole is in very early Parkinson patients who are just beginning to require treatment. These patients have been diagnosed with Parkinson's disease and may have slight tremor or a little bit of slowness and would have just begun to notice that these symptoms are beginning to bother them or disrupt their lives. We are enrolling patients who meet these criteria in the early trial of pramipexole in early Parkinson's disease.

If you feel that you meet these criteria and would like to participate in this study, please call **Carol Sheldon or Melodye Ololade at (305) 547-6200.**

# Clues From International Research On Schizophrenia

*Harriet P. Lefley, Ph.D. Professor of Psychiatry, University of Miami School of Medicne*

A great deal of research in recent years confirms the biological nature of schizophrenia. Studies in Scandinavian countries of adopted children who later develop schizophrenia show much higher incidence of schizophrenic-like disorders in their biological relatives than in their adoptive families. Adopted away children of schizophrenic mothers have much higher risk of developing the disorder than do other adoptees. Twin studies show that identical twins, who share the same genes, are much more likely to be concordant (if one is schizophrenic, the other is too), than are fraternal twins or siblings. Even identical twins, however, are not entirely concordant. Recent studies have indicated that when one identical twin is schizophrenic and the other is not, their fingerprint dermal ridges are different. Dermal ridges are formed during the second prenatal trimester when there is massive migration of neural cells to the cortex.

Intrauterine stressors during the second trimester seem to be especially important in reinforcing genetic vulnerability to schizophrenia. In 1957, a virulent Type A influenza epidemic spread through European countries. Studies in Helsinki and London showed that during the height of the epidemic, when women in the second trimester of pregnancy were exposed to the virus, their offspring were significantly more likely to develop schizophrenia than individuals born any other time that year or duirng the same time period in other years. A twenty-year analysis of mental hospital admissions in England and Wales showed a similar correlation between schizophrenia and second trimester prenatal exposure to influenza epidemics between 1939 and 1960. Scientists think the second trimester is a particularly vulnerable time because critical cortical brain structure develop during that period.

There is also evidence, however, that social and cultural factors can affect the course of schizophrenia. Collaborative studies conducted by the World Health Organization in many countries established that clinicians in all cultures could agree on universal symptoms of schizophrenia. However, follow-up studies showed a much better prognosis in the developing countries than in the industrialized west. Explanations were that in more traditional cultures people were expected to recover rapidly from acute episodes of psychosis and neither patients nor families were held responsible for mental illness. More opportunities were available to patients for normal work roles in agrarian village economies. Extended family systems were able to difffuse the burden of caregiving and families were likely to be more tolerant and less critical of difficult behavior. Overall, researchers feel that low-stress supportive environments, normalized work roles geared to an individual's level of functioning and respect and acceptance from others are therapeutic for people with schizophrenia.

## A Tribute to Elwyn Archibald

Elwyn Archibald, an energetic advocate of the Brain Bank and strong believer in the necessity of brain tissue endowment, recently passed away. A South Florida resident since 1983, Mr. Archibald first became interested in the work of the Brain Bank in 1989, providing a testimonial for a television program about the importance of brain research. Mr. Archibald and his wife, Ruth, then actively discussed the Brain Bank with friends and neighbors, resulting in 50 new donors.

Mr. Archibald was a metallurgical engineer and retired executive of Columbia Steel in California. He also worked in municipal government, serving as a county planning director. He and Ruth traveled extensively before moving to Florida.

Elwyn Archibald was a people person who gave service wherever and whenever he felt that it was needed. He lived by the principle that "God blesses and multiplies all that I am, all that I have, all that I give and all that I receive... and all is well!" We miss him very much and know that he is serving with the angels now.

*-Trudy Skoke, Program Coordinator*

**• A LIVING MEMORIAL/HONOR •**

***No one can take your place in supporting the critical research efforts of the UM Brain Endowment Bank. Help us ensure great advances during the "Decade of the Brain, 1990 - 2000"***

GIVEN BY: ___Ms.__Mr. __Mrs. __Dr. _____

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Please make checks payable to **Brain Research Fund.** Mail check and coupon to: University of Miami School of Medicine, Department of Neurology (D4-5), P.O. Box 016960, Miami, FL 33101. Attn: Ms. Trudy Skoke. Thank you for your support.