

Front Cover

The cover represents approaches utilized in conducting research on various mental health problems in the North Carolina Department of Mental Health. The upper left portion of the drawing depicts the facial expression of a depressed elderly patient; on the top right are nerve cells and the spinal cord whose malfunction appears causally related to mental disease. The arrows below pointing toward various circles indicate interaction between organizational components; the formula permits measurement of program success. In the bottom segment of the drawing the mouse inside the male and female symbols represents studies on reproductive behavior. On the lower left in the geometric pattern of the spider web, the builder's behavior is made measurable, and a chick embryo on the lower right stands for one time of life at which abnormal development can lead to behavioral disabilities after birth. (The drawing was made by Sandy Huttaker of Raleigh, N. C.).

I. ITS TASKS AND ORGANIZATIONAL STRUCTURE

Q. What is research?

A. Research can be conceived as the continuous endeavor of the human mind to ask the how and why of events around and within us, and it can be regarded as an exploratory mechanism which forms an integral part of human progress. Most frequently, scientific methods are used by trained researchers in seeking answers to these questions.

Q. What is mental health research?

A. Studies which are specifically concerned with an analysis of the causes of normal as well as abnormal behavior, and possible cures of abnormal behavior, comprise the field of mental health research. It also involves investigation of the management of mental health in the social and political setting and helps clarify thinking about the nature of mental health. In contrast to treatment of patients, research provides the long-range, preventive approach to problems in mental illness.

Q. What is the Division of Research in the North Carolina Department of Mental Health?

A. It is a sub-unit of the North Carolina Department of Mental Health consisting of a group of qualified research scientists who, in various mental health programs all over the state, investigate mental health problems and advise on methodology and recent progress in the field. An additional responsibility is to help improve services by carrying out their research functions as close to the services as possible, instilling a scientific approach into patient management and other practical problems.

Q. Briefly, what are the functions of the Division of Research in the North Carolina Department of Mental Health?

A. The basic function of the Division of Research is to contribute to the acquisition of new knowledge and to aid in the dissemination of current research findings. Because it is an integral part of the Department of Mental Health, the Division of Research can aid in the rapid identification of both administrative and clinical problems and thus contribute to their solution either by providing information or by conducting the necessary studies. These functions both improve the quality and efficiency of services and, furthermore, assist in the training and recruiting of high quality personnel.

Q. Is research in the Department of Mental Health in danger of duplicating efforts elsewhere in the state, particularly those of the universities?

A. The subject matter of mental health research is so extensive and inexhaustible that this constitutes no limitations. In addition, the research in the Department of Mental Health is related to its service functions, while university research is geographically and in subject matter closely linked to the universities' teaching functions. Mental Health Department personnel and young scientists work for periods of several months to a few years in mental health research to gain an in-service training experience.

- Q. What is the relationship between research conducted by the North Carolina Department of Mental Health and other research being carried out across the state and nation?
- A. Research scientists in the Department of Mental Health have one or more university appointments, and lecture at various universities in the state. At the national level, the scientists check their procedures and results with those of their peers at both national and international meetings and in specialty journals.

Q. How does the Division of Research influence the services provided by the Department of Mental Health?

A. The activities of the Division of Research yield both immediate and long-range benefits to the department. This atmosphere helps to attract high quality personnel and, by emphasizing a scientific approach to problemsolving rather than being oriented to specific subjects, the division stimulates an investigative approach to the many problems which the department must solve. The basic and clinical research conducted in the division is largely directed toward uncovering the roots and improving treatment of mental diseases and thereby contributes to the world-wide effort to prevent and treat mental illness.

Q. Is it possible to assess whether funding of research in a state agency is a good investment for the taxpayer?

A. Industry, which has to account in terms of immediate and long-term profits, has found that investment in research is of prime importance for the success of an enterprise. It can be safely assumed that state government, though in many aspects different from industry, profits as much from diverting some funds into research. Specifically, with costs rapidly rising in our hospitals, all possible efforts should be made to uncover preventive measures and to expedite the release of patients. The conversion of patients into productive citizens is advantageous to both the patients and to the state.

Q. Is all research in the North Carolina Department of Mental Health financed with state funds?

A. No. In addition to state funds, individual research scientists and institutions receive federal and private support, usually on a matching basis. All such support is administered by the North Carolina Foundation for Mental Health Research, Inc., a nonprofit, independent organization.

Q. How are federal funds for research obtained?

A. An investigator applies for funds for a specific project to be conducted within a limited amount of time. The aim of the research has to be significant and the investigator must demonstrate that he is qualified to carry out the work. The proposal is evaluated by scientific advisory panels, and based on their recommendation and other factors, an award is made. Each application to federal agencies competes for funds on a national basis.

Q. What is the function of the North Carolina Foundation for Mental Health Research, Inc.?

A. It is charged with the specific task of administering funds which are received from non-state sources, and of raising funds of its own for support for mental health research needs in the state.

Q. What is the administrative structure of the North Carolina Foundation?

A. It is governed by a board of directors, a group of 15 to 30 distinguished and interested citizens in the state, and administered by an executive committee consisting of the executive director, executive secretary, the chairman of the board, the president, and the vice president. None of these persons can receive payment for his services. The Foundation's offices are located on the campus of Dorothea Dix Hospital in Anderson Hall. The address is P. O. Box 7532, Raleigh, N. C. 27611.

Q. How can a donation for support of mental health research in North Carolina be made?

A. Anyone can designate or bequeath a sum of money or other property as a tax deductible gift for general or specific use in mental health projects in North Carolina. The foundation will see to it that the gift is used for its designated purpose and will, upon request, provide reports of its activities to the donor.

Q. Does the North Carolina Foundation restrict its support to research in the Department of Mental Health?

A. At present, the foundation mainly administers grant funds for research in the Department of Mental Health; it has only limited funds of its own for dispersal. It is, however, incorporated in such a way that it could handle any funds for mental health research in the state.

Q. How many research scientists are fully employed by the North Carolina Department of Mental Health at the present time?

- A. As of January 1, 1973, there are six: one psychiatrist, one pharmacologist, two psychologists, one zoologist and one biochemist. Their special areas of research are described under Section II.
- Q. Is additional research carried out, for example, on a part-time basis in hospitals and centers throughout the state?
- A. In more than half of the institutions of the Department of Mental Health some organized research is going on. This is frequently carried out in spare time and with little or no financial support from the state.

Q. Have any beneficial effects to mental health services been produced by such a program?

A. Small contracts have been used as seed money for the initiation of larger, federally funded research projects. The results of the investigations are reported in research papers and have found wide interest and application in mental health programs; i.e., the value of alternate treatment methods and social problems connected with community mental health services has been clarified.

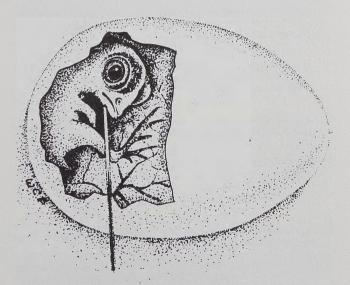
Q. Who will protect the interests of patients and institutions participating in research programs?

- A. Research committees have been formed all over North Carolina which screen protocols and monitor procedures for patients' and institutions' interests and their constitutional rights; they see to it that there is proper attainment of consent, and minimum danger in any mental health research project.
- Q. How do research scientists from different units in the state mental health system know each other, coordinate their efforts, and profit from central research facilities?
- A. A meeting of research scientists and mental health administrators has been held every year in North Carolina since 1968. Important mental health concerns like "child development" and "evaluation" have formed a central theme of such meetings. Every year a list of research publications and completed projects is distributed to all mental health units. In addition, a weekly seminar, dealing with wide-ranging problems in the areas of behavior, the nervous system and mental health, is held in the offices of the Research Division. Both local national and international speakers are featured at these weekly meetings. Research scientists are invited as speakers to various mental health programs all over the state and nation.

II. EXAMPLES OF CURRENT RESEARCH PROJECTS

Studies in Developmental Neurobiology

Psychology, biology and those other scientific disciplines which study the behavior of man and animals have, in the past, tended to neglect the period of time prior to birth. This neglect has subsequently led to a de-emphasis, or outright ignoring, of the possible important role this early



A chick embryo 10 days old (hatching occurs on the 20th day) is being stimulated with a probe to determine the extent to which the reflex connections in the nervous system have matured. A "window" has been made over the embryo by removing the eggshell. period may play in determining the capacities and capabilities of the adult organism. Over the past several years, however, there has been a noticeable trend on the part of scientists from all over the world — including those in the Research Division — to devote more of their efforts to understanding embryonic or prenatal behavioral and neural development.

The neuroembryology laboratory takes an anatomical and physiological approach to prenatal functional development, although behavior, per se, also receives equal attention. In short, an attempt is made to utilize the technology and knowledge of several scientific disciplines in order to better understand the challenging problem of how the normal functional and anatomical organization of the nervous system arises during ontogeny.

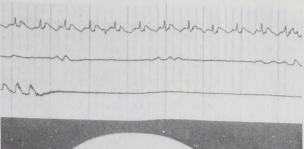
Currently in the neuroembryology laboratory, research scientists, research associates, postdoctoral and predoctoral students and research assistants are involved in several separate projects. These include: (1) the use of various pharmacological tools (e.g. neurotransmittors and their antagonists, neuromuscular blocking agents, and agents which *selectively* destroy parts of the developing nervous system) in order to better understand the role of various specific neural elements in behavior development; (2) an experimental examination of the neural and hormonal basis of coordinated motor behavior (i.e. hatching) in bird embryos; (3) the examination of early behavioral development in a primitive vertebrate such as a fish; (4) the detailed study of synapse formation with the electron microscope; the relationship between synapse formation and behavior development; and (5) the transplantation and extirpation of specific neural elements in bird embryos and the study of concomitant behavioral development in such preparations.

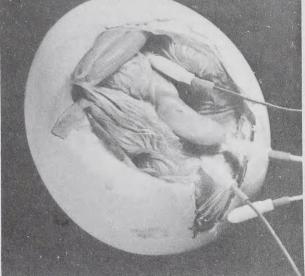
Through the joint efforts of the research scientists in the psychology and neuroembryology laboratories, preliminary attempts are being made to use a marsupial, such as the opossum, for studies in early behavioral and nervous system development. A marsupial was chosen because of the immature state of development of the young at birth, and because, being a mammal, information derived from a marsupial form will allow us to determine the extent to which the findings on bird embryos, discussed above, can be generalized to higher forms.

Prenatal Behavior

Many scientists now believe that both normal and abnormal behavior may be partly a consequence of events which occurred prior to birth (prenatal influences). Experiments conducted in the Research Division's psychology laboratory are aimed at unraveling some of the mysteries associated with the development' of behavior prior to birth, especially how prenatal sensory stimulation relates to normal and abnormal behavior after birth. By making windows in the shell of bird eggs, the behavior of the embryo can be observed and its reactions to stimuli measured. Since the early development of all vertebrate embryos follows essentially the same course with respect to the maturation of the brain, muscles, and sense organs, the results of experiments with bird embryos can reveal some general principles which apply to the behavioral development of both higher (mammals) and lower animal forms.

The advantage of working with bird embryos is that they can be directly observed without harmfully distorting their usual prenatal environment. Though a lot of research has been conducted on mammalian embryos, the embryos have been studied under adverse conditions and the results of such





For studies of the development of the nervous system and behavior, duck embryos are fitted with recording electrodes. The line at top shows the embryonic heartheat, the second line indicates occurrence of oral activity, and the third line depicts embryonic vocalizations.

experiments are almost always open to the question of whether the reactions observed are normal or typical ones.

In order to study how sensory stimuli affect the embryo's normal development, it was first necessary to determine when each sensory system becomes functional. This part of the research was done at the division's psychology laboratory, as well as other laboratories around the world. People are usually surprised to learn that all of the sensory systems (1) become functional prior to birth or hatching and (2) that they do not all become functional at one time.

The first sensory system to become functional in the course of embryonic development is touch or skin sensitivity. The embryo reacts when its own body surfaces come into contact (self-stimulation) or when it touches surrounding membranes and tissues. The next sensory system to mature is balance or gravitational sensitivity. The embryo's balance receptors are stimulated when the egg is turned or, in mammals, when the mother changes her position or posture. The third system to develop prior to birth or hatching is that of hearing. Mammals are exposed to internal noises as well as loud sounds which may be transmitted through the maternal abdomen. Bird embryos can even respond to low sounds coming from outside the egg, particularly the calls of their parent or other embryos. (Duck embryos begin vocalizing 4 days before hatching). Vision is probably the last sensory system to develop. Surprisingly, the bird embryo is capable of reacting to light even before hatching. It is not yet definitely known when taste and smell develop in the embryo; taste probably develops after hearing and before vision. As far as we know, the above sequence of sensory development holds for all vertebrate embryos including man.

Recently, the psychology laboratory staff has been incubating eggs in individual soundproof chambers to determine if isolation from sound affects the development of hearing. The question is whether the auditory system requires a certain amount of external stimulation to develop normally or whether internal stimulation from sounds in the egg is sufficient for the normal development of auditory perception. Preliminary results indicate that depriving the embryo of full exposure to the normal range of sounds from outside the egg slows down the development of the embryo's usual auditory perceptual ability so that its auditory perception is retarded at hatching, though the bird otherwise appears normal. If these results are validated, the next question is whether subsequent growth and experience after hatching can remedy the deficiency or whether it is irreversible.

Since the above auditory response involves the hatchling's behavior toward the call of its parent, it is a very important part of the hatchling's behavioral repertoire, one that occurs with such regularity under usual conditions that it is sometimes called "innate" or "instinctive." Since many people believe that innate behavior arises directly from genetic inheritance without the benefit of sensory stimulation or other prenatal experiences, the results of the present experimental program (if they are verified) will call for a modification in the way that we look at the process of behavioral development in both higher and lower animals.

Reproductive Behavior

The general goal of research in this laboratory is to identify the critical attributes of the environment responsible for behavioral changes and to unravel the physiological pathways lying between a change in the environment and a change in behavior. This research is aimed at identifying the proper types of environment necessary for healthy physical and psychological development. Although the environmental component in mental illness has long been recognized in a general sense, we must now become more specific and only through experimentation will we discover where the true cause and effect relationships lie between environment and mental disease.

To make broad goals such as the above obtainable, one relationship between environment and behavior was chosen for investigation—that between social stimulation and sexual behavior. To effect changes in sexual behavior we must alter the levels of hormones within the body, and these levels are controlled by centers in the brain. Such brain centers are affected by social stimulation and thus we have come full circle: social stimulation — changes in the brain — changes in hormone levels — changes in sexual behavior — and again to a change in social stimulation. Now that we know that such a marvelously balanced system exists, we must determine what types and amounts of social stimulation are necessary for the optimal development and expression of sexual behavior.

Using mice, hamsters and monkeys, experiments are being conducted to explore these relationships. For example, recent research on mice has shown that sexual maturation can be remarkably accelerated by specific male stimuli. This finding indicates that sexual maturation, formerly thought to be largely the result of heredity, is susceptible to influences from the social environment. In the past one hundred years, the sexual maturation of western man has been accelerating at a rapid rate; girls have been maturing about three months earlier in each of the last ten decades. The similarity in the process of sexual maturation in the mouse and in man permits us to use the mouse as a model system in an attempt to explain the accelerating rate of sexual maturation in humans. We must understand the physiological basis of puberty as well as the environmental factors that influence it because of the overwhelming social significance of early puberty. The period that today's youngsters have to cope with the flush of hormones and other metabolic changes that accompany puberty is much longer than that with which we, our parents, or our grandparents had to contend.

In addition to the work on puberty, two other studies are in progress to provide information in the relationship between the environment, hormones and behavior. In one of these, the role of sexually active females in stimulating increases in male hormone output and sexual activity is under examination. For this study, monkeys in a Puerto Rican colony are utilized. The results to date indicate that sexually active females can induce a remarkable increase in male hormone output and return a sexually inactive male to full capabilities.

The second area of investigation involves a series of studies to determine the role of neonatal imbalances in hormones on the expression of behavior during adulthood. Previous work has shown that exposing fetal or newborn female rodents to testosterone, the male sex hormone, induces permanent changes in adult sexual orientation. Such changes may result in reversed sex roles or a condition of bisexuality. These remarkable findings have forced a reexamination of the bases for sexuality. As a part of this reexamination we are exploring the role of neonatal hormones on the development of the ovary, its cyclicity and its effects on the behavior of females after they attain adulthood.

Biochemical Research

Current thinking views mental illness as a disease resulting from faulty adaptation to overwhelming psychological factors which, in turn, lead to disturbances in the metabolic balance of the body. Such disturbed body metabolism could play a key role in the development of mental disease.

Efforts of many scientists are directed towards identifying the particular substance or substances whose altered metabolism may be associated with development of mental disease. The biochemical laboratory of the Research Division has been conducting studies on the metabolism of calcium in depressed patients. The findings so far have indicated that the recovery from depression in patients treated with the antidepressant drug, imipramine, or electric convulsive therapy was associated with significant decrease in the concentration of calcium in the serum and in the amount of calcium excreted in the urine. This suggests a possible relationship between relatively high serum calcium concentration and depressive illness.

It is possible that the high serum calcium will affect the calcium metabolism in the brain. To explore this problem, the distribution of calcium in the brain of experimental animals is under investigation. The brain is secured from the skull, then homogenized in isotonic sucrose solution. The homogenized brain is subjected to high speed ultra centrifugation for resolving its subjected to high speed ultra nuclei, mitochondria, microsomes, synaptosomes and supernatant. It is hoped that these experiments will delineate the subcellular structure or structures which are operative in regulating calcium ion concentration in the cell. It is also possible that the metabolic function of these cellular ultra-structures may be affected due to excessive absorption of calcium.

Further work on the effect of psychoactive drugs, such as L.S.D., chlorpromazine, imipramine and amphetamine, on brain calcium distribution is planned for future research.

Another area of interest is the development of a test for the detection of micro amounts of the hallucogenic compound, L.S.D. Such a test will be helpful in identifying patients consuming the drug, and allows for effective treatment. Furthermore, blood samples of acute schizophrenics could be tested for the presence of L.S.D. This will test the notion that indogenous L.S.D. may be produced by these psychotic patients.

Studies in Depression

It has been said that the history of depression is the history of psychiatry. In the past three decades marked advances have been made in the symptomatic treatment of depression.

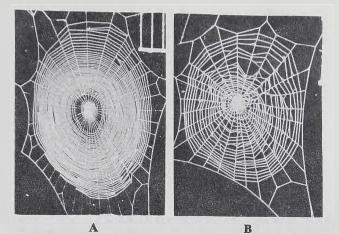
Despite these advances, several problems remain regarding the understanding and management of depressive illness: (a) delayed response to antidepressant medications exposes the patient to the physical and psychological complications of depression over a prolonged period of time; and (b) knowledge of the etiology and pathogenesis of depression is still obscured.

Our studies have been directed at (a) elucidating etiologic factors; (b) defining chemical pathogenesis of depression; and (c) studying the interaction of hormone substances with antidepressant medications.

On the Clinical Research Unit at Dorothea Dix Hospital, a cooperative program sponsored by UNC-Chapel Hill, the Research Division, and Dorothea Dix Hospital is underway. It has been determined by staff on the unit that profound interaction occurs between the tricyclic antidepressants and various hormones, namely, tri-iodothyronine, thyroid stimulating hormones, and ethinyl estradiol. By and large, these substances accelerate the speed of recovery from depression. Our interest at the present time is studying the antidepres-



Medical team on Clinical Research Unit tests reaction of patients to drugs.



The adult female cross-spider (Araneus diadematus Clerk) had built web A on the morning of the first day of observation, called "control web." That same day the spider drank 0.7 micro l of 1: 1000 d-amphetamine ("speed") dissolved in sugar water at 4:00 p.m. The next morning this spider built the web shown in B, which is characteristically smaller (see scale upper right corner) and less regular than the control. One day later the spider had recovered and built a web indistinguishable from the "control web."

sant effects of thyrotropin releasing hormone, a tripeptide substance secreted by the hypothalamus in the brain.

Our investigations of the etiology and pathogenesis of depression are directed at (a) defining possible genetic mechanisms involved in the transmission of depressive illness; (b) linking predisposition to depression with various anthromorphic characteristics; and (c) defining changes in various chemical systems during an acute depressive episode.

The Effects of Drugs on Motor Behavior

It is difficult to assess what goes on in another's mind, and there are several ways, all indirect, in which we try to do this. One of the purposes of such assessment is the wish to separate normal functioning from abnormal. This laboratory has approached the problem through a study of motor behavior under the assumption that many aspects of the functioning of the mind like fatigue, excitement, reaction to stress, and variation in mood find expression in subtle changes of fine movements of the hands and face.

The copying of a complex geometric pattern shows a great number of variations from person to person, from day to day, and from mood to mood. Placement of the lines in terms of exactitude, distance and shape can be measured and yield an enormous amount of data. The measurements are fed into a computer, and it prints out information about each drawing pattern in a few minutes, and compares one pattern with other patterns, drawn by other people and at other times. In this way, the effect of drugs, as well as stress, has been objectively assessed. In the future it is hoped that the evaluation of drawing patterns will make it possible to follow the ups and downs of mental patients under various treatment; in that manner we can evaluate the various influences of therapeutic procedures and weigh them against each other.

Because only a limited amount of investigations can be done with patients and because many behavioral functions are similar in animal and man, animals are used as models for the study of some aspects of human motor behavior. The elaborate and complex structure of the orb web of the spider Araneus diadematus Cl., as it is built in 20-30 minutes every 24 hours, has been found relatively easy to measure as well as sensitive to drugs and nervous system disturbances.

The method is simple; about a hundred spiders are kept in individual aluminum frames in the laboratory. They each build a web in the early morning hours, every animal in its frame. The web is lighted indirectly and subjected to contrast photography thus providing a permanent record for study. The effects of different drugs have been compared by evaluating web patterns which had been constructed after substances had been fed to the spider.

We have looked for possible permanent damage after repeated administration of hallucinatory drugs like marihuana. Efforts have been made, so far without success, to identify hypothetical disease-causing substances in the body fluid of mental patients by comparing spider webs built after the animal had received a patient's blood extract with those built after the animal had received the blood extract of a normal control subject. The disadvantage of using an animal so remote from man as the spider is partly outweighed by the advantage of being able to employ as many as 100 animals at a time and obtaining measurable results a few hours later.

Another concern of this laboratory has been the distribution of information on drug effects, particularly drugs of abuse, to university students and community drug training programs.

Sociological Research

The statewide organization of mental health programs and services is a complex everchanging network which seeks to administer effectively all available resources to meet mental health needs of North Carolinians. Successful administration of this mental health system requires sound management techniques, accurate and reliable information about the needs of the population, the extent to which programs and services meet these needs, and information concerning alternative methods of meeting these needs.

Several current projects employ scientific principles, methods and theories to identify, measure and understand factors which contribute to the effectiveness of mental health systems, to contribute to the understanding of organizational and behavioral changes, and to determine the relative merit of new and existing mental health programs and services. These include projects to develop measures of population change and manpower needs with special emphasis on particular sub-populations such as youth and aging minorities; develop and test computerized goals for inpatient care and treatment outcomes; refine and implement rating scales and goals for outpatient treatment; conduct follow-up studies of discharged patients; examine the structure and function of evolving area programs; evaluate the effectiveness of educational programs for the mentally retarded; develop a trainable achievement test for the mentally retarded; characterize children and adults with self-injurious behavior; and evaluate ESEA activities.

To provide better information for administrators, a series of projects focuses on components and programs in state psychiatric hospitals and community mental health centers. A central concern is to identify and measure factors associated with program success. Program success (the extent to which programs achieve expected results) is considered a function of personal attitudes and attributes of staff and clients, organizational structural variables, organizational process variables, environmental pressures and residual factors. New programs do not enter a vacuum but a network of relationships in and among these variables. These projects aim to develop prediction models of organizational change by isolating and measuring this network of relationships and using these data to explain the variation between programs with differential achievement of expected results. A similar study of statewide alcoholism programs is in the process of implementation.

In addition to extending scientific knowledge about organizational change, information derived from these studies will provide baseline data from which programs are evaluated; provide an accurate assessment of the role of psychiatric hospitals and community mental health centers in the delivery of mental health services; and provide for informed decision-making on the part of administrators and planners involved in the delivery of mental health services.

The Division of Program Evaluation also acts as a consultant to both state and community mental health administrators.



Research Personnel — North Carolina Department of Mental Health. January, 1973.