NIA ANNUAL REPORT

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OCTOBER 1, 1977 THROUGH SEPTEMBER 30, 1978
OFFICE OF THE DIRECTOR

The National Institute on Aging (NIA) implemented its comprehensive research program during Fiscal Year 1978, its second full year of operation after an initial year that emphasized organization and planning. Collaboration was the theme as the Institute engaged itself in work that crossed many disciplinary lines in the study of the aging process, specific diseases that may occur in old age, and the social and economic context in which the elderly live.

It was apparent that virtually no health or social concern was outside the range of NIA research interests. The search for understanding of the aging process begins with research on the molecular and cellular building blocks of life. At the other end of the spectrum, the Institute conducts research into the social and behavioral characteristics of aging populations. Both types of research can help to improve the quality of life at all ages, including the later years. The concerns of the Institute, then, as presented in the research plan developed during Fiscal Year 1977, cover the entire continuum of life--both the fundamental processes and the unexpected events that occur along the way.

The interdisciplinary nature of the Institute's work and the need for collaboration are illustrated by nutrition, a highly significant factor in many of the diseases and disabilities of the aged, as well as the health and well-being of the general population. Nutrition is an integrative issue that goes beyond any one discipline; it is not exclusively a function of biology, medicine or the behavioral and social sciences, but depends upon each of them. The major National Institutes of Health effort in this area is shared by three Institutes--the National Institute of Arthritis, Metabolism, and Digestive Diseases; the National Institute of Child Health and Human Development; and NIA--and supervised by the Nutrition Coordinating Committee. NIA earmarked $300,000 during FY 1978 for support of clinical nutrition studies and it convened a national conference on the subject in June (see below for details on this and similar interdisciplinary conferences).

Priorities

In order to organize its work most effectively, the Institute developed a set of priorities for immediate and long-range efforts based on its research plan entitled "Our Future Selves." Cost containment continues to be a major concern and, throughout Institute research programs, it is emphasized that knowledge must be applied to practical ends. NIA seeks to contribute to the effort to curb the staggering costs associated with the debilities of old age. Because mounting costs erect barriers to the delivery of the benefits of knowledge to people of all ages, including the elderly, we consider cost containment a legitimate goal of research.

The priorities of the NIA, refined and implemented to varying degrees during FY 1978, are as follows:

Research Geriatric Medicine

Research Approaches

Epidemiology and Demography
Longitudinal Studies
Clinical Trials

Research Resources

Biological Materials and Animal Models--Development and Availability
Research Personnel

Over-Arching Issues

Prevention-Related Research
Nutrition
Pharmacology
Prosthetics
Differential Life Expectancy

Biological Issues

Basic Biology
Neurosciences (Organic Brain Disease)
Immunology
Endocrinology (Hormone Dynamics)

Behavioral and Social Issues

Behavioral Aspects of Aging
The Family and Other Socio-Cultural Issues
Retirement

During Fiscal Year 1978, the National Institute on Aging operated with a budget of $37 million and had just over 200 staff positions. Funds were allocated as follows (estimates):

Research Grants	$21,985,000
Training	2,390,000
Research Contracts	2,158,000
Intramural Research	7,945,000
Operations and Management	2,522,000

Intramural research studies were conducted at the NIA laboratories in Baltimore. The extramural research program supported studies at other research institutions, including hospitals, medical schools, universities and research centers.

One major intramural program is the Baltimore Longitudinal Study of Aging at the Gerontology Research Center, which entered its second decade during FY 1978. Since 1958, the study has examined more than 1,000 men, ranging in age from 20 to 96 years, and continues to produce findings of value to a broad range of scientists working in the fields of aging and human development, as well as those investigating specific diseases.

Women were added to the study during the past year, an important addition that will make the research even more comprehensive. Because the women are, for the most part, wives and daughters of present volunteers, the study may become the first of its kind to also focus on family factors as they relate to aging.

One question being explored is why women outlive men by an average of eight years. Of the 23 million Americans 65 and older, more than 13 million are women. Those facts have important implications for economists, social scientists, and health care providers.

Key Staff Appointments

As the Institute moved from a period of defining critical research areas to careful development of work within the framework of the 18 priorities, several key staff appointments were made.

A Deputy Director was named to coordinate activities among the longitudinal and disease-categorical Institutes, the Public Health Service and HEW agencies, as well as other organizations in the Federal establishment with aging activities. In addition to a key role in forward planning evaluation, the Deputy Director will serve as liaison with various national aging organizations and coordinate international activities in aging.

An Assistant to the Director for Medical Program Development and Evaluation was appointed to monitor the developing body of knowledge of geriatric medicine and nursing and advise national and international organizations on progress in this area.

Also appointed was the first Director of the new Laboratory of Neurosciences at the Gerontology Research Center. It is expected that it will take several years to establish a neurosciences laboratory fully, but extensive research plans are already being developed. These plans include studies of genetic molecular control mechanisms and evaluation of neuroendocrine control and homeostasis, which involves exploration of the immune system, the muscular system and the central nervous system.

An eight-member Board of Scientific Counselors was established during the year as an advisory committee to the intramural research program of the Institute. After a review of Institute programs, the Board stressed that a strong program of fundamental research must be maintained in order to understand the aging process in chemical, molecular and biological terms.

Geriatric Medicine

There continues to be a serious shortage of trained professionals in geriatric medicine--in both research and medical practice--and a major effort

is being made by the Institute to encourage medical schools to incorporate the subject into their curricula. Although the Institute does not have the authority for clinical training in geriatric medicine, it is taking positive steps to help develop this field. A Geriatric Medicine Academic Award was recently established to stimulate the development of a curriculum in geriatric medicine in those schools that do not have one and to strengthen and improve the curriculum in those schools that do. It is only by supporting curriculum development now that we will interest future health practitioners in geriatrics and aging research.

The Institute is supporting by contract a study by the Institute of Medicine of the National Academy of Sciences on the need for gerontology and geriatrics in medical school curricula. This panel of representatives of medical academia is evaluating the best means of introducing material regarding human aging into medical school programs. The objective of the project is to determine how best to provide the necessary instruction in geriatric medicine.

The new Assistant to the Director for Medical Program Development and Evaluation recently spent six weeks in Great Britain observing how the British care for their aged. He found in most instances a well-integrated system providing medical care plus a full range of supporting services, including social assistance, occupational and physical therapy, day hospitals, home help, and even vacation admissions of healthy older patients to give the families caring for them time off. In the United Kingdom, contact with the aged is becoming an integral part of medical education because students are trained in clinics, hospitals, and other places where these services are provided. This contact with the elderly increases throughout five years of medical school and internship. While the U.S. medical student is more likely to see the older patient as a disease, his or her British counterpart is more likely to see the older patient as an individual for whom a variety of services is available.

The Institute has cooperated closely with the Veterans Administration, which has established Geriatric Research and Education Clinical Centers and a fellowship program in geriatric medicine. We also continue to collaborate along these lines with other Federal agencies, such as the Health Care Financing Administration and the Administration on Aging.

Under the Veterans Administration program, last July six of its hospitals began to train two Fellows in geriatrics. These are physicians who have qualified in internal medicine, family practice or neurology. Twelve more Fellows will be added to the program each year.

There are other signs of progress: universities and medical schools throughout the country are establishing institutes, programs and centers oriented toward geriatric medicine and gerontology and a National Advisory Council of Geriatric Medical Programs has been created.

Conferences

The interdisciplinary nature of NIA research and the cross-fertilization of knowledge and effort necessary to carry forward its programs are illustrated by several major conferences convened or co-sponsored by the Institute. The

contractions for up to 200 sec. Before, during or after stimulation, the fiber was frozen rapidly in liquid nitrogen. Perchloric acid at -35°C was used to extract metabolites. Protein, ATP, PCr and glycogen were determined by microanalytic procedures adapted specifically to extremely small quantities found in a single cell.

B. The right femoral nerve of anesthetized rats was stimulated by external electrodes at 0.2 Hz or 1 Hz for 75 min. DG was injected intravenously when stimulation began or immediately after stimulation. Arterial plasma radioactivity was followed, and animals were killed 75 min after tracer was injected. The left and right quadriceps femoris muscles were removed, frozen, sectioned and prepared for autoradiographic measurement of ^{14}C concentration. Sections were also stained for oxidative and glycolytic enzymes.

C. The perineurium of the frog sciatic nerve was isolated and mounted on cannulae within a bath of stirred Ringers solution. Radioiostopes were placed in the bath. Transport through the sheath was quantitated by measuring surface area and collecting Ringers that was perfused through the sheath via the inlet and outlet cannulae. Electrical resistance and capacity of the sheath were measured with internal and external voltage-recording and current-supplying electrodes.

Major Findings:

A. We first distinguished the time course of the fatigue process in single fibers from post-tetanic potentiation of the twitch, which is characterized by elevation and prolongation of the twitch and is due to intracellular calcium accumulation. Fatigue appeared after 20 sec of tetanic stimulation (at 20 Hz) as a decline in tetanic tension that took as long as 1 hr to be reversed. We then correlated the decline and recovery of tension with the instantaneous metabolic profile of the fiber. We found that prolonged tetanic stimulation reduced fiber phospho-creatine (PCr) in proportion to the internal work performed by the fiber, as measured by the isometric time-tension integral. However, despite the fact that ATP is the immediate energy source for muscle contraction, ATP concentration was normal or close to normal in fatigued fibers. ATP was not sequestered in internal compartments in these fibers, as residual ATP could be consumed when caffeine was applied to the fibers to produce maximal and irreversible contractures. Thus, we concluded that fatigue was not due to depletion of available energy stores for muscle contraction, but to failure of coupling between excitation and contraction. On the basis of measured lactate and ATP/PCr ratios in fatigued fibers, we suggested that H^+, as lactic acid, accumulates in repetitively stimulated muscle and interferes with the action of calcium in activating muscle contraction. Our findings have been presented as an abstract: Nassar-Gentina, V., Passonneau, J.V., and Rapoport, S.I.: Relation of muscle fatigue to muscle metabolism. Abstracts 27th Intern. Congress Physiol. Sciences 13, 543, 1977.

B. Unilateral stimulation of the femoral nerve at 0.2 HZ increased DG uptake in the vastus lateralis segment of the quadriceps muscle of the rat, whereas stimulation at 1 Hz increased uptake in the entire quadriceps muscle. Furthermore, uptake was significantly elevated in the 75 min after stimulation as compared to control muscles.

C. The normal permeability coefficient of ^{14}C-sucrose at the isolated perineurium equaled 5.6×10^{-6} cm/sec. This value is very low and shows that the sheath is extremely impermeable to water-soluble solutes. Impermeability would be important if the perineurium regulated the local environment of axons. Permeability to ^{14}C-sucrose was increased reversibly by stretching the perineurium by 10%, but was increased irreversibly by further stretch or by immersing the sheath in a Ringer solution made hypertonic with either NaCl or sucrose. We suggest that stretch or hypertonicity modifies the dimensions of tight junctions that connect perineurial cells, and thereby reduces the control by the perineurium of the axonal environment. An abstract of this work has been published: Weerasuriya, A., Taylor, R.E., and Rapoport, S.I.: Permeability of frog perineurium under conditions of stretch and hypertonicity. Abstr. Eighth Annu. Meeting Soc. Neurosciences, Nov., 1978 (in press).

Significance to Biomedical Research and the Program at the Institute:

A. Our finding that fatigue develops despite high levels of ATP, corresponds to observations of "power failures" in stimulated peripheral nerve and sympathetic ganglion. In these tissues, function also fails before energy supplies are exhausted. Protection of energy supplies from exhaustion, at the expense of function, may preserve survival of neuronal and muscle cells. Muscle wasting and fatigue commonly accompany senescence in man, but may be partially reversed, as endurance training can reduce their effects despite age (Suominen, et al., J. Gerontol. 32, 33, 1977). Endurance training also increases muscle aerobic metabolism. If our hypothesis is correct, that lactate accumulation rather than energy exhaustion can contribute to fatigue, then the results in man may reflect an enhanced ability of endurance-trained muscles to oxidize lactic acid.

B. We showed that the DG method can be employed to examine regional differences in muscle metabolism under different physiologic demands, in disease and aging. The quantitative relation between regional glucose consumption by muscle and DG uptake remains to be established.

C. Very little is known about how the perineurium regulates the environment of peripheral nerve axons, or whether defects in the perineurium contribute to peripheral neuropathy in disease or aging. Basic information on the perineurium is required to address these questions.

Proposed Course: Formerly done under Project Number Z01 MH 01082-13 LNP, "Muscle Function and Metabolism." Project to be continued. (A) Energy consumption associated with the independent steps of contraction and excitation in single muscle fibers will be analyzed. Excitation can be dissociated fr

contraction by stretching fibers beyond the point where actin and myosin filaments overlap, or by placing fibers in solutions made hypertonic with sucrose. (B) We shall explore the function and ultrastructure of the perineurial sheath so as to determine how the perineurium regulates the metabolic and ionic environment of peripheral nerve axons in relation to health, disease and aging.

Publications:

Rapoport, S.I., Ohno, K. and Schwartz, W.J.: Activity-related regional uptake of ^{14}C-labeled deoxyglucose by rat quadriceps femoris muscle. Experimental Neurology 60, 168-174, 1978.

SMITHSONIAN SCIENCE INFORMATION EXCHANGE PROJECT NUMBER (Do NOT use this space)	U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE NOTICE OF INTRAMURAL RESEARCH PROJECT	PROJECT NUMBER Z01 AG 00122-01 LNS

PERIOD COVERED
October 1, 1977 to September 30, 1978

TITLE OF PROJECT (80 characters or less)
Pharmacology of Central and Peripheral Catecholaminergic Nervous System

NAMES, LABORATORY AND INSTITUTE AFFILIATIONS, AND TITLES OF PRINCIPAL INVESTIGATORS AND ALL OTHER PROFESSIONAL PERSONNEL ENGAGED ON THE PROJECT

PI:	C.C. Chiueh	Sr Staff Fellow	LNS NIA
	S.I. Rapoport	Chief	LNS NIA
Others:	S.P. Markey	Section Chief	LCS NIMH
	A.P. Zavadil, III	Staff Physician	PT NIGMS
	I.J. Kopin	Chief	LCS NIMH
	K. Ohno	Visiting Fellow	LNP NIMH
	S.M. Nespor	Biological Laboratory Technician	LNS NIA

COOPERATING UNITS (if any)
Laboratory of Clinical Science, NIMH
Pharmacology/Toxicology Program, NIGMS
Laboratory of Neurophysiology, NIMH

LAB/BRANCH
Gerontology Research Center, Laboratory of Neurosciences

SECTION

INSTITUTE AND LOCATION
NIA, NIH, Baltimore, Maryland 21224

TOTAL MANYEARS:	PROFESSIONAL:	OTHER:
1.46	0.96	0.5

CHECK APPROPRIATE BOX(ES)

[ ] (a) HUMAN SUBJECTS [ ] (b) HUMAN TISSUES [X] (c) NEITHER

[ ] (a1) MINORS [ ] (a2) INTERVIEWS

SUMMARY OF WORK (200 words or less - underline keywords) The purpose of this project is to study the effects of central stimulant agents and stress on the neuronal activities of both central and peripheral catecholaminergic nervous system: 1) Cocaine-induced behavioral and neurochemical effects resemble those of amphetamine. Both cocaine and amphetamine caused an increase in the level of catecholamines in cerebrospinal fluid and in plasma. The increase in release of dopamine after amphetamine resulted in an increase in striatal 3-methoxytyramine rather than homovanillic acid. The results indicate that amphetamine acts directly on the nerve terminal to induce release whereas cocaine acts to increase neuronal firing by a local anesthetic effect on brain inhibitory neurons. The inhibition of re-uptake by both drugs further augments their in vivo catecholamine releasing actions. 2) Plasma levels of catecholamines were used as an index for activities of the peripheral sympathetic nervous system. It was found that plasma catecholamines depend upon the degree of stress. Resting levels of plasma catecholamine in conscious, undisturbed rats were less than 0.5 ng/ml. Plasma catecholamines were increased 2- to 4-fold in young rats (3 or 8 months old) but not in aged rats (28 months old). The exact mechanism for the lack of significant sympathetic responsiveness to stress in the aged rats remains to be investigated.

Project Description:

Objectives:

A. Pharmacological Actions of Cocaine and Amphetamine. (1) The systemic effects of cocaine are sympathomimetic and resemble those of d-amphetamine. Based upon in vitro radioactive tracer techniques, the sympathomimetic action of cocaine seems to be related to its ability to block re-uptake of catecholamines while amphetamine's effect is due to its ability to cause the release of catecholamines. However, other catecholamine re-uptake blocking agents failed to produce these amphetamine-like stimulatory effects. (2) In the present study, the effects of cocaine on the release of catecholamines from either brain or sympathetic nervous system are tested in vivo in order to provide a direct neurochemical basis for the similar actions of cocaine and amphetamine.

B. Stress and Sympathetic Activity. (1) To find a relatively unstressed procedure for the withdrawal of blood samples and monitoring of systolic and diastolic blood pressures in the conscious and freely moving rat, (2) to adapt the sensitive radioenzymatic method for catecholamine to quantities in less than 0.1 ml plasma, (3) to measure circulating catecholamines of conscious, developing and aged rats, and (4) to study the effect of aging on the responsivity of the sympathetic nervous system to stress or to drugs.

Methods:

A. Pharmacological Actions of Cocaine and Amphetamine.

1. Cerebroventricular perfusion technique. Due to the presence of a blood-brain barrier, the cerebroventricular perfusion technique was used to detect the release of neurotransmitters in vivo. Anesthetized cats were prepared for perfusion by placing an inflow cannula in the anterior horn of the lateral ventricle and an outflow catheter at the cisternal space. Artificial CSF was infused at a rate of 0.1 ml/min and collected every 10 min.

2. Radioenzymatic assay for catecholamines. Aliquots of CSF perfusate were incubated at 37°C with 0.2 ml of a mixture containing catechol-O-methyl transferase and ^{3}H-S-adenosyl-L-methionine for 90 min. ^{3}H-O-methylated amines were extracted and separated by chromatographic procedure. One nanogram of internal standard of dopamine, epinephrine and norepinephrine yields 17,000 cpm ^{3}H-3-methoxytyramine, 9,000 cpm ^{3}H-metanephrine and 10,000 cpm ^{3}H-normetanephrine, respectively.

3. Gas chromatographic mass-spectrometric assay for 3-methoxytyramine and homovanillic acid. Rats were irradiated by microwaves in order to inactivate brain enzymes and to minimize the decapitation stress. The striatum was homogenized in 0.2N HCl containing D_4 - 3-methoxytyramine. After centrifugation the supernatant descended into a 13 ml tube and dried under reduced pressure.

The sample was derivatized by incubation with 75 µl pentafluoropropionic anhydride and 50 µl dehydrated ethyl acetate at 75°C for 30 min. The solvent was evaporated in a stream of nitrogen and the dry residue was redissolved in in 25 µl ethyl acetate. Aliquots were injected into a GC-column coupled to mass spectrometer. The 3-methoxytyramine derivatives were monitored by their most abundant fragments M/e = 296 and 299 for D_0 - 3-methoxytyramine - PFP and D_4 - 3-methoxytyramine - PFP (after loss of one deuterium on β carbon) respectively. A standard curve was prepared using known amounts of D_0 -,D_4 - 3-methoxytyramine in cerebellum homogenate.

B. Stress and Sympathetic Activity.

1. Chronic indwelling tail arterial catheter. Rats were housed in groups of 6 in a 12-hr light cycle for at least one week. One or two days before an experiment, an indwelling catheter filled with 500 I.U./ml heparin was inserted into the tail artery. The cannula was led subcutaneously up to the neck and out at the back of the neck, where it was threaded through a spring wire which was anchored at the neck. The catheter was flushed twice daily with 0.5 ml of saline containing 300 I.U./ml sodium heparin.

2. Radioenzymatic catecholamine assay. (See Methods: A.2.)

3. Measurement of systolic/diastolic blood pressure and heart rate from the unrestrained rats. Systolic and diastolic blood pressures of the conscious, freely moving rats were monitored by a pressure transducer through the arterial catheter and recorded by a polygraph. Heart rate was obtained from the rate of pulsation of blood pressure either by manual calculation or by a tachometer.

Major Findings:

A. Pharmacological Actions of Cocaine and Amphetamine. (1) d-Amphetamine caused an increase in the release of catecholamines, mainly dopamine from the brain and norepinephrine from the sympathetic nervous system (heart, adrenal gland and spleen). It caused a relatively small increase in plasma levels of epinephrine. (2) The striatal level of 3-methoxytyramine but not of homovanillic acid was increased after d-amphetamine or decapitation stress. An abstract has been presented (Chiueh, C.C., Zavadil, A.P. and Markey, S.P.: Increased striatal 3-methoxytyramine but not homovanillic acid following administration of d-amphetamine or decapitation. Federation Proceedings 37: p 509 (Abstract 1554) 1978). (3) Although relatively less potent than d-amphetamine, cocaine released endogenous dopamine and norepinephrine from the brain mainly by a disinhibitory mechanism. (4) Systemically-administered cocaine elevated plasma levels of catecholamines, mainly of epinephrine. This effect of cocaine was more evident after inhibition of COMT and was attenuated, but not completely blocked, after bilateral adrenal denervation. (5) Desmethylimipramine (Desipramine) failed to increase plasma levels of catecholamines but inhibited completely the uptake of catecholamines.

B. Stress and Sympathetic Activity. (1) Arterial plasma levels of norepinephrine and epinephrine in unrestrained rats were less than 500 pg/ml, whereas levels of norepinephrine and epinephrine in blood obtained from decapitated rats were 7,600 pg/ml and 15,000 pg/ml, respectively. (2) Immobilization of control rats (3 - 10 months old) caused a 2- to 4-fold increase in the plasma levels of norepinephrine and epinephrine. (3) Plasma catecholamines in immobilized aged rats (28 months old) were only one-third of those in restrained young rats (3 months old). (4) Immobilization also produced a higher blood pressure (144 ± 2/116 ± 2 mmHg) and heart rate (418 ± 11 beats/min) in young rats than in aged rats. The results have been presented in abstract form: Ohno, K., Chiueh, C.C. and Rapoport, S.I.: Plasma norepinephrine and epinephrine concentrations in conscious, restrained young and old rats. Federation Proceedings, 37: p 888 (Abstract 3544) 1978.

Significance to Biomedical Research and the Program of the Institute:

A. Pharmacological Actions of Cocaine and Amphetamine. (1) Several hypotheses have been proposed for the mode of action of cocaine. In the past, the hypothesis that cocaine acts by inhibition of amine uptake has prevailed because evidence that it releases catecholamines from sympathetic nerve endings was not convincing. In the present study, a newly developed radioenzymatic assay for catecholamines provided direct evidence that cocaine increases plasma levels of catecholamines, mainly epinephrine. Cocaine also increases CSF levels of catecholamines. (2) The similarity of cocaine and d-amphetamine in releasing dopamine and/or norepinephrine from brain in vivo may be the neurochemical basis for their similar stimulatory behavioral effects. (3) Cocaine induces release of catecholamine from the sympathoadrenal medullary system largely via a central disinhibition mechanism, possibly by a local anesthetic action on small inhibitory neurons in the central nervous system. Disinhibition, rather than inhibition of uptake may also be responsible for the effect of cocaine on the release of dopamine from the nigrostriatal system. (4) The present results indicate that striatal 3-methoxytyramine rather than homovanillic acid is a better index for the release of dopamine in vivo. Levels of homovanillic acid mainly reflect the intraneuronal metabolism of dopamine.

B. Stress and Sympathetic Activity. (1) The tail arterial catheter procedure makes it possible to measure blood pressure and blood concentrations in the absence of stress. It can be used to study the release of neurotransmitters from the sympathetic nervous system, the release of neuroendocrines from the pituitary gland or the in vivo cardiovascular function of conscious hypertensive rats. (2) The finding of a positive correlation between plasma levels of catecholamine and changes in blood pressure or heart rate strengthens previous reports that plasma catecholamines in arterial blood obtained from the chronic arterial catheter of a conscious rat is a good index of sympathetic activity. (3) A decrease in sympathetic reactivity of aged rats in response to stress was supported by the lack of a significant increase in plasma catecholamines, blood pressure and heart rate after immobilization.

Proposed Course:

A. Pharmacological Actions of Cocaine and Amphetamine. (1) To explore the possible use of brain levels of O-methylated catecholamines as an index for regional neuronal activity or the functional turnover rate of catecholaminergic neurons, and (2) to measure the pharmacological and neurochemical changes in the aged or developing rat brain after central stimulants.

B. Stress and Sympathetic Activity. (1) To examine the effects of different stressors, cold stress, CO_2 stress, or immobilization - on the synthesis and turnover of peripheral and central aminergic nervous system (presynaptic events). (2) To study adrenergic receptor activity in vivo by measuring the levels of cyclic AMP in brain tissues or in the plasma (postsynaptic events).

Publications:

Chiueh, C.C. and Kopin, I.J.: Centrally mediated release by cocaine of endogenous epinephrine and norepinephrine from the sympathoadrenal medullary system of unanesthetized rats. J. Pharmacol. Exp. Ther. 205: 148-154, 1978.

Chiueh, C.C. and Kopin, I.J.: Radioenzymatic paper-chromatographic assay for dopamine and norepinephrine in cerebroventricular cisternal perfusate of cat following administration of cocaine or d-amphetamine. J. Neurochem., in press.

Chiueh, C.C. and Kopin, I.J.: Hyperadrenergic responsivity of SHR to indirect measurement of blood pressure. Amer. J. Physiol. 234: H690-H695, 1978.

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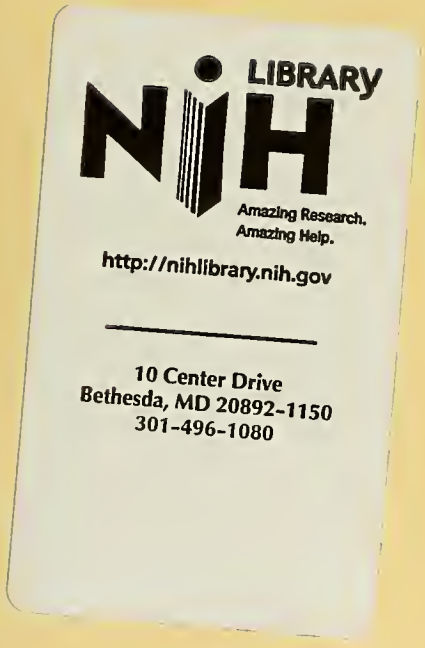
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