

Originally Processed With FOIA(s):
2005-0336-F

FOIA Number:
2005-0336-F

FOIA MARKER

**This is not a textual record. This is used as an
administrative marker by the George Bush Presidential
Library Staff.**

Record Group/Collection: George H.W. Bush Presidential Records
Collection/Office of Origin: Science and Technology Policy, Office of (OSTP)
Series: Bromley, D. Allan, Files
Subseries: Correspondence Files

OA/ID Number: 62010
Folder ID Number: 62010-002

Folder Title:
Invitations: General (4) [2 of 12] [1991]

Stack:

Row:

Section:

Shelf:

Position:

0

0

0

0

"INVITATION FOR DR. BROMLEY"

TYPE: INVITATION

DOCUMENT NUMBER: 9121202

SPEECH: YES NO

FROM: FRI, Robert W.: RESOURCES FOR THE FUTURE

DATE OF EVENT: 05/13/91

LOCATION OF EVENT: RESOURCES & CONSERVATION CENTER, 1616 P STREET, N.

TIME OF EVENT: 04:30PM

SUBJECT: INVITATION TO ATTEND A RECEPTION TO CELEBRATE THE
RELEASE OF THE DOCUMENTARY FILM ON GLOBAL CLIMATE
CHANGE, "FUTURE CONDITIONAL".

RSVP: 05/06/91

CONTACT PERSON:

CONTACT NUMBER:

INVITATION ACCEPTED? YES NO

COPIES TO: ENVIRONMENT

REMARKS: 5/1/91 - Regretted to Lawrence!
m r

DATE OF LETTER: 04/19/91

DATE RECEIVED: 04/23/91

FILE: P- INVITATION



RESOURCES
FOR THE FUTURE

9121202
RECEIVED

91 APR 23 P 4: 05

Robert W. Fri
President and Senior Fellow

19 April 1991

OFFICE OF THE
DIRECTOR

Mr. D. Allan Bromley
Science Advisor to the President
Office of Science & Tech. Policy
360 Old Executive Office Bldg.
Washington, DC 20506

Dear Mr. Bromley:

You are cordially invited to attend a reception sponsored by Resources for the Future to celebrate the release of our documentary film on global climate change called Future Conditional. The reception is being held on Monday, May 13, 1991, from 4:30 to 6:00 p.m., in the Thomas A. Kimball Conference Room at the Resources and Conservation Center, 1616 P Street, N.W. You will have an opportunity to view the film, which will run continuously, at your leisure.

The science involved in deciphering the changes in the world's climate as a result of greenhouse warming is extremely complicated; many uncertainties remain about the likely effects. But understanding what can be done to mitigate these effects and finding ways to adapt to changes that may already be under way are vital first steps toward a solution. Future Conditional explores climate change in a clear-sighted, balanced way and offers hope for steps that man can take to both mitigate and adapt to changes that may come.

The film was made possible by contributions from ARCO, Du Pont, Texaco Foundation, Union Carbide Corporation, and William and Flora Hewlett Foundation. Resources for the Future is anticipating that this documentary will be the first in a series of films on important environmental and natural resource issues.

We hope you will be able to join us and meet the film's producers, Hal and Marilyn Weiner of Screenscope, and the science advisor, Norman J. Rosenberg of RFF. We look forward to seeing you.

Very truly yours,

Robert W. Fri
President

"INVITATION FOR DR. BROMLEY"

TYPE: INVITATION

DOCUMENT NUMBER: 9121230

SPEECH: YES NO

FROM: FLANIGAN, John W.: ARMED FORCES COMMUNICATIONS &
ELECTRONICS

DATE OF EVENT: 05/14/91

LOCATION OF EVENT: OMNI SHOREHAM HOTEL

TIME OF EVENT: 11:15AM

SUBJECT: INVITATION TO BE A HEAD TABLE GUEST AT THE
WASHINGTON CHAPTER AFCEA LUNCHEON.

RSVP: 04/30/91

CONTACT PERSON: CLAUDIA LESH0

CONTACT NUMBER: 703/247-2966

INVITATION ACCEPTED?



NO

COPIES TO:

REMARKS: 4/30/91 - Regretted! m2

DATE OF LETTER: 04/17/91

DATE RECEIVED: 04/23/91

FILE: P, INVITATION

PRESIDENT
M. A. Brunner
AT&T Federal Systems
1120 20th St., NW
9th Floor
Washington, DC 20036

VICE PRESIDENT
J. W. Flanigan
ITT Aerospace Communications
Division

TREASURER
R. McCashin
Electronic Data Systems Corporation

SECRETARY
G. B. Shick, Jr.
Andrulis Research Corporation

GENERAL COUNSEL
J. Ennis, Esq.
Fletcher, Heald & Hildreth

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Programs - D. J. Cade
COMSAT Systems Division
Publicity - R. J. Lombardi
AT&T Federal Systems
Scholarship - E. F. Bronson
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OSD C!

ARMED FORCES COMMUNICATIONS AND ELECTRONICS ASSOCIATION



RECEIVED

17 April 1991

AFCEA—WASHINGTON CHAPTER
1990-1991

91 APR 23 P 4: 29

Dr. Allan Bromley
Assistant to the President for Science and
Technology
Office of Science and Technology Policy
Old Executive Bldg.
17th and Penn Ave., NW Rm 358
Washington, DC 20506

Dear Dr. Bromley,

On behalf of the Armed Forces Communications and Electronics Association (AFCEA), I would like to extend to you an invitation to be a head table guest at the Washington Chapter AFCEA luncheon, May 14, 1991. This will be Science and Technology Day and we will be recognizing the Science Fair Winners and awarding scholarships in hard sciences and engineering. Vice President Dan Quayle will be our guest speaker.

There will be a Head Table Reception prior to the luncheon. Pertinent information regarding the luncheon is as follows:

PLACE: Omni Shoreham Hotel
2500 Calvert St., N.W.
Washington, D.C.

DATE: Tuesday, May 14, 1991

TIME: 11:15 a.m. - Head Table Reception
Executive Room

12:00N - Luncheon
Regency Room

At the end of the reception period, the head table guests will be assembled to proceed to the dais in the Regency Room.

Please contact Claudia Lesho, (703) 247-2966, with your RSVP or if you have any further questions.

Sincerely,

John W. Flanigan
Vice President
Washington Chapter - AFCEA

"INVITATION FOR DR. BROMLEY"

TYPE: INVITATION-SPEECH

DOCUMENT NUMBER: 9121150

SPEECH: YES NO

FROM: Salam, Abdus

DATE OF EVENT: 06/07/91

LOCATION OF EVENT: TRIESTE

TIME OF EVENT:

SUBJECT: INVITATION TO TRIESTE FOR THE OPENING CEREMONY AND
TO ANNOUNCE THE US PLANS FOR THE AFRO-EUROPEAN
CENTRE FOR GLOBAL CHANGE.

RSVP: 04/30/91

CONTACT PERSON:

CONTACT NUMBER:

INVITATION ACCEPTED?

~~YES~~

NO

COPIES TO: Thomas Ratchford

REMARKS:

DATE OF LETTER: 04/13/91

DATE RECEIVED: 04/17/91

FILE: P- INVITATION

Withdrawal/Redaction Sheet

(George Bush Library)

Document No. and Type	Subject/Title of Document	Date	Restriction	Class.
01a. Letter	To: Abdus Salam From: Allan Bromley Re: Global Change Research Center (1 pp.)	4/29/91	(b)(1)	

Collection:

Record Group: Bush Presidential Records
Office: Science and Technology Policy, Office of (OSTP)
Series: Bromley, D. Allan, Files
Subseries: Correspondence Files
WHORM Cat.:
File Location: Invitations: General (4) [2 of 12] [1991]

Date Closed:	2/18/2010	OA/ID Number:	62010-002
FOIA/SYS Case #:	2005-0336-F	Appeal Case #:	
Re-review Case #:		Appeal Disposition:	
P-2/P-5 Review Case #:		Disposition Date:	
AR Case #:		MR Case #:	
AR Disposition:		MR Disposition:	
AR Disposition Date:		MR Disposition Date:	

RESTRICTION CODES

Presidential Records Act - [44 U.S.C. 2204(a)]

P-1 National Security Classified Information [(a)(1) of the PRA]
P-2 Relating to the appointment to Federal office [(a)(2) of the PRA]
P-3 Release would violate a Federal statute [(a)(3) of the PRA]
P-4 Release would disclose trade secrets or confidential commercial or financial information [(a)(4) of the PRA]
P-5 Release would disclose confidential advice between the President and his advisors, or between such advisors [(a)(5) of the PRA]
P-6 Release would constitute a clearly unwarranted invasion of personal privacy [(a)(6) of the PRA]

C. Closed in accordance with restrictions contained in donor's deed of gift.

PRM. Removed as a personal record misfile.

Freedom of Information Act - [5 U.S.C. 552(b)]

(b)(1) National security classified information [(b)(1) of the FOIA]
(b)(2) Release would disclose internal personnel rules and practices of an agency [(b)(2) of the FOIA]
(b)(3) Release would violate a Federal statute [(b)(3) of the FOIA]
(b)(4) Release would disclose trade secrets or confidential or financial information [(b)(4) of the FOIA]
(b)(6) Release would constitute a clearly unwarranted invasion of personal privacy [(b)(6) of the FOIA]
(b)(7) Release would disclose information compiled for law enforcement purposes [(b)(7) of the FOIA]
(b)(8) Release would disclose information concerning the regulation of financial institutions [(b)(8) of the FOIA]
(b)(9) Release would disclose geological or geophysical information

Withdrawal/Redaction Sheet

(George Bush Library)

Document No. and Type	Subject/Title of Document	Date	Restriction	Class.
01b. Letter	To: Allan Bromley From: Abdus Salam Re: Global Change Research Center (2 pp.)	4/13/91	(b)(1)	

Collection:

Record Group: Bush Presidential Records
Office: Science and Technology Policy, Office of (OSTP)
Series: Bromley, D. Allan, Files
Subseries: Correspondence Files
WHORM Cat.:
File Location: Invitations: General (4) [2 of 12] [1991]

Date Closed:	2/18/2010	OA/ID Number:	62010-002
FOIA/SYS Case #:	2005-0336-F	Appeal Case #:	
Re-review Case #:		Appeal Disposition:	
P-2/P-5 Review Case #:		Disposition Date:	
AR Case #:		MR Case #:	
AR Disposition:		MR Disposition:	
AR Disposition Date:		MR Disposition Date:	

RESTRICTION CODES

Presidential Records Act - [44 U.S.C. 2204(a)]

P-1 National Security Classified Information [(a)(1) of the PRA]
 P-2 Relating to the appointment to Federal office [(a)(2) of the PRA]
 P-3 Release would violate a Federal statute [(a)(3) of the PRA]
 P-4 Release would disclose trade secrets or confidential commercial or financial information [(a)(4) of the PRA]
 P-5 Release would disclose confidential advice between the President and his advisors, or between such advisors [(a)(5) of the PRA]
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C. Closed in accordance with restrictions contained in donor's deed of gift.

PRM. Removed as a personal record misfile.

Freedom of Information Act - [5 U.S.C. 552(b)]

(b)(1) National security classified information [(b)(1) of the FOIA]
 (b)(2) Release would disclose internal personnel rules and practices of an agency [(b)(2) of the FOIA]
 (b)(3) Release would violate a Federal statute [(b)(3) of the FOIA]
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 (b)(8) Release would disclose information concerning the regulation of financial institutions [(b)(8) of the FOIA]
 (b)(9) Release would disclose geological or geophysical information

Withdrawal/Redaction Sheet

(George Bush Library)

Document No. and Type	Subject/Title of Document	Date	Restriction	Class.
01c. Report	The Trieste System: A Description (11 pp.)		(b)(1)	

Collection:

Record Group: Bush Presidential Records
Office: Science and Technology Policy, Office of (OSTP)
Series: Bromley, D. Allan, Files
Subseries: Correspondence Files
WHORM Cat.:
File Location: Invitations: General (4) [2 of 12] [1991]

Date Closed:	2/18/2010	OA/ID Number:	62010-002
FOIA/SYS Case #:	2005-0336-F	Appeal Case #:	
Re-review Case #:		Appeal Disposition:	
P-2/P-5 Review Case #:		Disposition Date:	
AR Case #:		MR Case #:	
AR Disposition:		MR Disposition:	
AR Disposition Date:		MR Disposition Date:	

RESTRICTION CODES

Presidential Records Act - [44 U.S.C. 2204(a)]

P-1 National Security Classified Information [(a)(1) of the PRA]
P-2 Relating to the appointment to Federal office [(a)(2) of the PRA]
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(b)(8) Release would disclose information concerning the regulation of financial institutions [(b)(8) of the FOIA]
(b)(9) Release would disclose geological or geophysical information

"INVITATION FOR DR. BROMLEY"

TYPE: INVITATION

DOCUMENT NUMBER: 9121182

1

SPEECH: YES NO

FROM: COLLIER TROPHY BANQUET COMMITTEE

DATE OF EVENT: 05/17/91

LOCATION OF EVENT: OMNI SHOREHAM HOTEL

TIME OF EVENT: 06:30PM

SUBJECT: THE ROBERT J. COLLIER TROPHY PRESENTATION BANQUET TO
HONOR THE BELL BOEING V-22 OSPREY TILTROTOR TEAM

RSVP: 05/06/91

CONTACT PERSON:

CONTACT NUMBER:

INVITATION ACCEPTED?

~~YES~~

NO

COPIES TO:

REMARKS:

DATE OF LETTER:

DATE RECEIVED: 04/22/91

FILE: p, INVITATION

*The National Aviation Club
and
The National Aeronautic Association
of the United States of America*

*request the pleasure of your company
at the*

***Robert J. Collier Trophy
Presentation Banquet***

which will honor the

Bell Boeing V-22 Osprey Tiltrotor Team
*for the development of the world's first large-scale
tiltrotor aircraft*

Friday, May 17, 1991

6:30 p.m.

Reception, Ambassador Room

7:30 p.m.

Dinner, Regency Ballroom

The Omni Shoreham Hotel

Washington, D.C.

*R.S.V.P.
Accepts Only*

*Black Tie or
Military Equivalent*



Dr. Allan Bromley
Science Advisor to the President
360 Old Executive Office Bldg.
Washington , DC 20506

Collier Trophy Banquet Committee
1133 Fifteenth Street, N.W.
Suite 1200
Washington, D.C. 20005

RECEIVED

91 APR 22 P 2 : 10

OFFICE OF THE
DIRECTOR

9121182

*Rooms have been reserved in the name of the Collier Dinner at the
Omni Shoreham Hotel for Friday evening, May 17, 1991.*

Please call the hotel directly to make your reservations.

*The Omni Shoreham
2500 Calvert Street
Washington, D.C. 20008
(202) 234-0700*

*Collier Trophy Presentation Banquet
Friday, May 17, 1991
Reservation Card*

Name _____

Affiliation _____

Address _____

City _____ State _____ Zip _____ Telephone _____

Kindly reserve:

_____ table(s) of 10 seats each; _____ table(s) of 12 seats each;
_____ single seat(s)

I will make _____ seats available for DoD guests and their spouses.

My check for \$ _____ at \$125.00 for each banquet seat is enclosed.

Please make check payable to:

COLLIER DINNER COMMITTEE

Note: Refunds cannot be made after May 10, 1991.

signature

*Collier Trophy Banquet Committee
1133 15th Street, N.W., Suite 1200
Washington, D.C. 20005
(202) 785-1188*

COLLIER TROPHY BANQUET COMMITTEE
1133 FIFTEENTH STREET, N.W.
SUITE 1200
WASHINGTON, D.C. 20005

"INVITATION FOR DR. BROMLEY"

TYPE: INVITATION

DOCUMENT NUMBER: 9121158

SPEECH: YES NO

FROM: YOUNG, Judith A.: YALE GRADUATE SCHOOL ALUMNI
ASSOCIATION

DATE OF EVENT: 05/27/91

LOCATION OF EVENT: WOOLSEY HALL, YALE UNIVERSITY

TIME OF EVENT: 12:00PM

SUBJECT: INVITATION TO THE PRESENTATION OF THE CROSS MEDALS
AND DIPLOMAS, A RECEPTION AND A LUNCHEON.

RSVP: 05/01/91

CONTACT PERSON:

CONTACT NUMBER:

INVITATION ACCEPTED?



NO

COPIES TO:

REMARKS:

DATE OF LETTER: 04/15/91

DATE RECEIVED: 04/18/91

FILE: P- INVITATION



Yale Graduate School Alumni Association

9121158
RECEIVED

April 15, 1991

91 APR 18 A 9:18

OFFICE OF THE
DIRECTOR

Dr. D. Allan Bromley
Assistant to the President
for Science and Technology
Director, Office of Science and
Technology Policy
Executive Office of the President
The White House
Washington, DC 20500

Dear Dr. Bromley:

As you already know, the Yale Graduate School Alumni Association will award the Wilbur Lucius Cross Medal to W. Edwards Deming on Monday, May 27, 1991.

The presentation of the Cross Medals and of diplomas to the graduating Doctors of Philosophy will take place at 12:00 noon in Woolsey Hall. At the conclusion of these ceremonies there will be a reception in the courtyard of the Hall of Graduate Studies at 320 York Street. Guests will be joining this reception until just prior to 2 p.m. when the recipients and their guests move upstairs to the Faculty Lounge, Room 211 HGS, for cocktails and a luncheon in honor of the medalists.

I hope that you will be able to attend the presentation, reception, and luncheon. A return postcard is enclosed for your convenience in replying.

Yours sincerely,

Judith A. Young
Assistant to the Dean

JAY:sec

Enclosure



Carnegie Hall Centennial 1991

Judith A. Young
Assistant to the Dean
Yale Graduate School
P.O. Box 1504A Yale Station
New Haven, CT 06520-7425

9/21/54

"INVITATION FOR DR. BROMLEY"

TYPE: INVITATION

DOCUMENT NUMBER: 9121157

SPEECH: YES NO

FROM: FOSTER, John S. Jr.: DEFENSE SCIENCE BOARD

DATE OF EVENT: 05/01/91

LOCATION OF EVENT: SHERATON NATIONAL HOTEL, ARLINGTON, VA

TIME OF EVENT: 07:00PM

SUBJECT: INVITATION TO A SOCIAL HOUR AND THE DEFENSE SCIENCE
BOARD'S SPRING DINNER. (There is a fee of \$35.00)

RSVP: 04/24/91

CONTACT PERSON: DIANE L.H. EVANS

CONTACT NUMBER:

INVITATION ACCEPTED?

~~YES~~ NO

COPIES TO:

REMARKS:

DATE OF LETTER: 04/12/91

DATE RECEIVED: 04/18/91

FILE: P- INVITATION



DEFENSE SCIENCE
BOARD

OFFICE OF THE SECRETARY OF DEFENSE
WASHINGTON, D.C. 20301-3140

912/157
RECEIVED

91 APR 18 A 9: 19

OFFICE OF THE
DIRECTOR

April 12, 1991

Honorable D. Allan Bromley
Assistant to the President for
Science and Technology
Office of Science and
Technology Policy
OEOB, Room 360
Washington, DC 20506

Dear Dr. Bromley:

The Defense Science Board will have its Spring dinner meeting on Wednesday, May 1, 1991 at the Sheraton National Hotel, Columbia Pike & Washington Boulevard, Arlington, Virginia (Galaxy Room on the 16th Floor). There will be a social hour at 1900 hours, followed by dinner at 2000. We have invited Honorable Brent Scowcroft, Assistant to the President for National Security Affairs to be our after-dinner speaker.

If your busy schedule permits you and your spouse to attend, please forward your check for \$35.00 per person made payable to "Defense Science Board," to Mrs. Diane L.H. Evans, Defense Science Board, OUSD(A), Room 3D1020, The Pentagon, Washington, DC 20301-3140. This amount covers the dinner, tax, and gratuity. A cash bar will be available before dinner. The reservation deadline is April 24, 1991.

Sincerely,

for John V. C...
John S. Foster, Jr.
Chairman

"INVITATION FOR DR. BROMLEY"

TYPE: INVITATION

DOCUMENT NUMBER: 9121154

SPEECH: YES NO

FROM: CARNEGIE INSTITUTION OF WASHINGTON

DATE OF EVENT: 05/09/91

LOCATION OF EVENT: CARNEGIE INSTITUTE OF WASHINGTON

TIME OF EVENT: 08:45PM

SUBJECT: A LECTURE BY J. ROGER ANGEL, "MAKING BIGGER AND
BETTER TELESCOPES"... RECEPTION FOLLOWING.

RSVP: 04/29/91

CONTACT PERSON:

CONTACT NUMBER:

INVITATION ACCEPTED?

~~YES~~

NO

COPIES TO: Dr. Wong

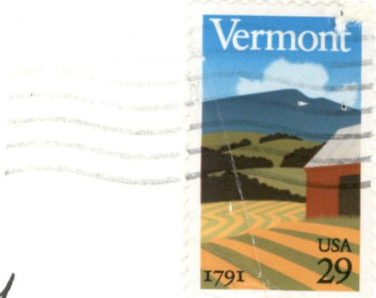
REMARKS:

*make mailing for
JRSR*

DATE OF LETTER:

DATE RECEIVED: 04/18/91

FILE: P. INVITATION



Dr. and Mrs. D. Allen Bromley
Assistant to the President for Science
and Technology Policy
Old Executive Office Bldg.
Suite 358
17th and Pennsylvania Avenue N.W.
Washington, DC 20506

9121154

RECEIVED

SI APR 18 A 9:16

OFFICE OF THE
DIRECTOR

CARNEGIE INSTITUTION OF WASHINGTON
1530 P STREET, NORTHWEST
WASHINGTON, D.C. 20005-1910

AP

THE PRESIDENT AND TRUSTEES
OF THE

CARNEGIE INSTITUTION OF WASHINGTON

CORDIALLY INVITE YOU TO A LECTURE BY

J. ROGER ANGEL

REGENTS PROFESSOR OF ASTRONOMY AND
DIRECTOR, STEWARD OBSERVATORY MIRROR LABORATORY
UNIVERSITY OF ARIZONA

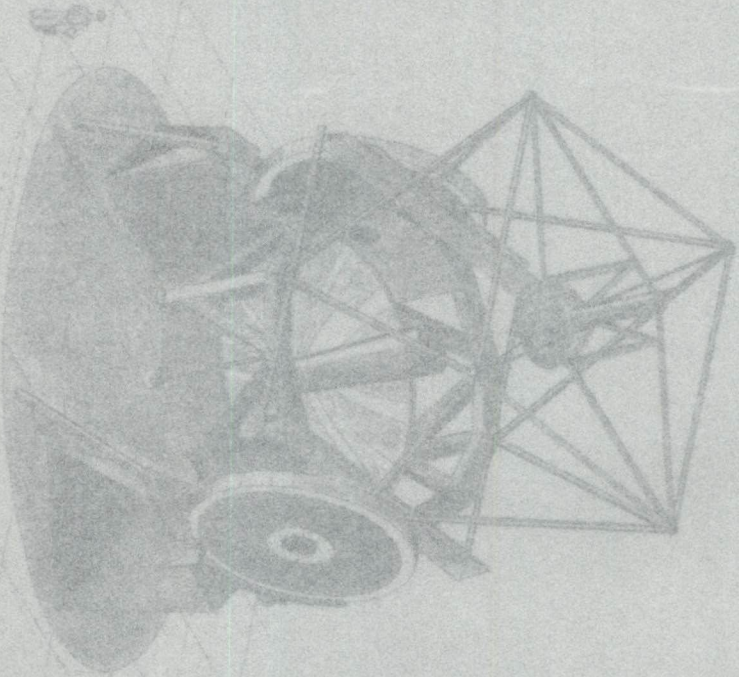
"MAKING BIGGER AND BETTER TELESCOPES"

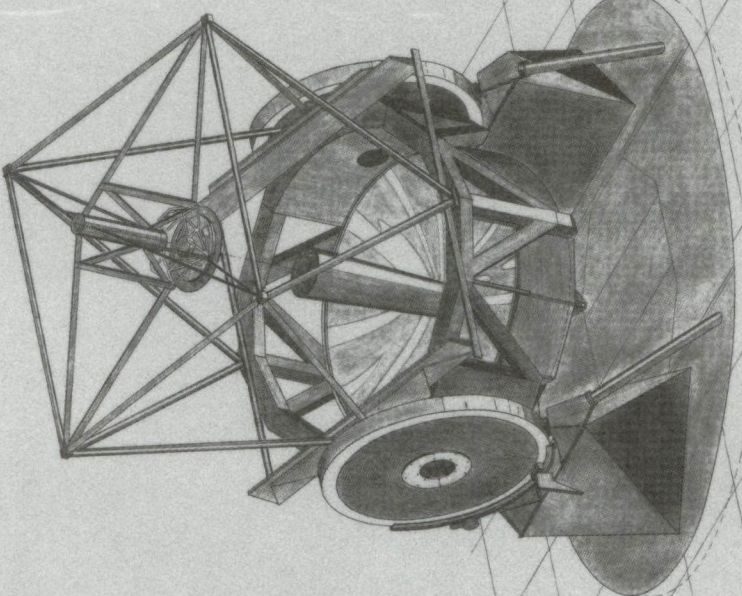
ON THURSDAY, MAY 9, 1991, AT 8:45 P.M.

RECEPTION FOLLOWING

ROOT HALL
ADMINISTRATION BUILDING
CARNEGIE INSTITUTION OF WASHINGTON
1530 P STREET, N.W.
WASHINGTON, D.C.

R.S.V.P.
BY REPLY CARD
ENCLOSED





WASHINGTON, D.C.
1230 P STREET, N.W.
CARNEGIE INSTITUTION OF WASHINGTON
ADMINISTRATION BUILDING
ROOF HALL

ENCLOSED
BY REPLY CARD
R-2-V-1

RECEPTION FOLLOWING

ON THURSDAY, MAY 9, 1921, AT 8:45 P.M.

MAKING BIGGER AND BETTER TELESCOPES.

UNIVERSITY OF ARIZONA

DIRECTOR, STEWARD OBSERVATORY MIRROR LABORATORY
REGENTS PROFESSOR OF ASTRONOMY AND

J. ROGER ANGEL

CORDIALLY INVITE YOU TO A LECTURE BY

CARNEGIE INSTITUTION OF WASHINGTON

OF THE

THE PRESIDENT AND TRUSTEES

Dr. D. Allan Bromley

PLEASE PRINT NAME(S)

☐ WILL

☒ WILL NOT

BE ABLE TO ATTEND THE
CARNEGIE EVENING LECTURE AND RECEPTION
MAY 9, 1991

KINDLY REPLY BY
APRIL TWENTY-NINTH

"INVITATION FOR DR. BROMLEY"

TYPE: INVITATION

DOCUMENT NUMBER: 9121142

SPEECH: YES NO

FROM: EMBASSY OF THE REPUBLIC OF POLAND

DATE OF EVENT: 05/02/91

LOCATION OF EVENT: 2640 16TH STREET, N.W., WASHINGTON, D.C.

TIME OF EVENT: 06:00PM

SUBJECT: INVITATION TO A RECEPTION ON THE OCCASSION OF THE
NATIONAL DAY OF POLAND AND THE TWO HUNDRETH
ANNIVERSARY OF MAY THIRD CONSTITUTION.

RSVP: 04/25/91

CONTACT PERSON:

CONTACT NUMBER: 202/234-0626

INVITATION ACCEPTED? YES NO

COPIES TO:

REMARKS:

DATE OF LETTER:

DATE RECEIVED: 04/17/91

FILE: P- INVITATION



April 4, 1991

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11th ANNUAL
CONVENTION
San Francisco, California
July 6 - 9, 1991

The Honorable D. Allan Bromley
Assistant to the President
For Science & Technology
360 Old Executive Office Building
Washington, D. C. 20506

Dear Dr. Bromley:

I am pleased to enclose copies of our most recent issue of The Decade of the Brain. We are all very grateful for your taking the time to write this article which I am sure will be of high interest not only to NAMI families, but to Congress and the scientific community as well. I certainly intend to call this to the attention of my former boss, Rep. Don Ritter.

This decade is indeed a critical ten years in which we must take optimum advantage of existing circumstances to reap incomparable benefits through unparalleled research opportunities. NAMI Executive Director, Laurie Flynn, and I would like to visit with you very briefly on ways we can be of mutual service in accomplishing these goals.

Also, please let me know if you can be on hand the night we honor Chairman Bill Natcher with the first annual Silvio Conte Public Service Award.

With best wishes,

Sincerely,

James H. Cromwell
Research Advocate
Editor, The Decade of the Brain

JHC:ac
Enclosures

NATIONAL ALLIANCE FOR THE MENTALLY ILL
2101 WILSON BOULEVARD, SUITE 302 • ARLINGTON, VA 22201
703-524-7600 • FAX 703-524-9094

9/21/40

*The National Alliance for the Mentally Ill (NAMI)
and the
NAMI Legislative Network
request the pleasure of your company
at a reception
celebrating the presentation of
the first annual*

Silvio O. Conte Public Service Award

to the

Honorable William H. Natcher

*on Monday, April 15, 1991
six to eight p.m.*

4/15/91
Regretted!

*Informal
R.S.V.P. (703)524-7600
Please respond by April 8th*

*First Floor Foyer
Rayburn House Office Building
Washington, D.C.*

THE DECADE OF THE brain

WINTER 1991
VOLUME II, ISSUE 1

COORDINATING THE FEDERAL DECADE OF THE BRAIN EFFORT

By D. Allan Bromley, Ph.D.*

It has always seemed astonishing to me that we know vastly more about the first microsecond of the existence of our universe, or about the constituents of any atom, or about the interior of the sun, than we do about the three pounds of tissue inside our own heads. Brain research is truly one of the great frontier areas of science. Of particular interest to the **National Alliance for the Mentally Ill (NAMI)** and the millions of people afflicted with mental disorders, it is a frontier that promises enormous practical payoff in the form of new treatments and possibly new ways of prevention. Even more important, it is a profoundly philosophical human adventure, an attempt by the human brain to understand itself.

To make significant progress in that effort during the 1990s -- the 10-year span President Bush has designated as the Decade of the Brain -- we will need to draw on every aspect of modern science, including molecular and cellular biology, computational science, behavioral science, brain imaging technologies, even aspects of theoretical physics. We will need the dedicated,

IN MEMORIAM

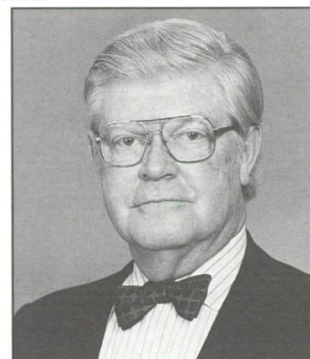
The Honorable Silvio Conte, a U.S. Representative from Massachusetts since 1959 and author of the Decade of the Brain (PL 101-58), the first Congressional Resolution to endorse a specific area of research since the National Geophysical Year, passed away on February 8th. He was a dynamic legislator and highly respected leader who gave new direction to research on serious mental illness. He will be deeply missed by NAMI families around the nation.

coordinated efforts of many individuals and organizations in the private and public sectors alike.

My office, the Office of Science and Technology Policy (OSTP), is charged with coordinating Federal scientific efforts concerning brain research during the commemoration of the Decade of the Brain. As this field is important to several Federal agencies, the Administration has begun this effort with an initiative on Brain and Behavioral Sciences in the Federal Coordinating Council on Science, Engineering, and Technology (FCCSET) Committee on Life Sciences and Health. This group is working on an integrated Federal effort to take advantage of the extraordinary opportunities now before us in neuroscience.

This initiative is headed by Dr. Roger Porter, Deputy Director of the National Institute of Neurological Disorders and Stroke (NINDS), with Dr. Alan Leshner, Acting Director of the National Institute of Mental Health, and Dr. Steven Zornetzer, Director of Life Sciences in the Office of Naval Research, as Vice-Chairs. Key government agencies involved in a broad spectrum of brain research are represented on the subcommittee developing this initiative, including many key components of the Public Health Service, including NIMH, NINDS, and other ADAMHA and NIH Institutes. Because brain research has such important implications for international competitiveness, technology transfer and international efforts to promote science, the group also includes representatives from the Departments of Commerce, Education, Defense and State.

Federal activities associated with the Decade of the Brain are directed toward two different audiences, the public and the scientific enterprise. We want to increase the public's awareness and understanding of the brain and its disorders. At the same time, we want to involve the



D. Allan Bromley, Ph.D.

scientific community in exploring both existing knowledge and promising new frontiers in brain research.

With these dual goals in mind, nine specific research areas have already been identified that can form the basis of an integrated program in this tremendously challenging frontier. These areas include: 1) human behavior and mental disorders; 2) addiction; 3) aging; 4) development; 5) learning and memory; 6) communication and sensory disorders; 7) environmental impacts; 8) brain and spinal cord injury; and 9) restoration of function. Using these topics as a framework, Federal agencies can receive input from the scientific community and voluntary health organizations, such as NAMI, in building a coordinated effort for this vitally important Decade.

We are also considering the possibility of creating a 10-year national research plan for the neurosciences. This will mark a very important strategic step in planning a decade ahead for what activities and initiatives the Federal Government should consider supporting and fostering.

OSTP will act as a central clearinghouse for this work. But we will need the cooperation of a great many other institutions and organizations, including NAMI. We intend to make the Decade of the Brain a cornerstone of Federal efforts in the life sciences.

With the cooperation of groups such as yours, we will be contributing to one of the most important initiatives in science and technology the Federal Government has undertaken in this decade. We expect that these efforts will contribute substantially to a new capacity to free the brain of illness and enhance its vast human potential in health.

*[About the author: Dr. Bromley is Science Advisor to President George Bush and Director, Office of Science and Technology Policy. He is on leave from his position as Henry Ford II Professor of Physics at Yale University, where he was founder and Director of the A.W. Wright Nuclear Structure Laboratory.]

BRAIN WAVES

Peer reviewers of grant applications submitted to the National Institutes of Health (NIH) and the Alcohol, Drug Abuse and Mental Health Administration (ADAMHA) will be selected from a new, computerized database pool of basic or applied research scientists. Other review activities and committee assignments will be made from the same database, and for some of those positions, according to Dr. Fred Bruner, lay persons with special interests and skills, but without scientific backgrounds, will not be ruled-out. NAMI members

interested in joining the pool should call Dr. Bruner (301)443-3936 or write to: Consultant File Department #02, Suite 725, 4733 Bethesda Ave., Bethesda, MD 20814. (Please send a copy of your application to Jim Cromwell, c/o The Decade of the Brain).

Rep. John Dingell, Chairman of the House Committee on Energy and Commerce, has requested the Office of Technology Assessment (OTA) to undertake a study of major new developments in neuroscience. OTA study director Dr. Laura Lee Hall and research analyst Claire Pouncey have already contacted The Decade of the Brain regarding new advances in mental illness research on the topics of: 1) neural transplants and nerve regeneration, 2) biological rhythms and shift work, 3) neurotoxic substances, and 4) the biological bases of mental illness.

Dr. Alan Leshner, Acting Director of the National Institute of Mental Health (NIMH), said, in connection with the dedication of the Harbor-UCLA Research Center on the Psychobiology of Ethnicity, "Although mental illness can strike anyone regardless of race or cultural origin, there appear to be some very important differences in the ways people of different ethnic backgrounds respond to medications in the treatment of depression, schizophrenia and other serious mental disorders." According to Leshner, the research undertaken by the new Center "will greatly enrich our understanding of the psychobiological bases of mental disorders and their treatment, and help ensure that every patient of every ethnic background receives appropriate treatment."

The Stanley Foundation Research Awards Program is intended to attract established scientists from other areas of biology and medicine into research on serious mental illnesses, as well as to provide support for innovative research by established scientists already in the field whose funding sources are limited. Grant applications for the Stanley Research Awards Program should be received by April 1st. Applications should consist of: a 80-120 word summary statement; a 1-2 page single-spaced outline of what the applicant plans to do and what relevance it has for serious mental illness; a condensed Curriculum Vitae; a list of current funding sources and pending grants; and a brief preliminary budget indicating how the funds will be used. Send applications to: E. Fuller Torrey, M.D., Chairperson, Stanley Research Awards Program, c/o NAMI, 2101 Wilson Blvd., Suite 302, Arlington, VA 22201. If you have questions concerning the Stanley Foundation Research Awards, please contact Kelly Peck at NAMI (703)524-7600.

SPOTLIGHT ON

DR. LYNN DeLISI

STANLEY SCIENTIST SEEKS DEFECTIVE GENE

Dr. DeLisi has been on the faculty of the Department of Psychiatry, State University of New York (SUNY) at Stony Brook for approximately three years. She previously was a staff member in the intramural National Institute of Mental Health (NIMH) research division -- beginning at St. Elizabeth's Hospital working closely with Dr. Richard Wyatt, then at The Clinical Center in Bethesda with Drs. Monte Buchsbaum and Elliot Gershon. She has always devoted her career to research on the etiology and pathogenesis of schizophrenia, initially examining peripheral neurochemical markers for brain pathology, then later moving to direct studies of brain metabolism by positron emission tomography (PET), brain morphology using magnetic resonance imaging (MRI) and molecular genetic markers in a large group of families with multiple ill schizophrenic members.

Her present program at Stony Brook focuses on the occurrence of brain structural changes in schizophrenia, how they relate to the genetic tendency for schizophrenia, and whether they progress with the course of illness. Patients who have a recent onset of a schizophrenic illness are being evaluated and followed in a prospective study design. These and other patients who have available first degree relatives with schizophrenia are also being examined and a registry is being maintained of all families who have multiple ill members.

Dr. DeLisi is currently expanding her registry of families nationally. "When I began to hunt for large families with multiple ill members, suitable for genetic



studies," said DeLisi, "NAMI chapters throughout the country aided me by placing ads in local and national newsletters. I eventually identified approximately 200 such families and continue to evaluate new ones." In recognition of this investigative work, Dr. DeLisi was presented

NAMI's annual Judith Silver Memorial Young Scientist Award.

She is also a Stanley Foundation awardee. The brain structural studies she has been conducting at Stony Brook, partially funded by that Foundation, have shown, thus far, that enlargement of the lateral ventricles appears to be present early on in the illness. The first group of patients studied had significantly larger ventricles than the control group, although smaller than a randomly selected group of chronic patients. A decrease in the size of the temporal cortex was not found in the first episode patients, while this was found in two separate series of chronic patients under study by other investigators. According to Dr. DeLisi, "These data suggest that brain structural pathology may be increasing with the duration of the illness and its chronic progression."

Two year follow-up examinations of these patients are now in progress. Thus far, the data indicate that the larger the ventricles at the onset of illness, the poorer the outcome two years later. Two years subsequent to the initial MRI scan, ventricular size varied greatly in a subgroup of patients. "Therefore," she emphasized, "the mystery to be solved from the clues is still a key element of my work."

Some patients had substantial increases, while others had decreases in ventricular size. However, the degree of change in ventricular size was not correlated with outcome at two years. Temporal lobe changes with time are presently being examined. Dr. DeLisi's methodical schedule includes serial scans annually in each subject over a five year period to clarify the extent of brain change early in the illness course.

"In addition," Dr. DeLisi points out, "concurrent genetic studies have focused on finding a defective gene for schizophrenia that may be related to abnormal brain growth." In collaboration with Dr. Timothy Crow and colleagues in Harrow, England, she has been focusing on the X and Y chromosomes as possible loci for the gene or genes. These studies are partially based on their observations that XXY and XXX subjects are more frequently found among hospitalized schizophrenics than in the general population. "Also," according to Dr. DeLisi, "these views are based on our recent finding that the pattern of inheritance of schizophrenia may be specific to sex chromosome inheritance."

The observation that pairs of siblings with schizophrenia tend to be more often of the same than of the opposite sex, has previously been published by other investigators. However, further examination suggested that if same sex concordance is to be explained by sex chromosome inheritance, then this would be expected specifically when the gene is transmitted from the father, but not the mother. This is because fathers transmit their X chromosomes only to daughters and their Y only to

sons, whereas mothers, with two X's can transmit genes on the X chromosome to either sons or daughters. In a combined UK/USA sample of schizophrenic siblings, investigators found a tendency for the gene to have been transmitted by the father.

Dr. DeLisi expressed optimism that her work will be helpful in "eventually making a link between the genetic and brain pathologic studies. It is possible that a gene for schizophrenia may be related to a number of inherited factors that contribute to brain growth and development, all of which could lead to the abnormal findings I have noted in the brains of some adult schizophrenics."

OVERCOMING STIGMA: A POWERFUL INFLUENCE ON PEOPLES' LIVES

By Bruce Link, Ph.D.*

Recent research has shown that stigma can have powerful effects on peoples' lives influencing their self esteem, their interaction with others and their chances for employment and the opportunity to earn a good living. As such it is appropriate that the theme of the 1990 American Psychiatric Association Meetings was "Overcoming Stigma."

Stigma Defined

Social scientists define stigma as a two part sequence. First, stigma involves an attribute or a "mark" that sets a person apart from others. In some instances the mark will be immediately apparent as it is for people with a harelip or for people who are dwarfs. In other instances it will not be immediately apparent as, for example, for people who have been hospitalized for mental illness.

The second part of the definition of stigma is that the mark links the person to undesirable characteristics even in the absence of any evidence that the person has the characteristics. For example, if a person is hospitalized for mental illness and is then assumed to be dangerous, incompetent, or untrustworthy, the person, according to this definition, is stigmatized. Similarly, if a mother is "marked" as a consequence of having a mentally ill son or daughter and is, as a result, linked to an undesirable characteristic such as being a "schizophrenogenic mother" then the mother is experiencing stigma.

Certainly, then, with this definition in mind, people with mental illness and their families are susceptible to stigmatization. But is the stigma of mental illness still an important influence on people's lives in contemporary society?

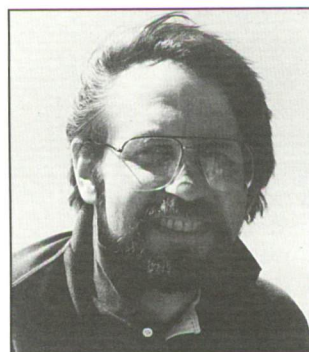
Research Evidence On the Stigmatization of People With Mental Illness

Most social scientists agree that mental illness was highly stigmatized up until the mid 1950's or so. At about that time public education campaigns were undertaken and some social scientists came to believe that mental illness was no longer severely stigmatized. Sociologist Walter Gove put it this way, "Most mental patients experience some stigma, however, in the vast majority of cases the stigma appears to be transitory and does not appear to be a significant problem." Other social scientists have put it in even stronger terms by stating that former mental patients "enjoy nearly total acceptance in all but the most intimate relationships." By the late 1970's and early 1980's this perspective came to have a profound effect on research about the stigma of mental illness. In fact when a panel of experts was called to the National Institute of Mental Health to discuss the stigma of mental illness in 1980 they decided to leave the word stigma out of the title of their proceedings. In their view the mentally ill were no longer significantly affected by the stigmatizing reactions of others. If former mental patients experienced rejection the cause was more likely attributable to deviant behavior caused by mental illness than to the stigmatizing reactions of others.

But the research that led to these conclusions shared two main problems. It relied too heavily on straightforward questions about whether members of the public would accept mental patients and it did not consider the subtle ways in which stigma can affect people's lives.

Consider first the matter of asking straightforward questions that ask members of the public whether they would be willing to hire, rent a room to or date someone who had been a mental patient. The problem with these so called "social distance" questions is that people have learned that the ideal response to such questions is one of acceptance. Moreover they are hypothetical and the person answering the questions knows it. It is easy for a person to say "certainly I would rent a room to a former mental patient," knowing full-well he/she will never really have to do so. In short, undisguised hypothetical questions allow socially desirable responses that do not reflect a person's true feelings.

One way to overcome this problem is to compare mental illness to other potentially



Bruce Link, Ph.D.

stigmatizing conditions such as cleft palate, psoriasis, cancer, diabetes, prostitution, drug addiction and criminal behavior. When this is done a general tendency to give socially desirable responses can be overcome by examining where in a hierarchy mental illness stands. Research studies have shown that mental illness is one of the most highly rejected conditions clustering with prostitution, drug addiction and crime, rather than with cancer, diabetes and heart disease. In fact, one study found that people viewed the ex-mental patient role as even less desirable than the ex-convict role. Respondents also thought that mothers would be more likely to trust an ex-convict with the care of their children than an ex-mental patient, and that an ex-convict would be much more reliable in an emergency than an ex-mental patient.

A second way to overcome the problem of social desirability is to make the situation more real. Stewart Page, a social scientist from Toronto, Canada, did this by gathering all the advertisements in the local newspaper concerning apartments to rent. For some of the advertisements a member of his research team called landlords and indicated that he was a patient in a mental hospital who would be released in a day or two, whereas in a control condition no mention of mental hospitalization was made. When mental patient status was known, landlords were much less likely to indicate that the apartment was available (27%) than in the control condition (83%).

To summarize, when we consider studies that avoid the problem of socially desirable responses, public attitudes reveal an enduring stigma of mental illness. While people may have learned that it is wrong to stigmatize the mentally ill their true attitudes may not have changed as much as their responses to straightforward questions would seem to indicate.

But if stigma exists how does it come to affect people who have been hospitalized for mental illness? What is the process through which stigma erodes confidence, disrupts interaction and makes employment and fulfilling social ties difficult to achieve? My colleagues and I have proposed the following explanation. As part of growing up in this society individuals develop a conception about how most people view and treat people who have been hospitalized for mental illness. They develop conceptions about whether most people will reject mental patients as employees, neighbors, and intimates, or whether they will devalue them, believing them to be less intelligent, trustworthy, and competent. Before entering treatment these beliefs are inconsequential -- they are beliefs about how other people, "mental patients", are viewed and treated. Upon entry into treatment, however, this set of beliefs takes on new meaning for patients -- they become personally relevant. The more patients feel that people devalue and discriminate against mental

patients the more they feel threatened by interactions with others. They may keep their treatment a secret, try to educate others about their situation, or withdraw from social interaction they perceive as potentially rejecting. The uncertainty, tentativeness and withdrawal that can result may affect performance in the job market, social network ties, and a patient's view of himself/herself.

Consistent with this explanation, my colleagues and I have found that community residents and patients agree on the extent to which most people are rejecting mental patients. Moreover, this view is decidedly more negative than positive. That is, both community residents and mental patients tend to believe most people will devalue and reject a former mental patient across a series of twelve questions forming a perceived devaluation discrimination scale. The more mental patients expect devaluation and discrimination as measured by this scale the less likely they are to be employed, to earn a good income and to have robust social support outside their immediate household. For community residents there is no association between scale values and these outcomes -- the items are about mental patients and are not personally relevant to them. This research suggests that some significant portion of the problems that former mental hospital patients experience in work and social relationships are stigma related.

Need for Future Research

While studies of the stigma of mental illness have investigated important issues, three areas of research are underdeveloped at the present time. First, we know relatively little about whether the fear of being stigmatized causes people with severe mental illness and their families to delay or avoid badly needed treatment. The person with mental illness may strenuously avoid psychiatric treatment because he or she fears the stigmatizing consequences of accepting the mental patient label. Perhaps family members avoid bringing their relatives for mental health treatment because they do not want to be told (possibly again and again) that they caused the mental illness of their relative. While these seem real possibilities, research documenting just how important they may be is lacking.

A second major area of research that needs development is research on families' experience with stigma. Does stigma cause the social isolation of some families? What are the consequences for a parent's self-esteem if they are told by a professional that one caused a child's illness? With what frequency do friends, relatives or acquaintances make stigmatizing comments about a family simply because a member has developed mental illness? What effects do these comments have and how do family members cope with them when they occur?

Thirdly, we need research concerning efforts to overcome stigma and its harmful effects. Our studies suggest that when patients are left to themselves to cope with stigma, the strategies they adopt -- keeping their treatment a secret, withdrawing from social interaction, or trying to educate other about mental illness -- are either not effective or, in the case of withdrawing, actually prove harmful. The missing ingredient in these efforts is the support of a group. Left alone it is far too easy for stigma to induce shame in the stigmatized. A group that explicitly rejects those who stigmatize the mentally ill can help patients see that stigma lies in the ignorance of such persons and does not reflect something shameful about them. Can we overcome stigma's effects by devising interventions that bring group support of this sort to the mentally ill? I believe that we can and that research on the stigma of mental illness should turn to the evaluation of such efforts.

*[About the author: Dr. Link is Associate Professor of Public Health at Columbia University. His works have been instrumental in the development of the research instrument for the new World Health Organization study on the outcome of schizophrenia in different cultures.]

A MEDICAL MODEL FOR INCORPORATING THE NEUROSCIENCE REVOLUTION INTO CHILD AND ADOLESCENT PSYCHIATRY

By Richard Peschel, M.D., Ph.D. and
Enid Peschel, Ph.D., Editor NAMI CAN News*

The scientific revolution in molecular biology and neurobiology has begun to have a dramatic impact on adult psychiatry. It has affected child psychiatry to a lesser extent. For example: (1) Recent magnetic resonance imaging (MRI) implicates cerebellar anomalies as the probable site of origin for autism (Courchesne et al, "Recent advances in autism", Current Opinion in Pediatrics, 1990). Autopsy data suggest that these cerebellar abnormalities may have occurred prior to 30 weeks gestation in utero. These findings have vast implications. (2) Positron emission tomography (PET) has localized an abnormality in the caudate nucleus of the basal ganglia as the probable anatomic site responsible for obsessive-compulsive disorders (OCD) in children (Rapoport, The Boy Who Couldn't Stop Washing, 1989). Advances in psychopharmacology such as the development of clomipramine (Anafranil) and fluoxetine (Prozac) have also had a major impact on the treatment of OCD in children.

In the long term, we are optimistic that basic science research will continue to make progress in the

understanding and treatment of biologically-based brain diseases (BBBD) -- for example, bipolar and depressive disorders, schizophrenia, pervasive developmental disorder (PDD), autism, OCD, Tourette's disorder, anxiety and panic disorders, and attention deficit hyperactivity disorder (ADHD).

Given the findings of the past 10 years of science research, it is essential to recognize that BBBD: (a) have biological causes and (b) are very different from "mental health" problems (e.g. abuse, neglect, poverty, crime, emotional, neurotic or life-adjustment issues), which have sociological or environmental causes.

Unfortunately, child psychiatry has been very slow to integrate the scientific revolution into daily practice. Even today, many child psychiatrists do not prescribe psychotropic medications for severe BBBD or are not expert -- or even trained -- in using these drugs. In addition, many hospitals and clinics use "milieu therapy" or behavior modification techniques universally without regard to the individual child's diagnosis and without any long-term scientific data demonstrating the efficacy of these approaches for children and adolescents with a BBBD.



Richard Peschel, M.D., Ph.D., and Enid Peschel, Ph.D.

Why has progress been so slow? (1) Many child psychiatrists were trained in the pre-neuroscience era. (2) Some physicians choose to ignore the scientific revolution. Most important, fewer than 20 full-time academic child psychiatrists in the U.S. devote 80% or more of their time to science research. (Institute of Medicine [IOM], Research on Children and Adolescents with Mental Behavior, and Developmental Disorders, 1989).

Without a major increase in the number of full-time researchers, the integration of the biological revolution into child psychiatry will remain suboptimal. How can we remedy this situation?

The best model for addressing the critical shortage of basic researchers in child psychiatry comes from the seven new Child Health Research Centers funded by the National Institute of Child Health and Human Development, part of the National Institutes of Health (NIH). These new research centers will use a multidisciplinary team -- including senior pediatricians,

geneticists, molecular biologists, cellular biologists and neuroscientists -- to teach basic science to pediatric researchers-in-training. These centers aim to incorporate and integrate all aspects of the biological revolution into the training of the next generation of pediatric researchers.

To start to remedy the dearth of science researchers in child and adolescent BBBD, we advocate the establishment of Child BBBD Research Centers to help encourage and support the most talented of our young physicians to seek careers in the basic science of child psychiatry. These research centers would integrate all the rapid advances in neurobiology, genetics, pharmacology, statistics, etc., with the principal focus of applying *only scientific methods and data* to the problems of BBBD in child psychiatry.

The 1989 IOM (Institute of Medicine) report estimated that some 7,500,000 children in the U.S. suffer from some type of "diagnosable mental illness." The creation of new training programs to produce scientifically-based child psychiatry researchers in BBBD is an essential component -- and should be a high priority -- of the "Decade of the Brain."

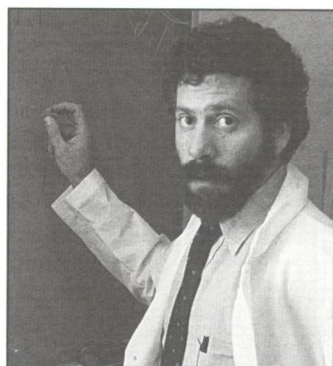
* [About the authors: Dr. Richard Peschel is Associate Professor, Department of Therapeutic Radiology Yale University School of Medicine and Medical Director, Phelps Radiation Center, Uncas on Thames Hospital; Dr. Enid Peschel is Co-Director, Program for Humanities in Medicine and Assistant Professor (Adjunct), Department of Internal Medicine, Yale University School of Medicine]

PHARMACOTHERAPY AND DRUG DEVELOPMENT IN THE DECADE OF THE BRAIN

By David Pickar, M.D.*

Today, over a quarter century since the discovery of the antipsychotic effects of chlorpromazine (Thorazine{R}), the first neuroleptic drug, there is a renewed sense of optimism regarding the pharmacotherapy of schizophrenia and other serious mental illness. There is certainly no more important goal for the Decade of the Brain than to improve the pharmacology of the seriously mentally ill. A brief overview of developments in the drug treatment of schizophrenia follows.

*[About the author: Dr. Pickar is Chief, Experimental Therapeutics Branch & Chief, Section on Clinical Studies, Experimental Therapeutic Branch, National Institute of Mental Health].



1. Neuroleptic "Augmentation"

The use of non-neuroleptic drugs to "augment or enhance" the antipsychotic effects of traditional neuroleptic treatment is now the focus of controlled investigations. While any augmentation strategy is likely to be effective only in a subset of patients, when it is successful, it may offer substantial clinical benefits. The most widely used "augmenting" drug is lithium in the treatment of schizoaffective illness. Anticonvulsants such as carbamazepine (Tegretol{R}) or valproate (Depocote{R}) appear to be useful adjuncts in treating impulsivity and aggression in schizophrenia, while benzodiazepines, particularly short-acting agents such as lorazepam (Ativan{R}) and alprazolam (Xanax{R}) are beneficial in patients whose psychosis is associated with prominent anxiety or panic-like symptoms. Antidepressants have now been shown to be effective in at least one controlled study of patients with schizophrenia who also suffer from depression. Finally, experimental approaches such as dopamine agonists or opiate antagonists may offer some benefits as adjunctive treatments when administered in the research setting.

2. "Atypical" Neuroleptics

The recent demonstration of the effectiveness of clozapine, the prototype "atypical" neuroleptic, in otherwise treatment resistant patients, has had enormous impact on the clinical treatment of the seriously ill patient with schizophrenia. Our new data support the notion that approximately one-third of the patients show enhanced therapeutic response to clozapine in comparison with "typical" neuroleptic treatment. The term "atypical" refers to the fact that clozapine produces little or no motor side effects such as Parkinsonism and may also not cause tardive dyskinesia.

The mechanism by which clozapine produces its unique therapeutic effects is only partially understood. Clozapine, like "typical" neuroleptics (neuroleptics which cause motor side effects), has important effects on dopaminergic systems in the brain. Unlike "typical" neuroleptics, clozapine has prominent effects on norepinephrine and serotonergic systems. One of the most important themes in new drug development is the identification of the key combination of pharmacologic properties which renders clozapine so uniquely efficacious. As has now become well-known, clozapine has one major liability: it can produce life threatening agranulocytosis (loss of certain white blood cells). A challenge for drug development is the discovery of a new drug with clozapine's therapeutic effectiveness without the risk of agranulocytosis.

There are a number of other new "atypical" neuroleptics which are currently undergoing clinical trials in the United States. Sulpiride, raclopride and

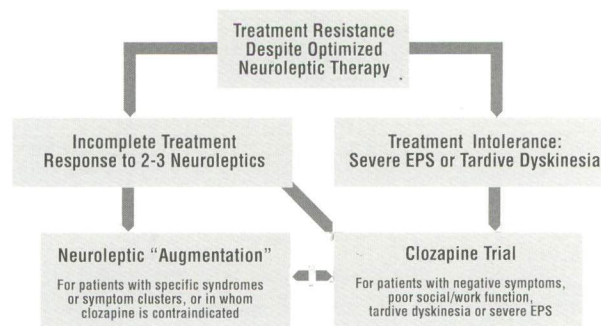
remoxipride are the best examples. They are potent dopamine antagonists but surprisingly produce little movement side effects. Some investigators have hypothesized that they may interact with specialized subtypes of the dopamine receptor. It is unclear whether they have any therapeutic advantages over typical neuroleptic treatment. The field is awaiting the results of current clinical trials.

3. New Directions

The prospects for new drug development are good -- particularly if the trend for collaboration between basic and clinical neuroscience continues to develop. For example, substantial evidence from clinical studies using functional brain imaging techniques such as Positron Emission Tomography (PET) suggest a deficit in activity of the prefrontal cortex in patients with schizophrenia. New drug development which is targeted to enhance the functional activity of the frontal cortex -- perhaps through interactions with receptor types which are specific for the frontal cortex -- may hold particular promise for the treatment of negative symptomatology of schizophrenia. Expect to see new treatments identified by functional brain imaging in coming years.

Despite the fact that there has yet to be a clear link established between a specific genetic defect and schizophrenia, don't be surprised to hear of a metabolic abnormality pertaining to the pathophysiology of schizophrenia which was first uncovered using genetic techniques. Once discovered, it may portend a unique and powerful pharmacotherapeutic "intervention." Look

for a close reliance on experimentally derived data -- clinical and basic -- in drug development during the Decade of the Brain.



Decision tree for treatment-resistant patients with schizophrenia

4 What to Do Now

Prospects of new drug development should not divert needed attention away from the benefits of currently available treatments. A great deal has already been accomplished and should be available to as many patients as possible. The figure illustrates a treatment approach for the seriously ill patient with schizophrenia which integrates currently available agents.

The Decade of the Brain will undoubtedly bring new scientific discovery to treat mental illness. Let it also bring awareness that the mentally ill have a "right" to receive the most advanced and effective treatments, regardless of setting or personal resources, enabling them to return to productive and fulfilling lives.

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The National Alliance for the
Mentally Ill
2101 Wilson Blvd.
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