

Perspective

An Historical Perspective on Psychiatric Genetics, the International Society of Psychiatric Genetics and the Role of Elliot Gershon

Lynn E. DeLisi^{1,2}

¹ Department of Psychiatry, Harvard Medical School, Boston, MA 02215, USA;
Email: Lynn_DeLisi@HMS.Harvard.edu

² Cambridge Hospital, Cambridge Health Alliance, Cambridge, MA 20139, USA

ABSTRACT

Psychiatric Genetics is a relatively new field that was defined by groups of researchers interested in the familial aggregation of psychiatric disorders, and spurred on by the escalating new field of molecular genetics beginning in the 1980s. This manuscript contributes to a special issue honoring the career of Elliot S. Gershon, a true pioneer and critical thinker, who contributed substantially to the development of this field and also its stimulating meetings that brought colleagues together to discuss the latest research findings. It details the role Dr. Gershon played in establishing the precursor of the *International Society of Psychiatric Genetics* (ISPG) and how he remains in a leadership role on its Board of Directors and was honored with one of the ISPG Lifetime Achievement Awards.

KEYWORDS: psychiatric genetics; ISPG; WCPG

The field of Genetics was likely born about the time that Mendel reported his experiments on traits of pea plants and how they were transmitted through generations of new seedlings [1,2]. The words “gene” and “Genetics”, originating from the Greek, meaning “of noble birth” or “to give birth”, came into scientific use when William Bateson used the term “genetics” to describe inherited variations [3], referring to Mendel’s work, and when Wilhelm Ludvig Johanssen [4], a few years later in 1909, coined the word “gene” to refer to a unit of Mendelian inheritance (<https://www.genome.gov/25520244/online-education-kit-1909-the-word-gene-coined>). Despite Emil Kraepelin and some of his colleagues having described clusters of psychotic illness within families, it was not until large family studies in the 20th century were collected and their illness patterns observed that psychiatric disorders were thought to have any familial vulnerability or relationship to genes. These prompted further twin concordance studies and then adoption studies that ultimately solidified the notion that genetic factors led to psychiatric illness. Psychiatric Genetics was not a field, nor a term used in psychiatry, until much later.

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Some of the earliest refinement of family study methodology was published by Elliot Gershon with colleagues in the 1970s and early 1980s (e.g., [5,6]). The landmark discovery of the Huntington's gene in 1982 [7] then led to early investigations in the Gershon laboratory to using similar methodology to finding a gene for bipolar disorder and schizophrenia (e.g., [8]).

I first met Elliot Gershon, the head of the National Institutes of Mental Health (NIMH) *Neurogenetics Laboratory*, sometime in 1978. I was at that time a post-doctoral fellow in Richard Wyatt's *Adult Psychopharmacology* NIMH Branch at the Saint Elizabeths Hospital in Washington, DC. It was Dr. Wyatt's idea that my first project should involve a collaboration with Dr. Gershon to examine a popular biological marker for schizophrenia, Platelet Monoamine Oxidase Activity (pMAO), and determine whether the activity was inherited and related to the inheritance of schizophrenia. The study design was to be using families with multiple ill members, comparing affected and non affected members. However, when, in preliminary studies, we determined that pMAO activity was lowered by antipsychotic medication [9], the family studies were never pursued. About the same time, I attempted to engage Dr. Gershon in studies of the "Genain" Quadruplets, 4 monozygotic women, all of whom developed chronic schizophrenia. Again, this collaboration failed because Dr. Gershon was adamant that any studies of these women were essentially an "N" of "one" and thus would not advance the field further. Nevertheless, my interest in genetics persisted and I joined the Gershon laboratory in 1984 to pursue the new field of molecular genetics in families with schizophrenia [10–12], initially beginning by confirming the extent of the genetic effect in a carefully controlled new family study [13].

On Friday, October 23, 1992 Theodore Reich, Professor of Psychiatry at Washington University in St Louis invited a handful of colleagues (T Crow, JFW Deakin, L DeLisi, R Elston, D Kirch, J Nurnberger, R Todd) to his department to discuss plans for a congress of psychiatric genetics to be held in the USA sometime in 1993. A few previous events led up to and initiated this landmark St. Louis meeting, one of which was a workshop organized by E Gershon, R Cloninger, P Propping and L DeLisi with funding and support contributed by Professor Hans Hippius from Bonn, Germany (Figure 1). It was an invited 2-day conference, held in Berlin in 1986, for approximately 30 international senior researchers focused on the genetics of mainly schizophrenia. Its aim was to discuss the unanswered questions and to form hypotheses to pursue in future genetic collaborations. The success of this workshop led to two of its attendees, Timothy Crow and Peter McGuffin from the UK, establishing *The World Congress of Psychiatric Genetics* (WCPG) as a meeting of the *Biological Psychiatry Division of the British Royal College of Psychiatrists*. The first 2 WCPGs sponsored by this division of the Royal College were held in Cambridge in 1989 (Figure 2) and London in 2001, and attracted

approximately 200 researchers. It was at the last one that there was talk among some of the American attendees about bringing the WCPG to the USA. Cold Spring Harbor was investigated by Dr. Crow as an obvious site, but was decided to be too small and then abandoned to the preferences of Dr. Reich who thought that having the first USA congress as a satellite of the *American Society of Human Genetics* annual meeting in New Orleans in 1993 seemed the best prospect for success. There was much discussion at that seminal October 1992 meeting about the further future of world congresses and how important it would be not to have one person surface spontaneously to decide it was time to organize a meeting. Chaos, competition, and unnecessary political dealings would ensue. Thus, in order to ensure some stability and transparency to the process for future WCPGs, it was decided to form a non-profit society of interested researchers and thus to have an advisory Board, program committee and officers that would rotate over the years according to a set of by-laws. Thus, while the other attendees at the St Louis meeting took roles in the planning of a 1st USA New Orleans meeting, I volunteered to look into the feasibility of forming a society, and proceeding with the necessary pieces. The first step would be to see if in fact there was interest among colleagues to belong to such a society. A flyer was developed announcing the society and stating for a nominal fee of 10 dollars one could become a member. The mail quickly began accumulating huge numbers of envelopes (and money) from people wishing to become members and it was only then that the administrative complexities of beginning a society and its pieces began to become apparent, *i.e.*, incorporation, application for legal charitable status in the USA, opening a bank account in the name of a “society”. These happened within a short time with the aid of a former psychiatric researcher in my laboratory, G Shields, who then lived in Nevada. Thus, the ISPG was incorporated with Dr. Shields as the “resident” administrator, in Nevada for a very small fee and over time gained 501c USA non-profit status. By the time of the New Orleans congress and the first in person Board meeting, the *International Society of Psychiatric Genetics* (ISPG) had a founding Board of Directors ($N = 8$), By-Laws, approximately 300 members, and 2 life-time achievement prize winners who were honored (Seymour Kety and George Winokur)(Figure 3) with an original sculpture of DNA designed and completed by NY artist, Charles Reina. The rest is “history” that many colleagues listed in Tables 1–4 have been part of at different times. The notable events during the past 27 years have been, (1) an established relationship by contract with the journal *Neuropsychiatric Genetics* and a lesser, but still important relationship with the journal, *Psychiatric Genetics* in the 1990’s. These two important journals were the first specialty journals in the field, having begun about the same time independently late 1980s early 1990s even before the society was officially born. (2) Grant support from the USA National Institutes of Drug Abuse and Alcohol Abuse, led by J Nurnberger and L

DeLisi from 1999 on for several years. These funds were able to provide a travel awardee program for students and young investigators. (3) A travel awardee rapporteur program was established in 2007 whereby coordinated reporting on sessions by travel awardees resulted in a later publication (e.g., [14–16]) documenting the notable events of the congresses. (4) the establishment of Chromosome Workshops to integrate data being produced during the era of early first-generation genome-wide linkage studies, (5) An *Educational Day* was established in 2005 to take place 1 day prior to each WCPG for reviews of different aspects of the field for new investigators beginning work in psychiatric genetics, as well as the informed public and media. (6) A notable field trip took place to Hadamar Psychiatric Hospital in 1998 during the Bonn WCPG to educate genetic researchers about the use of eugenics to form policies about psychiatric patients during the Nazi era and the resulting extermination of thousands of psychiatric patients, bringing to the forefront important lessons from history about the potential misuse of psychiatric information. (7) Other ethical issues were discussed and policies formulated, one dealing with the use of family members for ascertainment of information in genetic studies and the question of who were the “research subjects” requiring informed consent. Another discussion was on addressing the need for a collective society supported statement to the public about the use of genetic testing in psychiatry. (8) Collaborative efforts to enlarge numbers of subjects in large genome-wide studies were discussed at in person meetings during WCPG (most notably in a symposium at the end of the WCPG 2005 in Boston) and thus it can be said that the WCPG and ISPG facilitated the world-wide development of ideas for sharing of data and collections. These included both the NIMH Genetics Initiative, which then led to the Psychiatric Genomics Consortium in the years from 2005 to 2008.



Figure 1. Berlin, October 1986: Left to right: P Propping, H Hippius, B Bondi, unknown assistant to H Hippius, R Cloninger, L DeLisi, E Gershon.

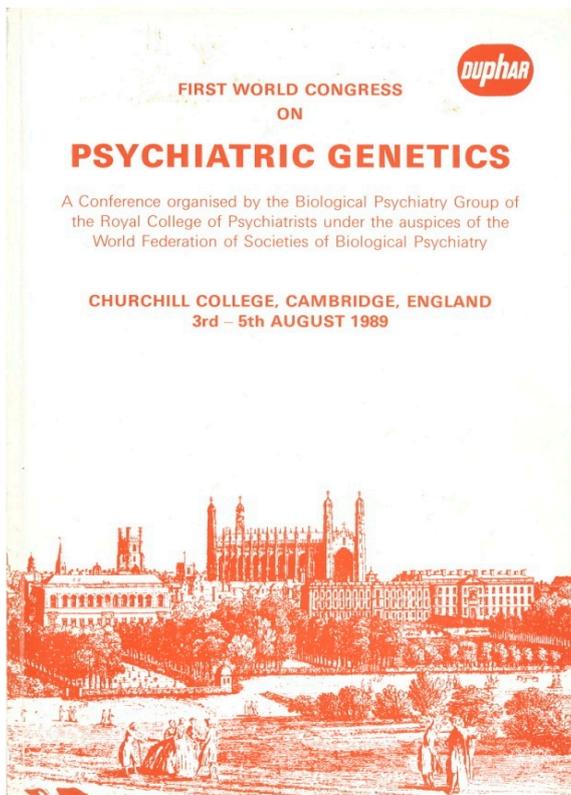


Figure 2. Preliminary meetings held by TJ Crow and P McGuffin in 1989 and 1991 in Cambridge and London as part of The Royal College of Psychiatrists, Biological Psychiatry group. The Cambridge program.



(A) George Winokur



(B) Seymour Kety with Fred Goodwin looking on

Figure 3. The First meeting of the incorporated International Society of Psychiatric Genetics in New Orleans, October, 1993. Both George Winokur and Seymour Kety were honored with the first society lifetime achievement awards for their landmark family (George Winokur) and adoption (Seymour Kety) studies of schizophrenia that led to the search for genetic causes of schizophrenia and all major mental illness.

Thus, while the main mission of the society is to educate and facilitate advancement in research on psychiatric genetics, important political and ethical issues involving the use of genetics were not ignored and will continue to be discussed. In 2011 the society executive office moved from my university academic office, to a professional society management company, Parthenon Management Company, under the auspices of the American College of Neuropsychopharmacology and Dr. Ronnie Wilkins as company president. This enabled the society to continue to expand its professional status in coming years and have a consistent organization to its annual congresses. These were and still are exciting times for the uncovering of genetic mechanisms for disease and the ISPG has been at the forefront in facilitating progress toward the understanding of the genetics of mental illness and facilitating large collaborative efforts to meet and do so.

The following tables summarize the notable researchers who contributed to the leadership of the ISPG in its first 27 years and to the field of Psychiatric Genetics in general. Table 1 lists the officers and terms of office. Table 2 lists the names of Board members and their estimated terms of office. Table 3 lists the many international venues and the chairs of each that were sponsored by the ISPG and the named *World Congress of Psychiatric Genetics* (WCPG). Until 1996, these were biennial meetings and then quickly became annual congresses beginning in 1997 in Santa Fe. Table 4 lists the many awards and their recipients given by the ISPG to recognize achievements in psychiatric genetics. The first award was founded by T Reich and myself to honor two of the most eminent leaders in the field of psychiatric genetics at that time in 1992, Seymour Kety (for his adoption studies in Denmark) and George Winokur (for the Iowa 500 family cohort).

Table 1. Officers from 1992 to Present.

PRESIDENT
Theodore Reich *: 1992–1996
Peter McGuffin: 1997–2000
Michael Owen: 2001–2005
Ming Tsuang: 2006–2010
Nicholas Craddock: 2011–2012
Francis McMahon: 2013–2015
Thomas Schulze: 2016–present

Table 1. *Cont.*

VICE PRESIDENT
Timothy Crow: 1992–1996
Michael Owen: 1997–2000
Christine van Broeckhoven: 2001–2005
Stephen Faraone: 2006–2010
Francis McMahon: 2011–2012
Marcella Rietschel: 2013–2015
Jordan Smoller: 2016–present
SECRETARY
Lynn DeLisi: 1992–2012
Thomas Schulze: 2013–2015
Elizabeth Binder: 2016–present
TREASURER
Richard Todd *: 2005–2008
John Rice: 2008–2015
James Potash: 2016–present

* deceased.

Table 2. Board members and estimated terms (some are based on best memory and may be inaccurate).

Kenji Abe: 1995–2002
Laura Almasy: 2008–2014
Jehannine Austin: 2018–present
Nicholas Barden: 2002–2004
Samuel Barondes: 1994–2011
Kate Berg: 1994–1998
Sarah Bergen: 2014–present
Elisabeth Binder: 2014–present
Margit Burmeister: 2008–present
Nicholas Craddock: 2000–2011
Timothy Crow †: 1992–2011
Lynn DeLisi †: 1992–2013
William Deakin †: 1992–2000
Robert Elston †*: 1992–1999
Steve Faraone: 2003–2012
Susan Folstein: 2000–2004
Barbara Franke: 2018–present
Elliott Gershon: 2008–present
Michael Gill: 2002–2016
Irv Gottesman *: 1995–2010
John Kelsoe: 2012–2018
Ken Kendler: 1995–2000
James Kennedy: 2008–present

Table 2. *Cont.*

Darryl Kirch †: 1992–1997
Douglas Levinson: 2000–2016
Jacque Mallet: 1995–2010
Peter McGuffin: 1994–2008
Francis McMahon: 2004–2016
Sarah Medland: 2018–present
Benjamin Neale: 2018–present
Markus Nöthen: 2000–2018
John Nurnberger †: 1992–2018
Michael Owen: 1995–2013
Lena Peltonen *: 1992–2009
James Potash: 2014–present
Peter Propping *: 1994–2010
Henriette Raventos: 2018–present
Ted Reich †,*: 1992–2003
John Rice: 1999–2016
Marcella Rietschel: 2010–2016
Dan Rujescu: 2014–present
Thomas Schulze: 2008–present
Jonathan Sebat: 2010–present
Jordan Smoller: 2010–present
Patrick Sullivan: 2016–2018
Richard Todd †,*: 1992–2008
Ming Tsuang: 1995–2013
Christine van Broekhoven: 1995–2009
Kenneth Warren: 1994–2000
Naomi Wray: 2016–present
Pamela Sklar *: 2016–2017
Maria del Zompo: 2006–2009

* deceased; † the 8 Founding Board Members.

Table 3. Venues for the World Congress of Psychiatric Genetics (WCPG) sponsored by ISPG and corresponding Chairs/Co-Chairs.

1993: New Orleans (Theodore Reich *)
1995: Cardiff (Peter McGuffin/Michael Owen)
1996: Interim San Francisco (Lynn DeLisi)
1997: Santa Fe (Lynn DeLisi)
1998: Bonn (Propping */Markus Nöthen)
1999: Monterey (John Nurnberger, Jr)
2000: Versailles (Jacques Mallet)
2001: St. Louis (Richard Todd)
2002: Bruxelles (Christine Van Broeckhoven)

Table 3. Cont.

2003: Quebec City (Nicholas Barden)
2004: Dublin (Michael Gill)
2005: Boston (Stephen Faraone)
2006: Sardinia (Maria Del Zompo)
2007 New York City (Lynn DeLisi/Douglas Levinson)
2008: Osaka (Hiroshi Yoneda)
2009: San Diego (John Kelsoe/Martin Schalling)
2010: Athens (Nicholas Craddock/George Papadimitriou)
2011: Washington D.C. (Francis McMahon/Thomas Schulze)
2012: Hamburg, Germany (Markus Nöethen/Marcella Rietschel)
2013: Boston, MA (Jordan Smoller/Lynn DeLisi)
2014: Copenhagen, Denmark (Thomas Schulze, Oli Mors)
2015: Toronto, Canada (James Kennedy)
2016: Jerusalem, Israel (Bernard Lerer, Elliot Gershon)
2017: Orlando, Florida (Stephen Faraone, Daniel Rujescu)
2018: Glasgow, Scotland (Mandy Johnstone, Benjamin Pickard, Jonathan Sebat)
2019: Anaheim, California, (Daniel Geschwind, John Kelsoe)

* deceased.

Table 4. Awards presented by ISPG.

Lifetime Achievement Awardees
1993: Seymour S. Kety * and George Winokur *
1995: Ming T. Tsuang
1997: Irving I. Gottesman *
1999: Theodore Reich *
2001: P. Michael Conneally *
2002: Jules Angst and Nikki Erlenmeyer-Kimling
2003: C. Robert Cloninger
2004: Peter Propping *
2005: NONE
2006: Elliot S. Gershon
2007: Peter McGuffin
2008: Jurg Ott
2010: Susan E. Folstein
2011: Kenneth S. Kendler
2012: Raymond Crowe
2013: John I. Nurnberger, Jr
2014: Margaret Pericak-Vance
2015: Michael Owen
2016: Raymond DePaulo, Jr.
2017: Pamela Sklar * and Marcella Rietschel
2018: Stephen Faraone

Table 4. Cont.

Reich Junior Investigator Award (Began in 2004)
2004: Carol Prescott
2005: Laura Almasy and Nigel Williams
2006: Thomas G. Schulze
2007: Alexander B. Niculescu III
2008: Shaun Purcell
2009: Jonathan Sebat
2010: Elisabeth B. Binder
2011: David Glahn
2012: Danielle Dick
2013: Stephan Ripke
2014: Benjamin Neale
2015: Sarah Medland
2016: Menachem Fromer
2017: Jonathan Mill
2018: Arpana Agrawal
Richard Todd Child Psychiatric Genetics Award (began in 2009)
2009: Robert Althoff
2010: Joseph D. Buxbaum
2011: Danielle Dick
2012: Anke Hinney
2013: Geert Poelmans
2014: Nadine Provencal
2015: Christie Burton
2016: Joseph Buxbaum
2017: Danielle Posthuma
2018: F. Kyle Satterstrom
Gershon Paper of the Year Award
2014: Thomas W. Muhleisen
2015: Michael O'Donovan and Stephen Ripke
2016: Liping Hou, Urs Heilbronner and Franziska Degenhardt
2017: Chi-Hua Chen
2018: Verner Anttila

* deceased.

The ISPG and WCPG continue to be successful for years to come recording progress toward understanding the genetics in a wide range of psychiatric disorders and how to apply research results to better the care of people at risk for or having psychiatric disorders.

CONFLICTS OF INTEREST

The author declares that she has no conflicts of interest.

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