# Toward a Philosophical Approach to Psychiatry

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## *The Writings of Kenneth Kendler*

Edited by

Kenneth S. Kendler and Peter Zachar

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# FOREWORD

## ROBERT FREEDMAN, MD

Kenneth Kendler is a unique intellect in psychiatry. As a psychiatrist, he is devoted to advocacy and the improvement of care for the people in our community who have mental illness. He passionately believes that if we improve the accuracy and rigor of our diagnostic evaluations, we can improve their care. Accordingly, he has been a major contributor to the American Psychiatric Association's *Diagnostic and Statistical Manuals of Mental Disorders* DSM-IIIR, DSM-IV, and DSM-5. What sets him apart from other psychiatrists who are clinicians and scientists is his inquisitive mind that delves deeply into the historical and philosophic basis of today's psychiatry.

Many contemporary philosophers who approach psychiatry reach the conclusion that its basis is at best crudely empirical and at worst totally flawed. They are often intellectual contributors to the current anti-psychiatry movement. Most psychiatrists, if they stop to consider the current philosophical community or at least its most vocal part, dismiss it as the idle speculation of people who have never witnessed the torment of an individual with schizophrenia. Both philosophers and psychiatrists overlook that psychiatry and philosophy share a common root in figures like Spinoza and Nietzsche, whose sufferings and isolation drove their genius in philosophy.

Dr. Kendler went to the philosophical community and their literature, not to confront it, but rather because he was seriously troubled in his own mind by the question of how we establish diagnosis. In the Introductions to the chapters of this book he explains his angst far better than I can recapitulate. Suffice it to say that he worried that without an external root in some sort of reality, psychiatric diagnosis ran the serious risk of being dismissed as either wrong-headed or trivial. As a committed clinical psychiatrist, he could not abide our patients' condition being labeled as trivial. Yet he struggled to see what the justification is for the diagnoses that we use to describe their illness.

This book describes Dr. Kendler's journey to search for the answer. It is twin stories of his philosophical framework to describe the process of

psychiatric diagnosis, and his historical recounting of how it was actually wrought in 19th and early 20th century Germany.

As Editor of the *American Journal of Psychiatry*, I felt fortunate that the *Journal* was able to publish much of this work. Often the *Journal* publishes articles in fields ranging from health care economic to molecular biology, knowing full well that most of our readers, busy clinicians, will not read these articles in detail. Yet, I felt that it was important to all of us in psychiatry to know the scope of efforts being made to push the frontiers of our knowledge further ahead. I was wrong to assume that Dr. Kendler's articles might not be widely read. "The Structure of Psychiatric Science," Chapter 13, was our most widely read Review and Overview when it was published in 2014.

Indeed, many people want to know that our understanding of patients' illnesses is more solidly grounded than 19th century theories and pharmaceutical companies' misinformation. Like Socratic Dialogues, Dr. Kendler's articles are unexpectedly quite readable. Dr. Kendler speaks not only to philosophers and historians, but also to clinicians as well.

In rereading the essays and, for the first time, their new Introductions, I was struck by how much the Introductions to each Chapter add to the value of the essay. In the *Journal* and other scientific publications, Dr. Kendler was not as free to say what he was seeking or what he thought he got right and where he thought he was still uncertain. That disclosure gives the book a fresh, personal perspective that greatly enhances its readability over a collection of previously published articles.

The best introduction to this body of work comes not from my pen, but from Dr. Kendler himself, beginning with the Introduction to Chapter 2, which lays out clearly to the readers what he was seeking. Each successive Introduction becomes the next chapter in a mystery novel, as Dr. Kendler sought out philosophers who could help him construct a basis for understanding psychiatric disorders.

Chapter 8 is pivotal. It resulted from Dr Kendler's sabbatical at the Stanford Center for the Advanced Study of the Behavioral Sciences. For the first time, he acknowledges "a bad case of the philosophy bug." Here the book becomes endearingly human. He had ventured boldly, yet with trepidation, into a field of philosophical inquiry for which he, like most physicians, was not trained. The often-dreaded review process at the hands of Bob Michels, the *Journal*'s action editor, resulted in an unexpectedly positive endorsement of his work, the first time he had received validation. The introduction to the chapter, the work itself, reads with all the freshness of a bildungsroman novel, a journey of discovery and maturation. For a

psychiatric reader, as interested in the development of the author as is in the content, it is an important article.

What would become the major object of his quest appears quickly, in the following chapter, Chapter 9, his intervention into the wave of biological reductionism that had begun with the Churchlands' attempt at a psychology based solely on elementary neurobiology and was then fueled by geneticists who sought to reduce schizophrenia and other mental illnesses to single genes. He continues that line of thought, forming his concept of how illness emerges from its elements, genetic and neurobiological, to become an entity that encompasses all the elements of human life. The approach, which he calls the dappled nature of psychiatric diagnosis, is a framework that he could then exploit in his landmark twin studies to extend the value of the studies beyond the traditional monozygotic-dizygotic twin differences that have long been useful as an indicator of heritability.

For example, one his scientific papers, not included in this book, finds that if a divorced mother has children and takes a second husband, her children's likelihood of becoming criminals is increased if her second husband is a criminal [*American Journal of Psychiatry* 172(6):553-60, 2015]. These family dynamics would seem the stuff of a previous generation of psychiatrists, who saw psychiatric illness primarily as a family disorder. Dr. Kendler's philosophical framework expands his conception of the transmission of psychiatric illness to include both genes and the family environment, both assessed with his characteristic scientific rigor.

The series of ten chapters on this theme of reductionism and emergence reminded me of a thought that I had attributed to the late Leon Eisenberg, although neither he nor I could find the source. The setting is the first biological machine to cure schizophrenia, eerily reminiscent of Viktor Trausk's influencing machine that sometimes appears as a delusion in psychotic individuals. When the patient emerges, cured, Dr. Eisenberg wondered if a clinician would be left in psychiatry to ask the patient, "How are you feeling?" Dr. Kendler's philosophical vision for psychiatry encompasses a psychiatrist who believes that how the patient feels is as important as the cure.

Initially, I thought that the last section of the book would not be well connected to what came before. The last section details Dr. Kendler's love of the 19$^{th}$ century historical roots of psychiatry and especially how Kraeplin's textbooks influenced the course of psychiatry for better and for worse through DSM-5. But Chapter 19 on the fall of Pluto from the planets of the heaven to become just another space rock convinced me otherwise. The chapter ostensibly compares the decision of the International Astronomical Union on Pluto to the decision of the American Psychiatric

Association to remove homosexuality as a diagnosis. In this admittedly witty essay, Ken describes the parallels well: both were in the end arbitrary decisions based on different sorts of observations from the characteristics of the orbit of Pluto to the equal cognitive abilities of gay men. However, he notes a fundamental difference but does not, to my mind, give it the credence it deserves. Robert Spitzer became convinced that homosexuality, a DSM-II diagnosis should not go forward to DSM-III, based on a clandestine meeting with gay psychiatrists. He listened to how they suffered because of the fear of the stigma attached to this diagnosis and, on that basis, he campaigned vigorously for its removal.

The rock feels no pain when it is no longer in the pantheon of planets, but diagnosis is not just a matter of the American Psychiatric Association's authority. Its Board of Trustees must serve a greater mission, to represent the suffering of our patients. That is why we fiercely defend schizophrenia against critics who claim it is a poorly constructed concept or worse, an oppression of those who think differently. As psychiatrists, we have witnessed the suffering of patients whose symptoms we call schizophrenia. And for the same reason we reject the suffering caused by the labeling of homosexuality as a mental disorder. If the Board of Trustees fails to speak for our patients, it loses its authority. That is why the National institute of Mental Health's Research Diagnostic Criteria fails as a diagnosis, despite it's superior ability to capture complex biology. It is not tied to the suffering of people with mental illness.

I had the privilege of serving as Ken's co-chair for the DSM-5 Scientific Review Committee. As one would expect, he was rigorous in requiring that any new change be fully justified by scientific research. But before a final decision was made, he would inquire about how many people might have their condition re-classified and, if we endorsed the change, how it would affect them. Would anyone who was suffering then be denied treatment? He recapitulates our process together in the chapter on premenstrual dysphoric disorder, Chapter 20, when women asserted their suffering that had been overlooked.

His empathy on an epidemiological scale was for me a touching reminder of who we are as psychiatrists. His empathy ties the history of the science of diagnosis to the concept that psychiatry is what emerges from the neuroscience that we need to treat our patients effectively. The neuroscience, as he articulately describes in the middle part of the book, can never describe who our patients are as people or who we are as psychiatrists. His recounting of the 19$^{th}$ century roots of psychiatry becomes alive if we remember that many of this first generation of psychiatrists, unlike most of

us today, lived in the same hospital as their patients. The intimacy of their lives with each other influences the evolution of today's diagnostic criteria.

An Introduction should invite readers to engage in the book. Perhaps this introduction will then be helpful in engaging readers, by demonstrating my immediate engagement. Dr. Kendler invites the engagement and without it, I suspect he would feel that the book had not achieved its purpose.

Robert Freedman MD
Denver, Colorado
February, 2019

# ACKNOWLEDGEMENTS

Both Kenneth Schaffner and John Campbell have, over many years, been generous with their time in guiding me through the wilds of the philosophical literature, which can often confuse and disorient the newcomer. Even more, they would, on occasion, gently suggest alternative approaches when my enthusiasm outran my good sense, or when I was going down blind alleys, typically because of my limited prior background.

Josef Parnas has been my partner, since 2006, in co-organizing five Philosophy and Psychiatry conferences held in Copenhagen. Each of them, in different ways, were wonderful experiences which broadened my philosophical horizons and brought me into personal contact with philosophers interested in things psychiatric. It was in these gatherings that I first met a number of philosophers including Sandra Mitchell, Dominic Murphy, James Woodward, Ian Hacking, Helen Longino and Miriam Solomon whose works I went on to read in depth and was much enriched by. Some have become my collaborators. Finding that such serious thinkers were interested in psychiatric issues in general and, even more remarkably, in some of my own thoughts on these matters, was a deeply satisfying experience.

Peter Zachar has been a co-traveler with me over many of these philosophical roads since we first met in 2003. He has reviewed and provided insightful comments on drafts of a number of the papers reprinted here. The idea of this volume arose first in discussions with him. He has indefatigably pursued this goal and deserves much of the credit for this resulting volume.

My chairman of over 30 years, Joel Silverman, was consistently supportive of my philosophical and historical interests and writings and so I never had to feel that the time spent on these endeavors was stolen from other duties.

Over the course of my career, on both philosophical and scientific fronts, and during the week and on weekends, I have spent much of my free time on my scholarship and other professional activities. Not surprisingly, my wife of more than four decades, Susan Miller, has not always been wildly enthusiastic about these commitments. Despite this, I have been very fortunate to have her consistent caring, support, and co-parenting that,

among other blessings, helped create the fertile ground on which the intellectual efforts contained in this book were built.

Kenneth S. Kendler, March 19, 2019

# I. OVERVIEW

# CHAPTER 1

# THE LIFE AND SCHOLARLY CAREER OF KENNETH S. KENDLER

PETER ZACHAR

## Introduction

Born July 12, 1950, Kenneth Seedman Kendler was the second child of Tracy Seedman Kendler and Howard Kendler, both experimental psychologists. As a college student in the late 1960s, he had the look of a California hippie from sunny Santa Barbara, but his roots go back to New York City and Roslyn Heights, Long Island where he spent the first twelve years of his life.

His parents met at Brooklyn College where their teachers included the social psychologist Solomon Asch and the humanistic psychologist Abraham Maslow (1). Asch encouraged them to pursue graduate studies with the gestalt psychologist Kurt Lewin at the University of Iowa (2). After making the move to Iowa, Tracy completed a master's thesis with Lewin, but she and Howard each completed their doctorates under the supervision of the neo-behaviorist Kenneth Spence. During his own career, Spence became the most cited experimental psychologist of the time (3). Kenneth Kendler was named after Spence.

Spence, associated with Yale University psychologist Clark Hull, is known for promulgating the "Hull-Spence" theory of learning in American Psychology. During the great depression of the 1930s, external funding for research became scarce, but Hull's program continued to be generously funded by the Laura Spellman Rockefeller Memorial Fund (4). This allowed Hull to establish a research paradigm whose adherents, most of them supervised by Spence at Iowa, populated university psychology departments throughout the country. As students of Spence, the Kendlers had prominent academic pedigrees in psychology and were leading figures in the dominant scientific paradigm of the 1940s and 1950s.

In the early 1960s the University of California system was expanding by adding campuses. While on a sabbatical at Berkeley in 1960, Howard Kendler fell in love with California and rather than waiting two years for a position to become available at Berkeley, he agreed to join the faculty at Santa Barbara. Prior to accepting this position, he had been Chair of the psychology department at the University Heights Campus of New York University in the Bronx.

Kenneth Kendler reports that in retrospect, this was not such a good career move for his father. Howard Kendler hoped that the Santa Barbara campus would develop into a prestigious public university like Berkeley, but that did not occur. His attempts to build a celebrated research department at Santa Barbara were not very successful and after the cognitive revolution took hold in American psychology, he was seen as an old-fashioned behaviorist and had difficulty securing funding for his research. This was quite unfair because in the Kendlers' most important scientific paper, they demonstrated that for adult humans, during learning internal representations mediate between stimulus and response and guide responding (5).

Tracy Kendler, however, finally secured at Santa Barbara the academic career she had long sought. Back in New York City, she was a tenured associate professor at Barnard College of Columbia University, but they did not have a graduate program. In California she became a professor of psychology and had the opportunity to train graduate students.

## College in Santa Cruz (1968-1972)

After the move from New York to California, Kenneth Kendler spent a year at Thatcher, an all-male boarding school in the hills behind Santa Barbara. This was not a good fit. He missed his parents. He also had one of his first encounters with anti-Semitism and reports being stunned. The next year he transferred to San Marcos High School and was able to move back home.

At San Marcos he was athletic, obtaining varsity letters in cross country and tennis, and in his last two years was selected for an experimental gifted student program. Classes were small and he received intense instruction in writing from a devoted English teacher. His politics, like those of his parents, were left of center and he was active in the Anti-Vietnam War movement, participating in demonstrations and in a school-wide debate. His main group of friends played together in a jug band. He was the percussion section, playing washboard and spoons.

He decided to attend college at the University of California at Santa Cruz. Only three-years old at the time, the Santa Cruz campus was the

newest, most experimental college in the California system. Organized like Oxford University into clusters of colleges, it emphasized undergraduate education in the liberal arts tradition.

At UC Santa Cruz, Kenneth Kendler was a resident of Cowell College, majoring in religious studies and biology. His interest in religion was especially puzzling to his father. Both Howard and Tracy were secular Jews. In fact, while growing up in the Jewish neighbored of Roslyn Heights, for religious holidays such as Yom Kippur, Kenneth, his older brother Joel, and a handful of Christian children were the only students attending school.

In his junior year of college, Kenneth Kendler participated in a six-month study abroad program in Israel, working at first on a Kibbutz and then later studying at a Yeshiva. The purpose of the Yeshiva was to convert assimilated Jewish youth back to orthodoxy. Kendler, who had also explored Zen Buddhism and still practices daily meditation, was not interested in becoming an orthodox Jew, but at the Yeshiva he developed an abiding interest in studying the Hebrew bible.

The trip to Israel was precipitated by an identity crisis which was resolved when, while still in Israel, he decided he wanted to study medicine. The stress of applying to medical school led to some sleepless nights, in part because Santa Cruz graded all courses pass-fail, and many medical schools treated a pass as a C. However, no one who knew Kenneth Kendler as a student, always sitting in the front of the class and asking a lot of questions, was surprised when he gained admission to medical school at Stanford University.

## Stanford Medical School and Psychiatry (1972-1977)

Tracy and Howard Kendler described how determined Tracy was to be a scientific researcher despite persistent barriers to women pursuing professional careers (6). Kenneth Kendler inherited his mother's determination in every respect, but the difference is that, rather than being closed, doors readily opened for him. Although, as will become evident, most of the doors opened after he took the liberty of knocking on them.

It was not clear to him initially, however, that he would become a researcher. At one point in medical school he briefly considered becoming a primary care doctor, a notion which his then future wife, Susan Miller, considered ridiculous as she knew he was an academic through and through.

He felt out of place at Stanford given that many of his fellow students were from other Ivy League institutions and, prior to college, elite prep schools. Beginning medical school was also psychologically trying because the task was to digest and then regurgitate a massive amount of factual

information, which was a different type of learning than what Kendler had been exposed to in his conceptually-oriented undergraduate education. He found the first semester to be an unsatisfying experience and coped by returning each weekend to the redwoods of the scenic Santa Cruz campus to spend time with Susan, who would herself begin medical school at UCLA the next year.

Stanford offered an option to complete the first two years of medical school over a three-year period, which became very attractive to Kendler after that first semester. When his request to pursue the extended track was granted, he used the extra time to get involved with research.

His first experience with research, however, had occurred many years earlier. When he was in kindergarten, his parents secured a National Science Foundation grant to apply the Hull-Spence theory to child development (6). Tracy developed the measures for these studies. She piloted them on her son and some of his friends and consulted Ken about what kinds of reinforcers a child his age would find most appealing (e.g. Lucky Charms versus M&Ms).

In the Stanford psychiatry department, a former student of his father, Seymour Levine, was doing groundbreaking research on the biology of stress. Kendler approached him about working in his lab, where he learned to put implants into rat hypothalami. Working in Levine's lab, he earned his first publication in a peer reviewed journal (published while he was still in medical school) (7). He approached the psychologist Albert Bandura, also a University of Iowa graduate, to meet with him once a week for a readings course. In addition, he worked at the primate study station in the hills above Stanford where he was trained to rate chimpanzee social interactions. Jane Goodall even made occasional appearances. Susan reports that after he began working with the primates and developed an interest in the problem of other minds, he turned more towards psychiatry.

The first idea he had for his own research study in medical school was a project on religious belief and coping among terminally ill cancer patients. He secured the help of a Stanford faculty member to conduct the study, but the Chair of the oncology department refused them access to the patients.

Growing up at home, Kendler had been exposed to the jargon of learning theory but avoided taking a psychology class in college. The soon to be dominant paradigm of biological psychiatry was in its toddler phase and seemed like a promising pathway to a successful scientific career – and its medical focus made it different from psychology. Indeed, Stanford was on the cutting edge of the new biological psychiatry. Among those he worked with at this time, particularly important were Kenneth Davis and Robert Rubin. Davis was interested in the biology of schizophrenia and later

Alzheimer's disease, eventually becoming the Chief Executive Officer of the Mount Sinai Health System. Rubin became a pioneer in the psychoneuroendrocrinology of affective disorders.

With Davis, Kendler wrote a review paper on the role of cortisol in depressive disorders, also published while he was still in medical school. Rubin ran a lab at Harbor General Hospital affiliated with UCLA where Susan was in medical school. The two of them were now spending time at each other's schools. With Rubin, Kendler published both a book chapter and a journal article. While working in Rubin's lab he decided, with Rubin's approval but without any other consent or supervision, to inject himself with the anti-psychotic drug haloperidol to gauge its effects on levels of the hormone prolactin. He had a strong akathisia reaction which he later described in a letter to the editor in *American Journal of Psychiatry* titled "A medical student's experience with akathisia" (8). For several years afterwards, he was best known as the author of that letter.

Why psychiatry? In part, as already noted, biological psychiatry held the promise for major scientific breakthroughs, but just as important was his fascination with mental disorders themselves. In his rotations he had encountered patients with schizophrenia and mania, as well as a classic psychopath in a prison setting. He was captivated and wanted to understand what could be causing people to be like this. An additional appeal of the field was the broader perspective on humanity that came with studying human behavior and its dysfunctions. Somehow, psychiatry seemed to best combine his college interests in biology and religion.

After he decided to become a psychiatrist, other than an outpatient rotation in psychotherapy with Irving Yalom, he avoided psychiatry rotations for the remainder of medical school in favor of gaining experience in general medicine, where he continued to distinguish himself. At one point, a couple of senior professors approached him and wanted to know why such a bright boy was going to work in psychiatry rather than in a scientifically valid branch of medicine. Kenneth Kendler, however, was determined to join that community of biological psychiatrists who intended to transform psychiatry into a scientifically valid branch of medicine.

## Residency at Yale (1977-1980) and Early Publications

In the mid-1970s, the first year after medical school was called an internship – the completion of which was required to obtain a medical license. Specializing in psychiatry required further training after the internship – which was called the residency. Kendler was accepted into the psychiatric residency program at Yale University.

Although he chose to complete his first two years of medical school in three years, he finished medical school in four and a half years – and residency did not begin until July 1977. For the first six months of 1977, Kendler did a general internship at Waltham Hospital in Massachusetts. He and Susan were married in November 1976 and she moved with him to complete the last months of medical school at Mass General Hospital before entering a Residency in the new specialty of Family Medicine at Hartford Hospital and the University of Connecticut, beginning what she has described as a pattern of being the "trailing spouse" (9).

There are two somewhat contradictory trends to Kendler's residency. The first trend was his fascination with the clinical work, especially for cases involving psychosis. When he had the option to transition away from seeing severely ill patients to working with better functioning outpatients, unlike his fellow residents, he chose to continue following the psychotic patients. He describes his success at helping one of his long-term patients avoid a sustained psychotic break as a peak experience.

While at Yale his two closest resident colleagues were Alan Gruenberg and Peter Kramer. In medical school, Gruenberg had worked with Hagop Akiskal and had extensive experience with the careful assessment of manifest symptomatology – a skill which had recently been re-introduced in the United States by Eli Robins and colleagues at Washington University in St. Louis (10, 11). This was an interest he and Kendler shared. The Yale program still had a strong psychoanalytic component and Kendler's experience with those supervisors was mixed. Unlike, Peter Kramer (of *Listening to Prozac* fame), speculative psychoanalytic ideas did not excite him.

The second trend was his impatience to begin a scientific research career. Yale was also an early leader in the biological psychiatry revolution. At the Connecticut Mental Health Center (CMHC), an entire floor was devoted to caring for patients participating in research studies. Kendler successfully competed for a National Institute of Mental Health (NIMH) grant that funded him to be a half-time researcher for the last 18 months of his residency. Decisively entering the domain of biological psychiatry, he focused on the role of dopamine, working with Robert Roth, Jr. and George Heninger studying rats and Gene Redman studying Vervet monkeys. Roth and Heninger were both psychiatrists and psychopharmacologists. Heninger played a role in the development of molecular psychiatry. Redman became known for his research in support of the cellular repair of neurodegenerative disorders like Parkinson's disease.

In his first six months on the in-patient research unit at CMHC, Kendler was responsible for the care of the patients who were all also research

participants. An important event occurred when one of the senior faculty at Yale, Malcom Bowers, Jr., asked Kendler to write an order for a lumbar puncture for a patient who Bowers wanted to include in a study evaluating the dopamine hypothesis of schizophrenia. Kendler had conducted the initial intake assessment of this patient and knew that he had paranoid delusions, but neither hallucinations nor signs of a thought disorder. When he informed Bowers that the patient had paranoia and not schizophrenia, Bowers responded that he was "close enough." This was an arresting experience for Kendler who thought to himself, "how do you know that it is close enough?"

In one his seminars, students were required to conduct a research project. Kendler chose to spend hours in the basement of Yale New Haven Hospital reviewing clinical, epidemiological, and family studies relevant to the diagnostic validity of paranoia (delusional disorder). To organize his findings, he expanded the Robins and Guze (10) notion of validators into antecedent, concurrent, and predictive validators. The resulting paper, in which he argued that delusional disorder is likely distinct from schizophrenia and does not seem to be a subtype of mood disorder, earned him a publication in the prestigious *Archives of General Psychiatry* (12) (recently renamed *JAMA Psychiatry*).

A decade earlier, Seymour Kety and colleagues began publishing data from their groundbreaking adoption study of schizophrenia using adopted children and their biological and adoptive relatives. Their finding that relatives who were diagnosed with schizophrenia or schizotypal personality disorder were much more likely to be biologically related to an adoptee with schizophrenia was groundbreaking (13). It also helped establish the notion of a schizophrenic spectrum. Kendler wondered what the data from this Danish Adoption Study would say about the prevalence rate of delusional disorder in the biological relatives of adoptees with schizophrenia. So, he wrote Kety who invited Kendler to come to Harvard Psychiatry's McLean hospital and look for himself. He would provide Kendler with the interview data but blinded to who was a relative of whom. Once the diagnoses were complete, Kety would break the blind.

Alan Gruenberg enthusiastically joined Kendler on this project. On select weekends over the next several months they drove to Boston and spent 12 hours on Saturday and 10 hours on Sunday going through piles of charts and re-diagnosing the cases using the recently revised *Diagnostic and Statistical Manual of Mental Disorders* (DSM-III) criteria. Kendler was amazed at how rich the raw interview data were and developed several additional hypotheses while reviewing the files. He describes what they found when the blind was broken as a profound experience for him.

Supporting the notion of a schizophrenic spectrum, 82% of the people they diagnosed with schizophrenia or schizotypal personality disorder were biological relatives of an adoptee with schizophrenia. None of their cases of delusional disorder were biological relatives of an adoptee with schizophrenia, contrary to Bowers "close enough" claim. The work they did in Boston led to multiple publications in the *Archives of General Psychiatry* beginning in 1981- which Kendler found thrilling to write (14-16).

One of these articles, which examined the relationship between anxiety disorders and schizophrenia, was also the basis of Kendler's first conference presentation at an American Psychiatric Association (APA) meeting in San Francisco. While he was at Stanford, he had asked Jack Barchas to do a readings course with him. Barchas was later the editor of *Archives of General Psychiatry* and the Chair of the Department of Psychiatry at the Weill Cornell Medical College. Although he did not have the time to do the readings course, at the APA meeting Barchas came to Kendler's talk and praised him for such a beautifully designed study.

Another connection from Stanford would lead him to leave the Yale residency six months early. Kenneth Davis had been hired to run the psychiatric service at the Bronx VA Medical Center in Mt. Sinai and wanted Kendler to join him to run the research ward and be the chief resident. At this time, Susan was pregnant with their first child, a daughter, and was not in favor of her husband leaving Connecticut six months early. Nor was this looked upon favorably at Yale. But Kenneth Kendler was anxious to begin his research career and was in New York by January to be joined by Susan in June.

## From Biological Psychiatry to Psychiatric Genetics

In July 1980, Kenneth Kendler became an assistant professor in the Mt. Sinai School of Medicine Department of Psychiatry and a Research Associate at the Bronx VA Medical Center. Setting up a rodent lab, a clinical research unit, and running a ward was challenging. Kendler would also end up wanting more autonomy than had originally been negotiated with Davis.

As the project with the Danish adoption study data had been so fulfilling, Kendler wrote Ming Tsuang at the University of Iowa to see if he could do something similar with the data from Iowa 500 and non-500 studies – a 35 year follow up of former psychiatric inpatients and their first degree relatives (17). Tsuang agreed and thus Kendler and Alan Gruenberg began making trips to Iowa City to spend a week at a time going through interviews and assigning DSM-III diagnoses. Interestingly, in some of these

files they came upon notes written by his mother Tracy Kendler who many years before had taken a job doing psychological testing at the University of Iowa Hospitals while working on her PhD because the psychology department would not give graduate assistantships to women (18). The results from the work in Iowa City began to be published in 1985 (19-21).

A 1969 study by William Pollen and colleagues using National Academy of Sciences-National Research Council Twin Registry data found high concordance rates for schizophrenia spectrum symptoms among monozygotic twins. After reading this article, Kendler realized that by the early 1980s they would have a lot more data. He took the liberty of contacting Dennis Robinette at the National Academy of Sciences about doing a follow-up. Robinette agreed to collaborate with him and in 1983 their new analysis led to Kendler's first research article in *American Journal of Psychiatry* (22).

One he embarked on his research career, Kendler had significant success. He secured a Research Career Development award through the Veteran's Administration and a National Institute of Health (NIH) grant. He was publishing many scientific papers with Kenneth Davis. Unfortunately, the research turned out to not be intellectually engaging for him and he began to doubt the potential for work with rodents to inform the treatment of actual patients. It took some time, however, for this to sink in because he was committed to conducting basic science. These side projects in nosology and genetics were fun, but not as respectable as his front line, hard core biological psychiatric work in dopamine neuropharmacology.

In 1982, as he became increasingly aware of his dissatisfaction with his chosen career path, Kendler decided to take a night class offered for adult learners at SUNY Purchase taught by the geneticist Lee Ehrman. He was quite taken by the elegance of the evolutionary theory underlying population genetics. After the course ended, he and Susan were taking the children to California for a family visit and he brought along Douglas Falconer's book on quantitative genetics. Although he did not follow a lot of the mathematics, the clarity of the conceptual basis of genetics was deeply attractive to him especially in comparison to the somewhat arbitrary and to him increasingly boring activity of incrementally collecting facts in the study of neurotransmitters. He was also increasingly disillusioned with the leading etiologic theory driving much of his research – the dopamine hypothesis of schizophrenia. Genetics also seemed to hold a lot of potential for being applied to psychiatric disorders.

After two years at Mt. Sinai, he knew that he did not want to be a biological psychiatrist studying dopamine metabolites in rodents and humans. With his interests and preferences now clarified, he decided to

pursue psychiatric genetics. His wife Susan thought that this would be a temporary intellectual enthusiasm. Complicating matters, their second child, a son, had been born in January 1982 and they now had two children under the age of 3.

Upon returning to New York from California, he informed Ken Davis that he intended to switch to psychiatric genetics. Hoping to keep Kendler there, Davis released him from running the clinical ward. Other than his continuing responsibility for the grants, he now had much more free time to pursue his own interests.

Over the next year he tried to learn all he could. He commuted to Yale to study with the population geneticist Ken Kidd and to Columbia to study with the statistical geneticist Neil Risch, but with his lack of training in mathematics, he knew that he could not apply these ideas to psychiatric disorders on his own. It became apparent that he needed more intensive training with experienced geneticists and at the end of the year he informed Ken Davis that he intended to leave.

At this time, he was also struggling with some of the data from the National Academy of Sciences-National Research Council Twin Registry for the project with Robinette. He read a paper written by an Australian statistical geneticist named Nick Martin that seemed relevant to his problem. Responding to a letter from Kendler, Martin mentioned that his own mentor, Lindon Eaves, had just moved to Virginia from Oxford University and if Kendler needed further help, Eaves would be the best person to contact.

Washington University in St. Louis was a leading center for psychiatric genetics in the U.S. and the logical place for Kendler to target for his next faculty position. His visit there, two weeks after receiving Nick Martin's letter, was not what he had hoped. The position available to him would be to run Theodore Reich's genotyping lab, and the package that the Chair of psychiatry, Samuel Guze, was willing to offer him did not allow enough research time or autonomy. While in St. Louis, Kendler took the opportunity to meet with the behavioral geneticist Irving Gottesman who told Kendler to not take the position at Washington University. "They will be more interested in getting work out of you than helping you with your career," said Gottesman - "and besides there is an absolutely brilliant guy that no one knows about yet who you should look up. His name is Lindon Eaves and he just moved to Virginia Commonwealth University."

## Richmond, the Virginia Twin Registry and the Roscommon Family Study of Schizophrenia

Ken, Susan, and their two children moved to Richmond, Virginia in 1983. Susan thought that this detour to the South would be a temporary position before moving back to California. As of 2019, they are still in Richmond.

Kendler was warned by colleagues to not make this move. There was very little research coming out of the Department of Psychiatry at the Medical College of Virginia/Virginia Commonwealth University School of Medicine. Kendler's colleagues opined that choosing Virginia Commonwealth University (VCU) and Eaves over Washington University and Reich could ruin his promising career. But the draw of Lindon Eaves was too much to resist. For one, Eaves had what Kendler calls "a sparking intellect." He completed his degree in England at the University of Birmingham which was a world leader in statistical genetics (23). Eaves was also an ordained Anglican Priest, and shared Kendler's interest in religion.

By the time Kendler arrived, Nick Martin had joined Eaves from Australia and soon thereafter, they were joined by the behavioral geneticist Andrew Heath who had studied under Eaves at Oxford. Nick Martin stayed until 1986, after which they would be joined by Michael Neale. Neale came from the University of London where his dissertation advisor was also a graduate of the Birmingham biometric school.

The Chair of the psychiatry department, Robert Freidel, realized that a rising star had dropped into his lap and found enough money to hire Kendler as associate professor on a three-year contract until he could obtain external funding. After running an inpatient unit for two to three months a year, his time was his own. He spent most of it working in little cubicles learning from his new colleagues and felt very lucky as they were generous with their time, introducing him to the theoretical and practical side of statistical genetics.

In this first year at VCU, Kenneth Kendler began working on two long term projects upon which a good deal of his early scientific reputation would be based – one utilized the Virginia Twin Registry and the other was the Roscommon family study of schizophrenia.

### The Virginia Twin Registry

The Virginia Twin Registry was established by Walter Nance and Linda Corry in the mid-1970s. A comprehensive record of twin births in the state, the registry offered Kendler the opportunity to draw large samples from a