

# The Debate Between Two of the Founders of American Psychiatric Genetics, Aaron Rosanoff and Abraham Myerson, on Mendelian Models for Psychiatric Illness

1911–1917

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**Abstract:** In 1911, Aaron Rosanoff published among the first pedigree studies of psychiatric illness, and the first ever in the United States, claiming that the neuropathic constitution was transmitted in as a Mendelian recessive disorder. In 1917, Abraham Myerson harshly critiqued that study, focusing on the very wide phenotypic definition of neuropathic constitution. Here, I describe Rosanoff and Myerson's backgrounds, the details of Rosanoff's study, and Myerson's critique and put this controversy in the context of the history of psychiatric genetics, emphasizing four themes: a) the close interrelationship between psychiatric diagnosis and models of genetic transmission, b) the strong attraction of Mendelian models to psychiatric geneticists after their 1900 rediscovery, c) the controversy about whether familial transmission of psychiatric illness is largely homogeneous or heterogeneous, and d) the methods taken by researchers to the problems of psychiatric genetics that typically emerged as part of their broader approach to the nature of psychiatric illness.

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In two articles published in the *American Journal of Insanity* (renamed the *American Journal of Psychiatry* in 1921) in 1911 and 1917, two of the most prominent American psychiatric geneticists in the first decades of the 20th century—Aaron Rosanoff (1878–1943) and Abraham Myerson (1881–1948)—debated the value of Mendelian models for psychiatric illness. The subject of the controversy was Rosanoff's analyses—conducted in 72 pedigrees—of the pattern of genetic transmission for what he termed the “neuropathic constitution” (Rosanoff and Orr, 1911a). The study represented the first detailed Mendelian analysis of psychiatric disorders ever reported in the United States and among the first in the world. An important background figure in this debate, and then a close collaborator of Rosanoff's, was Charles Davenport (1866–1924), who was an influential figure in the history of human genetics in the United States during this period (MacDowell, 1946; Rosenberg, 1961). I review both sides of this controversy with added italics to the quotes in places for emphasis starting with Rosanoff.

## AARON ROSANOFF

Rosanoff was born in Belarus in 1878 from a Jewish family and emigrated to the United States at the age of 13 (Mehler, 1988). He received his MD from Cornell University in 1900 working as a physician at Kings Park State Hospital from 1901 to 1922, rising eventually to the role of clinical director. From 1922 until his death, Rosanoff worked at

the Los Angeles Psychiatric Diagnostic Clinic and was appointed in 1933 as California's State Director of Institutions and State Commissioner of Lunacy.

While working at Kings Park, Rosanoff collaborated extensively with Charles Davenport at the Eugenics Record Office in Cold Spring Harbor and went on to be a member of the American Eugenics Society Advisory Council from 1923 to 1935, a member of the editorial board of the *American Journal of Psychiatry*, and editor of a popular psychiatric textbook (Rosanoff, 1920).

We begin by reviewing Rosanoff's article published in 1911 (Rosanoff and Orr, 1911a), entitled “A study of heredity of insanity in the light of the Mendelian theory.” The potential importance of this work to Davenport is illustrated by the fact that it was reprinted in its year of publication by the Eugenics Record Office at Cold Spring Harbor, then under Davenport's direction (Rosanoff and Orr, 1911b).

Writing barely more than a decade after the rediscovery of Mendel's work and 5 years before the classical Mendelian-informed sibling study of dementia praecox by Rüdin in Kraepelin's clinic in Munich, Rosanoff and his coworker Florence Orr (hereafter R&O) began by summarizing the standard prior approach to genetic studies in psychiatry—dividing the hospitalized patients into those with and without a hereditary predisposition (Kendler, 2021; Kendler and Klee, 2020, 2021b). They then quoted from Kraepelin's seventh edition textbook (Kraepelin, 1903) his summary of the decades of prior research on this topic: “We must therefore regard the statistics of heredity in insanity merely as facts of experience without finding in them the expression of a ‘law’ which should hold in every case.”

Referring to the rapid expansion of work on human heredity in the previous decade, which has provided promise of such a “law,” they then write that recently:

...it has been shown that human heredity, at least as far as certain traits are concerned, is subject to *general biological laws*. Special mention may be made of color of eyes, color of hair, form of hair, brachydactyly, some forms of cataract, and retinitis pigmentosa, as human traits which have been shown to be transmitted from generation to generation in accordance with the Mendelian theory. (Rosanoff and Orr, 1911a, p 222)

Would these laws, they wondered, apply to “insanity and *allied neuropathic conditions*?” We should note the specific way in which R&O framed their question: “... the present study has been undertaken with a view to determining whether indeed *the neuropathic constitution* is transmitted in the manner of a Mendelian trait” (Rosanoff and Orr, 1911a, p 222). That is, R&O do not follow the approach that would, over the ensuing decades, dominate studies applying Mendelian models to psychiatric illness—attempts to uncover the mode of transmission of specific psychiatric disorders, most commonly dementia praecox (Rudin, 1916) or manic-depressive insanity (Hoffmann, 1921; Kusters et al., 2015). Rather, they used a far wider phenotypic category initially

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popularized by French psychiatrists in the mid-19th century and later by the Charcot school, in part as a result of their interest in degeneration theories (Dowbiggin, 1991). The French term for this construct—*famille neuropathique*—bears obvious resemblance to the term adopted by R&O (Kendler and Klee, 2021a). Rosanoff was not, however, the only investigator collecting pedigrees at this time to investigate the pattern of “neuropathic inheritance” (Mott, 1914).

R&O proceeded to a basic review of Mendelian theories, outlining the six expected mating types of a risk locus for which they label D to be the wild-type allele and R the risk allele for the neuropathic constitution: a) RRxRR, b) DRxRR, c) DDxRR, d) DRxDR, e) DDxDR, and f) DDxDD. They note that, if the neuropathic constitution is transmitted as a fully penetrant recessive condition, rates of affection in the offspring should equal a) 100%, b) 50%, c) 0%, d) 25%, e) 0%, and f) 0%.

They then describe the methodology of their study. From patient samples available to them at Kings Park State Hospital, in Kings Park New York, R&O a) excluded patients with clear exogenous causes (*e.g.*, trauma, alcoholism, or syphilis), b) included only families with at least two generations of affected individuals who resided in the United States and were “accessible to investigation,” and c) included subjects on whom they were able to gather sufficient information to distinguish “neuropathic states from the normal state and in the case of a neuropathic state to identify, if possible, the special variety” (Rosanoff and Orr, 1911a, p 226). They summarized their approach to the field work:

Such diagnosis often enough presents great difficulty when there is opportunity for direct observation, but when it has to be based upon observations of untrained informants related from memory the difficulty is, of course, greatly increased and with it the chance of error. We have endeavored to reduce the amount of error from this source by interviewing personally as many as possible of the nearest relatives of the patients whose pedigrees were being investigated, and by the practice of tracing almost all the families not farther than to the generation of grandparents... (Rosanoff and Orr, 1911a, p 226)

It is important to note the novelty of this methodology, which was based on developments by Davenport and his team at Cold Spring Harbor. The vast majority of the prior extensive literature on the influence of familial factors on risk for mental illness had used information contained in hospital records, occasionally supplemented by additional information from relatives or physicians (Kendler, 2021). To my knowledge, the only prior extensive pedigree study of psychiatric illness that attempted to interview as many members as possible was conducted by Ludvig Dahl in Norway in the mid-19th century (Dahl, 1868; Porter, 2018) and was, of course, not concerned with Mendelian transmission patterns. However, the field workers employed by Rosanoff were not physicians but were trained for their work.

R&O then provided information about their field work and analytic assumptions. Most importantly, they note that it “appeared early in the course of our study that the normal condition was dominant over the neuropathic condition” (Rosanoff and Orr, 1911a, p 226). When an affected individual had normal parents, they preferred to support the evidence that the parents were heterozygote carriers “on the basis of the existence of neuropathic manifestations in the ancestors or collateral relatives of the subject” (Rosanoff and Orr, 1911a, p 226). However, if there was no such information, they still assigned the parent as a DR heterozygote. However, to their credit, R&O presented the results of these “assumed” heterozygote parents separately from those parents where they derived the presumed heterozygote status from other pedigree data.

R&O then summarized their pedigree sample: “the entire material now includes the pedigrees of seventy-two families, representing two hundred and six different matings, with a total of one thousand and ninety-seven offspring” (Rosanoff and Orr, 1911a, p 227). Their key Table II where they report the number of offspring observed in each

of their mating types and the number of who were diagnosed as neuropathic versus those predicted by a fully penetrant recessive model can be seen in Table 1.

A review of the table demonstrates, for mating types b, c, d and e, a striking similarity between the expected and observed number of affected individuals under their assumption that the neuropathic constitution is transmitted as a fully penetrant autosomal recessive condition. In the observed mating types b and d, where the imputation of parental genotype was based on information from grandparents or collateral relatives, the observed and expected cases were quite close. However, in those matings where the parental genotype was inferred on the basis of the children, the fit was considerably poorer. R&O added that many of the anomalous unaffected offspring from mating type a could arise from the fact that 8 of the 10 of them were younger than 23 years old and could manifest the neuropathic trait later in life.

It is noteworthy that Rosanoff’s effort to evaluate Mendelian was based on segregation patterns ascertained through parents for which no proband correction is necessary. No statistical test was used even though the chi-square goodness-of-fit statistic had been developed Pearson in 1900 (Pearson, 1900). The quality of fit of the observed to the expected data, for R&O, is self-evident. In reporting these results, R&O were not hesitant in their conclusions (*italics in original*):

As is shown in the table the correspondence between theoretical expectation and actual findings is in some cases’ exact and in all cases remarkably close. *It would seem, then, that the fact of the hereditary transmission of the neuropathic constitution as a recessive trait, in accordance with the Mendelian theory, may be regarded as definitely established.* (Rosanoff and Orr, 1911a, p 228)

A challenging feature of this study is understanding their phenotype of focus—the neuropathic constitution. Here is R&O’s main description, putting it in the context of the debate within psychiatric genetics, dating back to the early 19th century over whether psychiatric disorders of close relatives tend to be of the same (*i.e.*, “similar heredity”) or more often quite different syndromes (*i.e.*, “dissimilar heredity”) (Kendler, 2021; Kendler and Klee, 2021b).

Heretofore we have dealt with the neuropathic constitution as a unit, comparing it with the normal condition... The phenomenon of dissimilar heredity has, indeed, in the opinion of some cast a doubt upon the validity of conclusions which are in part based upon the assumption of the existence of an essential relationship between the most diverse clinical neuropathic manifestations. It must be admitted that the burden of proof rests upon those who assume that imbecility, epilepsy, deteriorating psychoses, periodic psychoses, paranoic conditions, involuntional psychoses, the slighter psychopathic states, and certain eccentricities are all etiologically related. (Rosanoff and Orr, 1911a, p 229)

Table 2 lists the brief diagnostic descriptions of all affected members of 10 of the 73 pedigrees, selected at random, and which contained 73 affected individuals. Nearly every family contains at least one individual with severe mental disorder that resulted in hospitalization. Figure 1 contains two such example pedigrees and the legend explaining the meaning of the various symbols used.

The diversity of individuals with a neuropathic constitution is substantial. Among the 73 affected individuals in these 10 pedigrees, the following are included: 21 described as nervous, 13 as eccentric or queer, 7 as alcoholic, 6 as high-strung, 4 with dementia praecox, 4 with manic-depressive insanity, 4 as imbecile or feeble-minded, and 1 as microcephalic. Several had short vignettes, presumably provided by informants including “visionary, had no idea of the value of money, always trying big schemes, became a complete wreck from drink,” “awful temper,” and “crazy, fits of temper, gets wild; violent headaches.”

**TABLE 1.** Results of Mating Types in the Analysis of Rosanoff and Orr

Mating Type	No. Matings	No. Offspring	Died in Childhood	Not Available	Neuropathic		Normal	
					Observed	Expected	Observed	Expected
a. RRxRR	17	75	11	0	54	64	10	0
b. DRxRR observed	37	216	46	1	84	84.5	85	84.5
b1. DRxRR assumed	56	284	20	4	106	130	154	130
c. DDxRR	14	61	13	3	0	0	45	45
d. DRxRR observed	7	34	5	0	8	7.25	21	21.75
d1. DRxRR assumed	55	335	39	3	99	73.25	194	219.75
e. DDxDR	20	92	12	3	0	0	77	77
f. DDxDD	0	0	0	0	0	0	0	0
Totals	206	1097	146	14	351	359	586	578

R&O provided seven conclusions in their study. The first begins “The neuropathic constitution is transmitted from generation to generation in the manner of a trait which is, in the Mendelian sense, recessive to the normal condition” (Rosanoff and Orr, 1911a, p 259). They then provide detailed summaries of what would be expected from various mating types based on Mendelian theory, the following of which is a typical example where both parents are heterozygotes:

Both parents being normal, but each with the neuropathic taint from one grandparent, one-fourth of the children will be normal

and not capable of transmitting the neuropathic make-up to their progeny, one-half will be normal but capable of transmitting the neuropathic make-up, and the remaining one-fourth will be neuropathic. (Rosanoff and Orr, 1911a, p 260)

They then commented on the diversity of clinical symptoms of affected individuals within the same family.

Among the actual results from such matings, the following have been met with:

- a. Brothers and sisters with clinically identical neuropathic manifestations.

**TABLE 2.** Descriptions of Individuals Affected With Neuropathic Traits in 10 Representative Pedigrees for the Rosanoff and Orr Study

Chart Number/No. Affected Persons	Description of Affected Individuals by Pedigree Number
XV/5	1. Nervous, little things bothered her, worried a great deal; her daughter was nervous and melancholy. 3. Excitable, nervous, worries. 4. Nervous temperament; easily excited; has “weak spells.” 6. Dementia praecox, paranoid, in state hospital. 7. Had “nervous hysteria” when his sister died, had hallucinations of sight and hearing; was disturbed and had to be restrained.
XVIII/4	1. Deaf and dumb imbecile. 2. Sunstroke affected his mind, became childish and foolish. 3. Nervous temperament, fidgety. 4. Allied to manic-depressive insanity, in state hospital
XXI/6	1. High strung, excitable. 2. “Awful temper.” 5. Nervous breakdown early in life, unable to work, recovered. 6. Dictatorial, abnormally selfish. 7. Very queer, lives alone, boards cats for living. 8. Allied to manic-depressive insanity, in state hospital.
XXIX/3	4. Epilepsy, in state hospital. 5. Seems to have lost interest in life; when interviewed would say only “I know nothing more than sister told you.” 6. Moderately alcoholic, never settled down to anything, but roamed around all his life until he died of pneumonia at the age of 62 years.
XXX/11	1. Alcoholic. 2. Feeble-minded. 3. Feeble-minded. 4. Hypochondriacal, had nervous prostration. 6. “Visionary, had no idea of the value of money, always trying big schemes, became a complete wreck from drink.” 7. Eccentric. 8. Allied to manic-depressive insanity, in state hospital. 9. “Visionary, unsound, goes wild in arguments, imagines he owns everything.” 10. “Crazy,” fits of temper, gets wild; violent headaches. 11. Dementia praecox, paranoid, in state hospital. 12. Microcephalic, defective, died in infancy.
XXXVIII/13	1. Died insane at an advanced age. 2. Eccentric. 3. Died insane; son also died insane in an asylum. 4–7. Eccentric, very queer. 8–10. Eccentric, alcoholic. 11. Eccentric, “very queer. 12. “Peculiar.” 13. Manic-depressive insanity, in state hospital.
LV/8	1. “Worrier.” 2. Nervous temperament, fidgety, depressed spells, was in sanitarium. 3. Nervous breakdown, “hysterical” a few years ago, recovered. 5. Nervous temperament, worries, at times pessimistic, considered queer though bright. 6. Nervous temperament, worries. 7. Insane, depressed, “religious mania,” in state hospital four months, recovered. 8. Insane, in state hospital about six years, onset after birth of sixth child; imagines he is a detective and has immense treasures. 9. Dementia praecox, paranoid, in state hospital.
LIX/3	1. Feeble-minded. 2. Queer, never saw neighbors, stayed in the house, kept doors and windows locked. 3. Dementia praecox, in state hospital.
LXII/12	1. High-tempered, excitable, impulsive. 2. High-strung, excitable, alcoholic. 3. Alcoholic, daughter high-strung. 4. Extremely nervous, eccentric. 5. Daughter has nervous temperament, fidgety, easily excited. 6. High-strung, periodically alcoholic. 7. Had nervous prostration eleven years ago, lasted 2 years, never fully recovered. 8. Alcoholic, wanderer. 9. High-strung, nervous temperament. 10. Very excitable, high-strung. 11. Constitutional inferiority, in state hospital. 12. Fidgety, cannot keep still.
LXVI/8	2. Eccentric, very suspicious. 4. Nervous, irritable, quick-tempered; suffers from neuralgia. 5. Very eccentric, suspected wife of trying to poison him, later suspected others as well. 6. Insomnia for 2 years during menopause, extremely nervous. 7. Nervous, quick-tempered. 8. Very irritable, nervous, quick-tempered. 9. Very irritable, nervous, quick-tempered. 11. Constitutional inferiority, in state hospital.

"In all charts the following symbols have been employed: a square indicates a male subject; a circle indicates a female subject; □ or ○ = normal subject with normal progeny; ⊠ or ⊙ = normal subject without progeny; ■ or ● = normal subject with neuropathic progeny; ▣ or ● = neuropathic subject; ⊠ or ⊙ = subject died in childhood; ⊠ or ⊙ = data unascertained. The type of mating is in each instance indicated by a small letter: a, b, b<sub>1</sub>, c, d, d<sub>1</sub>, e, as in Table II.

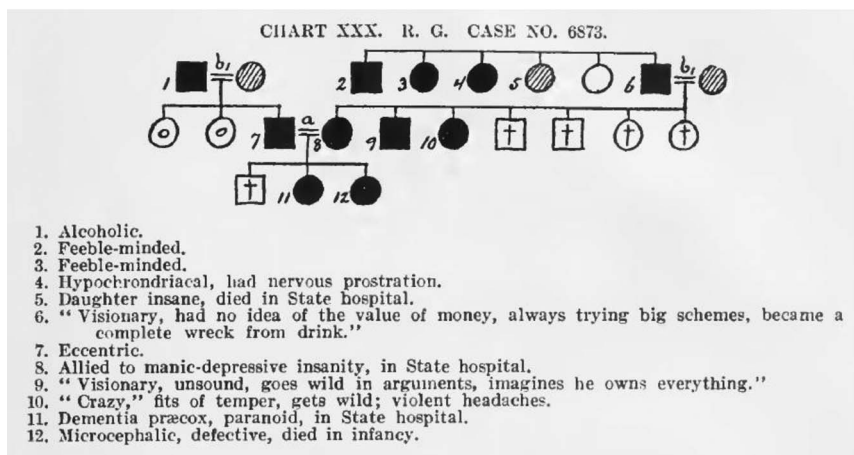
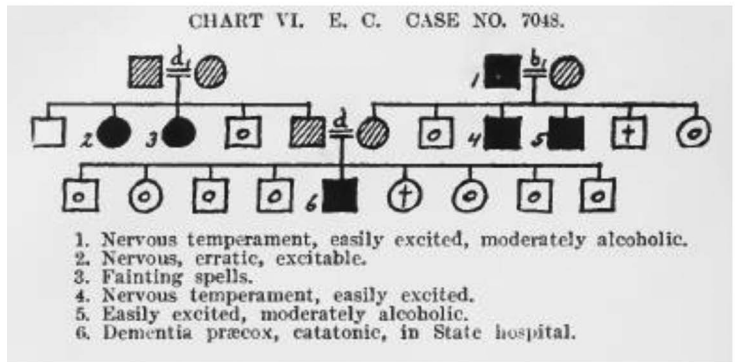


FIGURE 1. The legend and two representative pedigrees from the Rosanoff and Orr 1911 paper.

- b. Psychosis in one subject and peculiar or abnormal disposition, but no actual psychosis, in brothers or sisters.
- c. Psychosis in one subject and isolated but clinically related symptoms in brothers or sisters; we find with particular frequency dementia præcox = fainting spells or convulsions in childhood.
- d. Psychoses clinically not known to be related: senile deterioration = peculiar hysteriform psychoses.

They closed with estimates that approximately one fourth of individuals with a neuropathic constitution are psychiatrically hospitalized; the phenotype is seen in 1.5% to 2.0% of the general population, but 30% "carry the neuropathic taint from their ancestors."

**ABRAHAM MYERSON**

Myerson was born in Lithuania in 1881, the son of a Jewish schoolteacher who emigrated to the United States in 1885, soon sending for his family when Myerson was 5 years old. They lived first in Connecticut and then moved to Boston where he attended public schools. Myerson first went to the College of Physicians and Surgeons of Columbia University and later Tufts Medical School, graduating in

1908. He completed his residency in neurology at St. Louis University, returning to Boston in 1912 to join the first group of residents at the newly opened Boston Psychopathic Hospital. From 1914 to 1918, he served as the clinical director and pathologist at Taunton State Hospital.

In 1927, Myerson became the director of research at Boston State Hospital, where in 1933, a new laboratory was built for him with funds provided by the Rockefeller Foundation. In 1935, he was appointed professor of clinical psychiatry at Harvard Medical School in recognition of the accomplishments in his research. In 1940, he became professor emeritus.

During the first decades of the 20th century, the eugenics movement in the United States became prominent and widely supported by lay and professional groups (Kevles, 1985). Unlike Rosanoff, Myerson was not supportive of many of the goals of the eugenics movement and specifically disagreed with involuntary sterilization of the "feeble minded" and mentally ill, often favored by Eugenicians at that time.

Myerson published two important psychiatric genetic articles, based on family data collected through the records of Taunton State Hospital, in the *American Journal of Insanity* in 1917–1918 (Myerson, 1917, 1918). It is the first of those articles that contains a critique of Rosanoff's early article (Rosanoff and Orr, 1911a) and begins as part of a review about the theory of the "polymorphism of insanity":

The classical doctrine on the transmission of insanity is that of the French school...who evolved the doctrine of the polymorphism of insanity [which]...affirms, first, that all forms of mental disease and a large part of nervous disorders, together with some constitutional states, are various and interchangeable manifestations of hereditary degeneracy. Thus, the central doctrine assumes that such varied diseases as idiocy, cretinism, moral insanity, hebephrenia, catatonia, mania, melancholia, involution and senile diseases, neurasthenia, hysteria, epilepsy, criminality, and eccentricity in all its thousand and one forms, are not really separate conditions but merely manifestations of one condition. (Myerson, 1917, pp 356–357)

After reviewing other French and German authors' views of the subject, he notes

In America the question of polymorphism has scarcely been considered.... [but] Davenport and his co-workers and Rosanoff and his have contributed the most to the subject - Davenport to the question of feeble-mindedness and epilepsy and Rosanoff to clinical psychiatry. These two writers have worked entirely from the standpoint of Mendelism, and their efforts seem to me to be directed not so much to discover the laws of the transmission of insanity as to fit the facts to Mendelian theory. To do this with any show of plausibility it has been necessary to divide mankind into two types—the normal and the neuropathic. The latter...includes a list which starting from A proceeds alphabetically - apoplexy, alcohol, blindness, Bright's disease, criminality, cancerous, choreic, cripple, and so on through the various letters, including paranoia, locomotor ataxia, tuberculosis, tumor, and vagrant! All these varied diseases are to be considered as dependent upon the absence of a unit determiner and therefore the "neuropathic" constitution is to be considered as a unit character from the Mendelian standpoint. This is really *polymorphism with a vengeance but disguised as Mendelism*. (Myerson, 1917, pp 359–360)

The tone is sharply critical, the most pointed claim being that Rosanoff (following Davenport) sought a phenotype that might fit Mendelian theory rather than objectively studied, without preconception, the genetics of major psychiatric disorders. Myerson continues:

The laws of Mendel have not been shown to apply for any single normal human character of simple type, except perhaps eye color. To assume then that the vast range of the psychoses (the feeble-minded, the epileptic, character anomaly, criminality, and neuroses) is related to a unit determiner or group of determiners acting as a unit is, to say the least, premature. Moreover, to relate the varying picture of normality to a unit group is at present presumptuous, knowing as we do that normality is an abstraction rather than an entity. (Myerson, 1917, pp 360–361)

## DISCUSSION

This story of scientific controversy, occurring at the origins of systematic psychiatric genetics research in the United States, is of historical interest because it illustrates four key themes in the history of the discipline, which have continued to appear and reappear over its more than 200-year history. First, our debate demonstrates how, in psychiatric genetics, genetic and diagnostic models for psychiatric illness are closely and often irrevocably intertwined. This interdependence is well illustrated by the nature of Myerson's rejection of Rosanoff's results. His negative evaluation was not focused on the genetic model and how it was evaluated. Rather, his criticisms were almost entirely of the viability of the phenotype of neuropathic constitution. Myerson was saying, in essence, that even if the statistical model for a Mendelian recessive fitted the data well, the proposition that such a diverse group

of complex phenotypes could arise from a single inherited unit was too implausible to be worth serious consideration.

Interestingly, in the same year that Myerson was critiquing Rosanoff's Mendelian model for mental illness, Eugen Bleuler, best known for the renaming of dementia praecox as schizophrenia (Bleuler, 1911), wrote an essay criticizing Ernst Rüdin's Mendelian model for dementia praecox on similar grounds (Bleuler, 1917; Kendler, 2020). Bleuler writes (in translation [Kendler, 2020]):

The first basis of a heredity study should be the determination of the concept and the extent of the feature [being studied] which here is the psychosis. But it is precisely these norms that are problematic in mental illnesses and, conversely, should be determined by heredity. Rüdin first demonstrated his method of working by means of the example of dementia praecox, because he believes that this psychosis can be determined with the greatest certainty. I am of the opposite opinion. I think that dementia praecox is a psychosis [the boundaries of] which is most difficult to determine. (Bleuler, 1917, p 24)

He goes on to note that Rüdin's proposed Mendelian model—two-locus recessive—based on a risk of illness in siblings approaching the expected 0.0625% (or 0.25<sup>2</sup>) is entirely dependent on his narrow Kraepelinian view of dementia praecox. Applying his own broader concept of schizophrenia would, he argues, result in quite different estimated recurrence risks and, hence, Mendelian model. Most disorders in medical genetics—including most of those phenotypes first shown to have Mendelian transmission—have unambiguous phenotypic boundaries, so the results of genetic modeling rest on a relatively firm diagnostic foundation. However, this is not the case, to this day, for psychiatric illnesses, where major debates continue to define the limits of key diagnostic categories such as schizophrenia, bipolar illness, or depression.

Second, this story illustrates the strong (and continued) attraction of Mendelian models to psychiatric geneticists. The simplicity and potential reductive power of these hypotheses, along with the prestige and scientific credibility that such discoveries would convey upon the young field of psychiatric genetics, were hard to resist. Rosanoff's mentor and collaborator, Davenport, was a Mendelian "zealot" who proposed Mendelian models, based on pedigree data collected using the same methods as R&O, for a range of disorders and traits including outbursts of temper (dominant) (Davenport, 1915a), the wandering impulse (sex-linked recessive) (Davenport, 1915b), and temperament (two-locus model) (Davenport, 1915b). With the first successes of human linkage analyses with Huntington's chorea in 1983 (Gusella et al., 1983), the psychiatric genetics community again saw a burst of activity seeking to verify simple Mendelian models for schizophrenia and bipolar disorder, which, after prominent positive reports (Baron et al., 1987; Egeland et al., 1987; Sherrington et al., 1988), ended in a series of demoralizing nonreplications. Only with the rise of genome-wide association studies—with the undisputable evidence for the highly polygenic structure for key psychiatric disorders—have the dreams of finding "the gene for" major psychiatric disorders finally faded.

Third, as noted above, a major debate in 19th psychiatric genetics is whether psychiatric disorders are largely transmitted homogeneously within families (*i.e.*, like-predicts-like) or whether disorders within close relatives are more frequently heterogeneous, suggesting that the familial vulnerability to illness is quite broad and syndromally nonspecific (Kendler, 2021). This debate is at the core of the disagreement between Rosanoff and Myerson. Indeed, Rosanoff adopts the position of the Charcot school in the late 19th century that postulated one of the more extreme models of heterogeneous familial transmission. Myerson, by contrast, finds such a position highly implausible. This debate is still quite active in the Psychiatric Genetics of the 21st century, where molecular genetic evidence of sharing of many risk alleles between schizophrenia and bipolar disorder has resulted in calls for a

repudiation of Kraepelin's diagnostic framework (Craddock and Owen, 2010). Others have proposed a “P-factor” for psychopathology that reflects a broad risk to virtually all forms of psychiatric illness (Caspi et al., 2014) and that can be viewed as a something approaching a modern incarnation of the “neuropathic constitution” of Charcot and Rosanoff.

Fourth, despite both being Jewish emigres from Europe, Rosanoff and Myerson had different perspectives about the role of genetics both in human society more broadly and in psychiatry more specifically. This illustrates another enduring theme in the history of psychiatric genetics—that the particular conceptual and/or analytic approach to psychiatric genetics taken by individual investigators typically emerged as part of their broader approach to psychiatric illness and indeed to their understanding of sources of human differences more generally. Rosanoff was closely associated with the US Eugenics movement in the early 20th century. In a short review of his study published in *JAMA* in 1912 (Rosanoff, 1912), in a section entitled “Heredity and Practical Eugenics,” he noted the possible increased risk in the population for the neuropathic constitution. His attraction to Mendelian models continued for some years. In the fifth edition of his psychiatric textbook, published in 1920 (Rosanoff, 1920), he wrote, in the introductory chapter on etiology of psychiatric illness, “According to the assumption that most of the inheritable mental disorders are, like the trait of blue eyes, transmitted in the manner of Mendelian recessives...” (Rosanoff, 1920, p 5), and then presents his table from the 1911 study showing how well met that assumption was. In 1935, in his later twin study of manic-depressive illness, Davenport and colleagues harkened back to Mendelian models of temperament published decades earlier by his collaborator Davenport (Davenport, 1915b), proposing a “...mode of inheritance of manic-depressive psychoses, in which the existence of a cyclothymic factor (C) in the autosomes is assumed, and an activating factor (A) in the X-chromosomes” (Rosanoff et al., 1935, p 760). Davenport was generally comfortable with reductionist approaches that explained the etiology of psychiatric disorders solely on the basis of Mendelian genetic units.

Myerson, by contrast, was skeptical of eugenic goals and instead put considerable emphasis on the importance of adverse environmental conditions, particularly the social environment, on risk for insanity (Myerson, 1925). He had a more pluralistic view about the etiology of psychiatric illness that supported his strong and consistent skepticism about Mendelian models. Indeed, 8 years after his key article, we review above (Myerson, 1917), in his book *The Inheritance of Mental Diseases* (Myerson, 1925), the vigor of his attack on the work of Rosanoff and Davenport had not diminished. He writes:

Davenport, the director of the Eugenics Laboratory at Cold Springs Harbor, New York, an eminent biologist, whose attention to eugenics has received world-wide attention... is a Mendelian and I am frank to say that he seems to be determined to find in the mental diseases a Mendelian significance and postulates in advance conclusions which he is able to verify. (Myerson, 1925, p 64)

Much later in the book, he recruits the then leading American biologist, Edwin Conklin, to aid his attack:

Recent studies have shown that the development of such simple characteristics as coat color (Wright), eye color (Morgan) and sex... are exceedingly complex and that very many hereditary factors may be involved in the process. When we come to the development of more complex things such as temperament, feeble-mindedness, insanity, personality we are dealing with the most complex phenomena in all he world... if eye color in the fruit-fly is dependent upon a large number of inheritance factors as Morgan and his pupils have shown... how much more probably is it that epilepsy... and insanity are dependent upon a still large number of inheritance factors, as well as an unnumerable number of

environmental causes? We may be sure the when the whole “alphabet of degeneracy from alcoholism to wander-lust” is attributed to the lack of a single hereditary factor, there has been a pitiful failure to recognize the complexity of the phenomena in question. (Myerson, 1925, pp 278–279)

## DISCLOSURE

The author declares no conflict of interest.

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