

METHODOLOGY OF TWIN STUDIES

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## The Twin-Family Method in Psychiatric Genetics Illustrated from the Investigations of Franz J. Kallmann

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The present paper is aimed to celebrate Franz J. Kallmann's memory, by illustrating the twin-family method, which he developed. His phenomenal powers of organization are testified to by his extensive samples. Their representative nature has the built-in check of the ratio of MZ : DZ twins. He brought a refinement of his own to the existing methods of calculating expectancy from nett figures, that permits comparison of studies of varying age distributions relative to manifestation period. His investigative design allows not only for the standard global concordance comparisons between DZ and MZ twins as well as for those reared together and apart, but exploits the implications of the hitherto neglected comparison of the categories of sibs and DZ twins also. Further, his combined twin-family method comprehends in its extended range the powerful analytical tool of comparative figures for the series step-sibs, half-sibs, sibs, DZ twins and MZ twins (Kallmann and Sander, 1947; Kallmann, 1953). Kallmann (1954*a*, 1954*b*) has moreover given minute attention to controversies concerning legitimate inferences from twin studies, and has drawn attention to a point made by Darlington (1953), which is often overlooked by the best of geneticists. Discordance between MZ twins is not a measure merely of postnatal or even of prenatal environmental effects: it may also have a genetic component through the action of genes sensitive to cytoplasmic asymmetry.

It will doubtless be for his studies in schizophrenia that Kallmann will best be remembered. His earlier German work published in 1938, extended by his New York twin-family study and reported definitively in 1946 and 1950, has settled for all time the single-factor genetic predisposition to the disease, and its autosomal and probably recessive nature. Moreover, his concept of a graded constitutional resistance mechanism based on polygenic modifiers finds fruitful application in relation to somatotypes and the course and prognosis of both schizophrenia (Kallmann, 1948*a*, 1948*b*) and tuberculosis. In the latter, his clinico-pathological studies with Reisner (1943)

won the acclaim of Barbara Burks. In these and other genetic diseases Kallmann has always sought to apply therapeutically the hope-laden paradox of our present era of Biochemical Genetics. Genetically disordered metabolism can be reversed by physicochemical modification of the specific predisposing or polygenic resistance mechanism.

Hospitable to the notion that a genetic basis to psychiatric conditions does not exclude psychoanalytic or other interpretations of psychological content, Kallmann's genetic studies in schizophrenia nevertheless invalidate cultural causal theories of this condition (namely, the belief of a schizophrenogenic mother), as further shown by the following findings:

- 1) The father enters equally into the parental background of schizophrenics;
- 2) Only 14% of the sibs develop the disease, whereas 100% have potentially equal exposure to the mother;
- 3) The sibling series (step-sibs, half-sibs, sibs, DZ twins and MZ twins) manifest the condition in proportion to their genetic loading, and not equally according to their exposure to the mother;
- 4) A large part of the morbidity distribution is in the collateral line of descent through phenotypically unaffected parents, in proportions predictable in genetic terms.

In Kallmann's repertoire, the interrelationships of schizophrenia with mental defect (Kallmann et al, 1941) and with epilepsy (Kallmann and Sander, 1947) form the subjects of separate enquiries, and preadolescent schizophrenia (Kallmann and Roth, 1956) is found to be of a piece with its elder brother. That type of emotional instability, which may lead to an involitional psychosis, is somewhat unexpectedly linked up genetically with the group of schizoid personality traits, rather than the cycloid ones of his manic-depressive study (Kallmann, 1954a, 1954b), where irregular autosomal dominance is disclosed. Kallmann draws upon both his schizophrenic and manic-depressive data to bring precision into a conception of *folie à deux* which avoids the common error of overlooking the genetic contribution to the situation (Kallmann and Mickey, 1946).

Another central ideological contribution based upon the twin-family method is in the area of the psychology of adjustment. Kallmann (1951) insists on the recognition, as an integral part of the psychiatrist's clinical approach, of the assets and disabilities brought to the process of adjustment to life, rather than assuming an equality, as many psychodynamic theories, by implication or neglect, are inclined to do. He illustrates his adjustment theme by reviewing the series suicide (total failure of adjustment) (Kallmann and Anastasio, 1946; Kallmann, 1949; Kallmann et al, 1949), adult male homosexuality (distorted adjustment to one of life's major orientations) (Kallmann, 1952a, 1952b) and senescence and senile psychosis (gradual and progressive failure of adjustment) (Kallmann and Sander, 1948, 1949; Kallmann et al, 1951; Kallmann, 1952c, 1952d, 1952e; Falek et al, 1960; Jarvik et al, 1960; Kallmann, 1961a, 1961b, 1961c; Jarvik et al, 1962a, 1962b). The concordance finding

in the twin suicide research of not above chance expectancy indicates the absence of genetic causation and reveals the neutrality of genetic methodology in assigning a predominance to environmental factors. In striking contrast, the concordance figures in MZ and DZ homosexual twins, and the disturbed sex-ratio in their sibships indicate a substantial genetic organic component, that should be taken into consideration clinically. In senescent twins, MZ pairs show significantly smaller intra-pair differences in the longevity and tests of intellectual performance than do DZ pairs. Moreover, in senile psychotics a substantial concordance rate in MZ twins testifies to the significant role of genetic factors in psychiatrically pathological aging.

In the field of early total deafness, Kallmann carried out an extensive programme of genetic and demographic research and clinical insights, as well as of education and treatment for this large body of handicapped persons in the State of New York, in Philadelphia and Washington, D.C. (Kallmann, 1956*a*, 1956*b*; Sank and Kallmann, 1956; Rainer et al, 1963*a*, 1963*b*). Psychogenic induction of schizophrenia in the deaf was for the first time accurately refuted, a psychiatric service for the schizophrenic deaf was established at Rockland State Hospital, and community educational counselling and psychotherapeutic facilities were initiated for children and adults alike.

Kallmann's eugenic orientation has found expression in his comprehensive marriage and fertility aspects of his twin-family studies of schizophrenia (Kallmann, 1938*a*, 1938*b*; Kallmann et al, 1962, 1964; Erlenmeyer-Kimling et al, 1966). In particular, the overtaking in marriage and fertility rates by schizophrenics of the New York State general population, coinciding with the era of active therapeutic development between the study of the thirties (1934-1936 sample) and that of the fifties (1954-1956) is a finding that no worker in the preventive field can afford to overlook. The planning that Kallmann has put into his pleas for the education in genetics of various professional workers (Kallmann, 1952*a*, 1952*b*; Kallmann and Bondy, 1952; Kallmann, 1956*a*, 1956*b*; Kallmann and Rainer, 1963, 1964; Kallmann, 1961*a*) further underlines the earnestness of his desire for the effective development of scientifically enlightened eugenic policies.

In his genetic counselling philosophy Kallmann is committed to a programme of minimal voluntary scientific eugenics, with the heredity clinic as its focal point. How deeply scientifically informed this approach should be, is illustrated by his paper on the applicability of the twin study method to the analysis of variations in mate selection and marital adjustment (Kallmann and Bondy, 1952). But genetic and marital counselling should not be regarded merely as a matter of delivering to clients empiric risk figures; there is a psychological dimension as well, not only where specifically psychiatric conditions are under consideration, but in cases of serious physical ills also. Every counsellor should heighten his natural compassionate awareness to the fact that his client is undergoing one of the deepest emotional experiences of his life, when he has to seek guidance on the advisability of marriage and parenthood. Kallmann adduces in detail the considerations entering into the resulting psycho-

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therapeutic situation, which the counsellor may handle for good or ill, depending on the extent of his psychological preparation, sensitivity and insight (Kallmann, 1956*a*, 1956*b*; Kallmann and Rainer, 1963, 1964).

Those present in this great city at Professor Gedda's Conference of 1961 will remember not only Franz Kallmann's formulations of the Hybrid Specialty of Psychiatric Genetics (Kallmann, 1961*b*), with the Twin Family Method as its core. but can picture him at the Opening Session (Kallmann, 1961*c*), as he set new goals and perspectives in Human Genetics that are as relevant, vital and inspiring today as when he made them:

“ We need the scientist as well as the medical practitioner, the psychologist as well as the statistician, the specialist as well as the family physician, provided they are willing to undergo adequate genetic training, at least in some sector of specialised counseling work... They have to be told somewhere why they should feel responsible for a general comprehension of the fact that mankind as a whole must learn how to survive safely. Only then can real benefits be derived from the multitude of important contributions that human genetics is able to make to our scientific schemes and therapeutic programs... ”.

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