GENE INTERACTION IN THE PHENOTYPIC EXPRESSION OF MENTAL DISEASES

A Twin and Family Study

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A genealogical analysis is carried out on the pedigrees of 10 twin pairs with two or more psychoses. The probands' symptoms reveal some peculiar aspects, i.e., an atypical phenomenology possibly due to the interference of more pathological genes.
Schizophrenia, depression, epilepsy, and obsessive neurosis, are found in the pedigrees in different combinations.
The study of these pedigrees would lead to the conclusion that interaction of more than one psychosis gives rise to atypical forms as a result of an attempt to establish a state of balance between opposing dynamic actions, as in reversible chemical reactions. Probands' symptoms are less severe and with an often more favourable prognosis. Epilepsy tends to become independent and the major psychoses seem to be epistatic on it.
As for obsessive-compulsive neurosis, probands may progress into schizophrenia or depression if one of theses psychoses is present in the pedigree, or may represent the neurotic form of the major disease.

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A NEGLECTED ELEMENT IN TWIN-STUDY GENETICS OF HUMAN MENTAL DEVELOPMENT

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The usual asymmetry of human brain programming is sufficiently prevalent (over 96% by the best estimate) to suggest that it must have a genetically-coded cellular basis, and there are in the literature observations of structural asymmetries consistent with known functional specialization of brain substructures.
Departures from that usual asymmetry, manifested in unusual laterality of motor dominance and/or speech representation, seem to have some genetic basis, and have been found associated in statistically significant excess with: schizophrenia, epilepsy, alcoholism, dyslexia, dysphasia, autism, and mental retardation.
Unusual or reduced brain program asymmetry, and most of the above-named related disorders, can also derive from embryonic disturbances, as evidenced by excessive association with: first births, late births, birth difficulties, and twinning.
MZ twins are never in fact identical, and the differences most likely begin long before the effects usually considered under the label " environmental " can take place. A basic fact which has almost unanimously gone unmentioned in twin genetic studies of human mental development is that MZ twins develop from embryos which have split, in many cases and probably in most, after at least some commitments to the cellular development of bilateral symmetry have been made.
The earliest visible precursors of bilateral symmetry in the human embryo occur in the head region, with the mouth as focus, just after amniogenesis. The molecular commitment to this development must in fact have occurred still earlier, and estimates range from 15% to 30% for the fraction of MZ twinning events which occur at or after this stage.
The effects of such a split are visibly recorded in mirror-imaging; in tooth emergence patterns, in shapes of mouth, nostrils, eyes, and ears, in hairwhorl placement and pattern. The ectodermal precursors of these structures surround on three sides the cellular precursors of the brain. And brain-function laterality is also found to be subject to mirror-imaging; of 40 pairs in an unpublished study by Paul Satz, 35% mirror-imaged in speech laterality, motor dominance, or both, with handedness very strictly defined.
Data from the 1972 publication of the Gottesman and Shields genetic twin study of schizophrenia will serve to illustrate the power of the neglected embryonic discriminator: Fully one-third of their MZ schizophrenic sample (nearly ten times the best population estimate) were characterized as lefthanded or ambidextrous. If the sample is divided, between *Pairs* with and without