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Twins. Part 2. The Twin Study Method in Behavioral and Clinical Research

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There are many anecdotes about identical twins who were separated early in life and later reunited. Although reared in different environments, their remarkable similarities include mannerisms, tastes in food, choices of hobbies, and vocations. Some people even believe that there is an almost extrasensory sympathy between identical twins—shared pain and moods and vague awareness about how the other is doing or what the other is thinking. While these anecdotes receive widespread attention in the media, the truly profound research on twins is not so well known outside the scientific community.

In the first part of this essay,[1] we reviewed the unique biology involved in the conception and birthing of twins. In this part, we'll review what researchers in the behavioral, cognitive, and medical sciences have learned about twins. Much of this research has profound implications for the old philosophical "nature vs. nurture" debate. The extent to which intelligence, personality, and even health and life span are determined by genetics or environmental factors is still very controversial.

As discussed in the first part of this essay, there are two types of twins—monozygotic (MZ) and dizygotic (DZ). DZ twins are like any other siblings—that is, on the average, only *half* of their genes are the same. They can be of the same or opposite sex. MZ twins are genetically *identical*. They have duplicate genes and they are always of the same sex. Thus, by comparing MZ and DZ twins, researchers are able to study the genetic and environmental factors in various human characteristics and diseases. Before we review the results of these twin studies, we'll briefly discuss some of the various ways twins are used in research.

The classic twin study method is a tool for estimating the relative influence of genetic and environmental factors on a specific trait. If one assumes that environmental effects are the same in MZ and DZ twins, then a greater similarity between members of MZ pairs than between members of DZ pairs would indicate that the similarity is a result of their matching genes.

Twins are said to be concordant when both members of the twin pair are alike in a trait or discordant when one twin is different from the other in that trait. The concordance rate, or the percent of MZ and DZ twin pairs sharing similarity for a given trait, is used as a measure of the genetic contribution to that trait. However, if the research is concerned with a continuously variable trait, such as IQ score, a statistical measure known as correlation is used to gauge similarity. The higher the correlation, the more alike are the twins. A correlation of 1.0 indicates complete identity for a given trait.

A major criticism of this classic twin study method is that the childhood envi-

ronment shared by MZ twins may be more similar than that of DZ twins. For example, parents may treat nonidentical twins differently from the way they treat identical twins. And MZ twins were once thought to spend more time together than DZ twins. However, these speculations are not supported by research. Hugh Lytton, Department of Educational Psychology, University of Calgary, Alberta, Canada, found that parents respond to the differences between DZ pairs, rather than create them by treating the individual twins differently.[2] Nor do parents by their actions introduce greater similarity into the behavior of MZ twins. In fact, when zygosity is unknown to parents, their treatment of the twins is in line with the actual rather than the perceived zygosity of the pair. Steven G. Vandenberg, Institute for Behavioral Genetics, University of Colorado, Boulder, suggested that most twin characteristics, such as having the same friends, do not cause similarity, but result from existing similarity.[3]

Another method, which uses only MZ twins, eliminates this potential environmental bias. By looking at differences between MZ twins separated when they are infants and reared apart, psychologists have been able to examine the extent to which variation in a given trait is environmentally determined. However, use of this method is limited by the small number of MZ twins who are raised apart.

Still another twin study strategy is the co-twin control method. First used in studies of the acquisition of skills, the co-twin control method is more frequently used today in testing various treatments, such as the effectiveness of vitamin C in preventing the common cold. In the co-twin control study, one twin of the MZ pair is treated while the other remains untreated and serves as a control. One variation on this method compares MZ twins discordant for a specific trait. By using MZ twins, genetic factors are controlled, and the effects of environmental factors can be determined.

Of course, all these methods require accurate knowledge of zygosity; that is, the ability to distinguish MZ from DZ twins. A variety of genetically controlled traits, such as blood type and blood serum antigens, physical appearance, and finger ridge count, can be used to determine zygosity. However, in large twin studies, it may be more feasible to use a questionnaire that assesses early physical resemblance on the basis of selected traits. Discordance for any trait indicates that the pair is dizygotic, but a question arises when concordance occurs. Since they are genetically identical, all MZ pairs will be concordant. However, because approximately half of their genes are the same, concordance may also occur in DZ twins who may be mistaken for MZ.

Although comparison of blood groups and blood-group antigens is often thought to be the most accurate method for determining zygosity, subjective methods are necessary when researchers study large groups of twins. These methods are surprisingly accurate. For example, C. Dennis Robinette, National Academy of Sciences-National Research Council (NAS-NRC), Twin Registry, Washington, DC, noted that he and his colleagues were able to determine zygosity with 96 percent accuracy by asking two questions: (1) "Were you and your twin ever said to be alike as 'two peas in a pod,' or only of ordinary resemblance?" (2) "Did close friends, relatives or school teachers have difficulty telling you and your twin apart?"[4]

Paolo Parisi, University of Rome and Gregor Mendel Institute for Medical Genetics and Twin Studies, Rome, Italy, noted that an experienced observer can classify twins according to zygosity simply by looking at them.[5] This is not surprising, because physical traits such as eye and hair color, ear form and attach-

ment, and the shape of the nose are under strict genetic control. In a 1983 study, Nancy L. Segal, Department of Psychology, University of Minnesota, Minneapolis, compared the accuracy of a skilled observer in determining zygosity with the blood typing procedure. She found the observer's judgments to be the most accurate. Of 53 twin pairs classified by laboratory tests, 5 disagreed with the observer. On retest, researchers found an error in blood typing, and the observer's judgments thus were confirmed in all cases.[6] However, blood typing continues to be the preferred method for an objective diagnosis.

This interesting and important research would be either impossible without twins, or at least difficult and ambiguous. As noted in part one of this essay, twins are a small population, and identical twins occur only in 4 per 1,000 births. Fortunately, twin registries mitigate the relative rarity of twin births. Table 1 presents a selected list of these registries, which maintain extensive databases of demographic and other information about twins. Researchers can use the data in a registry or contact the twins through the registry. One of the largest registries in the US is at the Medical College of Virginia and includes over 29,000 pairs. The NAS-NRC Veterans Twin Registry includes the 16,000 US twins who served in World War II. Registries in the Scandinavian countries are generally based on birth records and include all of the twins who were born in each country. These registries facilitate studies from a wide variety of disciplines.

The first scientific study of twins took place more than 100 years ago when the British anthropologist and eugenicist, Sir Francis Galton, introduced the classic twin study method.[7] Galton's early genetic studies centered on the inheritance of intellectual ability. However, he was unable to distinguish between inherited and environmental factors. Galton realized that twins provided a natural laboratory for studying the nature vs. nurture controversy. Although Galton's studies were based on erroneous ideas about the biology of twinning and zygosity, his general conclusion that there is a genetic component to intelligence was reasonably accurate.

More recent studies of intelligence that used Galton's twin study method found that MZ twins become increasingly similar while DZ twins begin to diverge as they reach school age. Psychologist Ronald S. Wilson, University of Louisville School of Medicine, Kentucky, observed the same children for several years. He reported that prior to the age of 18 months, correlations for intelligence were 0.69 and 0.63 for MZ and DZ pairs, respectively. Between the ages of 18 months and 4 years, these correlations averaged 0.83 and 0.72, respectively. By age 6, correlations stabilized at 0.85 for MZ and 0.63 for DZ twins.[8] Wilson concluded that intelligence is guided by a genetic template that acts throughout childhood and into adolescence.

In a study of intelligence in MZ twins who were reared apart, David T. Lykken, Psychiatry Research Unit, University of Minnesota, Minneapolis, estimated that about 70 percent of intelligence is genetically determined.[9] The largest study of intelligence in MZ twins reared apart was published by the well-known British psychologist Sir Cyril Burt. According to Burt's biographer, L.S. Hearnshaw, University of Liverpool, England, the validity of this work has been questioned, since he chose to create fictitious collaborators with whom he published further confirming studies.[10] To say the least, the question of heritability of intelligence is still hotly debated, there being studies that both support and contradict his studies. However, Burt's work in no way reflects on the more recent studies of MZ twins reared apart.

Table 1: A list of some major twin registries.

Danish Twin Registry
University of Odense
Arvepatologisk Institut
Odense, Denmark

Finnish Twin Registry
Department of Public Health Science
University of Helsinki
Helsinki, Finland

Institute of Medical Genetics
Academy of Medical Sciences of the USSR
Moscow, 115478, USSR

Kaiser-Permanente Twin Registry
Department of Medical Methods Research
Kaiser-Permanente Medical Care Program
Oakland, CA 94611

Medical College of Virginia Twin Registry
Department of Human Genetics
Medical College of Virginia
Richmond, VA 23298

National Academy of Sciences-National Research Council Twin Registry
National Research Council
2101 Constitution Avenue, N.W.
Washington, DC 20418

Norwegian Twin Registry
Institute of Medical Genetics
University of Oslo
Blindern, Oslo 3
Norway

Swedish Twin Registry
Department of Environmental Hygiene
Karolinska Institute
Stockholm, Sweden

Language is one means of expressing intelligence. It is a complex function that is influenced both by genetic and environmental factors. Psychologists Patricia L. Mather, Utica College of Syracuse University, New York, and Kathryn N. Black, Purdue University, Lafayette, Indiana, found that in preschool children, vocabulary comprehension is significantly influenced by heredity. Verbal skills are more closely related to the home environment.[11]

Twins are generally slower to speak than singletons. Lytton found that MZ pairs are even slower than DZ pairs to develop speech and vocabulary skills.[12] Verbal interaction with the mother appears to be the most important factor in learning to speak for all children. Dorice Conway and colleagues, Department of Educational Psychology, University of Calgary, Alberta, Canada, found that, because they lack time, mothers speak to twins less frequently and in shorter and less complex utterances than do mothers of singletons.[13] Jennie P. Betton and Lynne S. Koester, Family Research Center, University of North Carolina, Greensboro, observed that twins provide support and encouragement for each other and need their mothers less than singletons do to develop cognitive skills.[14]

Certain speech disorders seem to have a hereditary component. Until recently, few researchers considered stuttering, a disorder in the timing of speech, to be of genetic origin. However, Pauline M. Howie, School of Psychiatry, University of New South Wales, Sydney, Australia, found a concordance of about 63 percent for MZ twins and about 19 percent for DZ twins.[15] To better understand the nature and degree of similarity of symptoms in MZ twins, Howie examined twin pairs with at least one stutterer to determine which characteristics were under genetic control. She found evidence for a genetic contribution to the frequency and type of speech disruption, for example, blocked or prolonged sounds. However, there was little evidence for a genetic influence on the types of speech repetitions and interjections associated with stuttering.[16]

Language skills and intelligence are related to basic brain function. One reflection of basic brain function is the electroencephalogram (EEG). EEG patterns reflect electrical activity within the cerebral cortex, that part of the brain responsible for intelligence. The resulting brain-wave tracings are influenced by factors such as the size and shape of the skull in relation to the underlying cerebral cortex, the anatomy of the cortex,

and by the microstructure associated with cognitive and emotional reactions. Generally, each person has a unique brain-wave pattern. However, since MZ twins are genetically identical, it is not surprising that their EEG patterns are very similar, while those of DZ twins are no more alike than those of unrelated individuals. Lykken and colleagues found these patterns to be similar for MZ twins whether they were reared apart or together.[17] This suggests a strong genetic influence on basic neural circuitry.

Certain aspects of personality also seem to be strongly influenced by genetic factors. In a 1980 study of 7- to 10-year-old twin pairs, Adam P. Matheny and Anne B. Dolan, Louisville Twin Study, University of Louisville, Kentucky, found significantly higher MZ correlation than DZ correlation on tests of emotionality, sociability, and activity.[18] Psychologists John C. Loehlin, University of Texas, Austin, and Robert C. Nichols, State University of New York, Buffalo, found a strong genetic contribution to various aspects of personality and measures of general ability in teenagers.[19] Additional evidence comes from studies of MZ twins reared apart. According to psychologist Thomas J. Bouchard, University of Minnesota, Minneapolis, MZ twins who were reared apart are as similar in some personality traits as MZ twins reared together.[20] For example, he reported that aggression, introversion and extroversion, impulse control, and neuroticism are significantly more similar in both types of MZ than in DZ pairs.

Galton also noticed the similar personalities of like-sex twins. He noted that these twins occasionally had similar types of mental disorders.[7] More recent twin studies of mental illness suggest that genetic factors play an important role. One example is schizophrenia. According to Irving I. Gottesman, Department of Psychiatry, Washington University, St. Louis, Missouri, and James Shields, then of the Institute of Psychiatry, London, concordance for schizophrenia in MZ twins is 46 percent while it is only 14 percent for DZ pairs.[21] In her re-analysis of several studies, psychologist Susan L. Farber, then of New York University, New York, reported 67 percent concordance for MZ twins raised apart.[22] Concordant MZ twins also become schizophrenic at similar ages. Although the large difference between MZ and DZ concordance figures provides strong evidence for a genetic contribution, MZ concordance is far less than 100 percent. This indicates that schizophrenia is probably due to a combination of environmental and genetic factors. However, Gottesman and Shields claim that studies of discordant MZ pairs have not provided evidence of a specific environmental factor.[21] Also, David W. Fulker, Institute for Behavioral Genetics, University of Colorado, notes that the provoking environmental circumstances are probably highly specific to the individual.[23]

Some of the most definitive results of twin research have come from the study of diabetes mellitus, a pancreatic disorder that affects carbohydrate metabolism. There are two pathologically distinct types of diabetes: insulin-dependent diabetes (IDD) and noninsulin-dependent diabetes (NIDD). IDD generally develops in childhood while NIDD usually occurs in mid- or late-life. The fact that the occurrence of diabetes is familial has long been known. However, a 1981 study by A.H. Barnett and colleagues, Diabetic Clinic, Kings College Hospital, London, found a little over 50 percent concordance for IDD in MZ twins.[24] This seems to imply that, while there is a genetic tendency to develop the disease, IDD is not entirely of genetic origin. Further support for this is the fact that more discordant than concordant twin pairs between the ages of 20 to 39 years were living apart at the time of diagnosis.

A study of the unaffected members of MZ twin pairs may have provided a marker for early diagnosis of the prediabetic state in IDD. S. Srikanta and colleagues, Department of Medicine, Harvard Medical School, Boston, Massachusetts, periodically examined the unaffected twin in 24 discordant MZ pairs for 21 years. They found that these patients began to produce antibodies to the insulin-producing beta cells of the pancreas several years prior to the onset of IDD.[25] The antibody can be used as a marker for the disease. In the future, susceptible people may be identified early enough to prevent diabetes. Srikanta's findings also suggest that IDD develops slowly, rather than suddenly, as researchers had previously thought.

Apparently there is a stronger genetic component in maturity-onset NIDD than in IDD. Of 53 NIDD twin pairs in Barnett's study, only 5 were discordant for the disease. The interval between the two diagnoses in concordant twins is also short, averaging about five years. These concordant twins had usually been living apart for many years and were often of different weights. This suggests that environmental factors, such as obesity, may be less important in NIDD than previously thought.[24]

Questions about possible environmental factors important to the etiology of neurologic disorders such as multiple sclerosis (MS) may also be answered by long-term follow-up of discordant MZ twins. MS is a degenerative disorder of the central nervous system. Like IDD, concordance rates for MS indicate that factors other than genes contribute to this disease. Neurologist Adrian Williams and colleagues, National Institute of Neurological and Communicative Disorders and Stroke (NINCDS), Bethesda, Maryland, reported concordances of 20 to 40 percent in MZ pairs and 15 percent in DZ twins.[26] Henry F. McFarland and colleagues, also at NINCDS, suggest that discordant twins may also provide an opportunity to evaluate various therapeutic approaches to MS.[27] One approach, based on a hypothesized immunological etiology, was to treat the affected twin with lymphocytes from the unaffected twin. However, this treatment had no long-term effect.[27]

Several recent twin studies examined the genetic contribution to risk factors for heart disease. A 1981 collaborative study between the Institute of Medical Genetics, University of Oslo, Norway, and the Department of Human Genetics, Medical College of Virginia, Richmond, reported by Kare Berg, University of Oslo, found an overall concordance of 66 percent in MZ and 25 percent in DZ twins for coronary heart disease. Studies of several serum lipoproteins associated with coronary artery disease indicate a strong genetic influence.[28]

Longevity and factors that contribute to human life span are of increasing interest to twin researchers. Twins provide a living laboratory for studying the genetics of biological time. In a 1981 study of more than 2,000 twin pairs from the Mormon genealogy born between 1800 and 1899, Dorit Carmelli and Sheree Andersen, Department of Medical Biophysics and Computing, University of Utah, Salt Lake City, reported greater similarity in life span in same-sex twins, who may be MZ, than in opposite-sex pairs, who must be DZ. Females had a higher concordance rate than males.[29] A study of twins who served in World War II, conducted by Zdenek Hrubec, then of NAS-NRC, and geneticist James V. Neel, University of Michigan, Ann Arbor, found greater concordance in MZ than in DZ twins for death due to disease.[30] However, their study group had not reached old age, so much of the full genetic effect could not be measured. Luigi Gedda and Gianni Brenci, Gregor Mendel Institute for Medical Genetics and Twin Studies, concluded from their research on the genetics of the human life span that there is a basic, built-in

genetic timetable.[31] They discuss one unusual example: 73-year-old MZ twins who died of the same cause only 10 days apart.[32] Galton described a similar case.[7] Undoubtedly, twin studies will teach us more about the genetic component of the human life span as the populations of the various twin registries reach old age.

A large number of papers on twin research is published each year. For example, we accessed *SCISEARCH®* using the word "twin" as a stem, which retrieves articles containing terms such as "twin," "twins," "twinning," and so on. We found 445 articles published in 1983 that contained such terms.

Some of the journals covered in *Current Contents®* (*CC®*) and *Science Citation Index®* that publish papers on twins are listed in Table 2. We selected for inclusion in the table those journals that most frequently published articles on twin research. The interdisciplinary nature of twin research is indicated by the wide range of disciplines represented in the table. Also included in the table is the 1983 impact factor for each journal. Impact was calculated by dividing the number of citations a journal's 1981 and 1982 articles received in 1983 by the number of articles it published in that two-year period.

Although twin studies do not provide a conclusive or definitive answer to the nature vs. nurture question, they are generally useful in providing a direction for further research. For example, Walter E. Nance and colleagues, Department of Human Genetics, Medical College of Virginia, Richmond, note that by extending twin studies to include families of twins, more detailed information can be obtained on the source of genetic and environmental variation.[33] As we have seen, most human traits and clinical problems result from a combination of genetic and environmental factors. This brief survey of twin studies is by no means exhaustive. For reasons of space, I cannot review all the areas that use twins in research. However, by highlighting some of the significant twin studies, we realize the impact they have made on our understanding of behavioral genetics and some clinical problems. It would appear some of the folklore about twins is in fact confirmed by science. But clearly there is a great deal more to be learned from this exciting area of research.

Table 2: Some of the main journals publishing research on twins. The 1983 impact factor for each has been listed.

Journal	Impact Factor
Acta Geneticae Medicae et Gemellologiae	0.4
Acta Obstetricia et Gynecologica Scandinavica	0.6
American Journal of Human Genetics	4.0
American Journal of Medical Genetics	1.6
American Journal of Obstetrics and Gynecology	1.9
American Journal of Psychiatry	3.2
Annals of Human Biology	0.6
Archives of General Psychiatry	6.1
Behavior Genetics	1.3
British Journal of Obstetrics and Gynaecology	1.5
British Journal of Psychiatry	2.4
Child Development	1.6
Clinical Genetics	1.2
Developmental Psychology	1.7
European Journal of Obstetrics, Gynecology and Reproductive Biology	0.3
Fertility and Sterility	2.4
Human Genetics	2.0
Human Heredity	0.7
Obstetrics and Gynecology	1.7

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