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Are the Brains of Monozygotic Twins Similar? A Three-Dimensional MR Study

A. Biondi, H. Nogueira, D. Dormont, M. Duyme, D. Hasboun, A. Zouaoui, M. Chantôme, and C. Marsault

PURPOSE: **The role of genetic mechanisms and the influence of environmental events in human brain development have been difficult to evaluate. The purpose of this study was to compare the cerebral cortical morphology and midline structures of monozygotic twin pairs using MR imaging.**

METHODS: **Six observers, blinded to twin pairings, evaluated the 3-D renderings of the cortical surface and midline structures from MR images of seven monozygotic twin pairs. A morphometric analysis of the corpus callosum and of the distance between the anterior and posterior commissures was also performed.**

RESULTS: **Despite surprising anatomic differences, the brains of the twin pairs were similar enough to enable the observers to distinguish twin pairs from unrelated subjects. Five of six observers correctly identified the brains of all seven twin pairs; the remaining observer failed to make a correct match in only one of seven pairs. Three of six observers identified the midline sagittal images of the related twins in all seven pairs, and the other three identified the related midline sagittal images in five of seven pairs. The results were statistically significant.**

CONCLUSION: **Although the observed differences in morphologic characteristics between twins necessarily reflect nongenetic influences, the cortical patterns and midline structures of monozygotic twins probably are genetically similar.**

The factors affecting the gyral and sulcal patterns of the human brain are poorly understood (1). In particular, the role of genetic mechanisms and the influence of environmental events in human brain development are difficult to evaluate. The use of MR imaging has contributed to the study of cerebral cortical anatomy, permitting investigators to identify noninvasively the surface features of the brain in living subjects (2–5). Anatomic differences in cerebral gyral and sulcal patterns between pairs of monozygotic twins suggest that development of the convolutions of the human brain is not only genetically determined but also influenced by nongenetic factors. Some researchers have found differences in morphologic characteristics of the cortical surface on MR imaging studies in pairs of monozygotic twins (6, 7). Others have reported differences in the corpus callosum in monozygotic twin pairs (8). However, except for a single recent study (9), the contribution of genetic and nongenetic factors to the detailed cortical anatomy of the brain has not been evaluated.

The purpose of our study was to use three-dimensional MR imaging to examine the cortical pattern and midline structures in pairs of monozygotic twins and to test whether, despite previously reported anatomic variations, it is possible to identify the brains of monozygotic twin pairs. A morphometric study of the corpus callosum and the distance between the anterior and posterior commissures (AC-PC) within twin pairs was also performed to quantify the resemblance of such midline structures, in which a minor interaction of environmental factors has been suggested.

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Methods

We evaluated cerebral gyral patterns on volumetric renderings of the cortical surface on MR images of seven pairs of healthy monozygotic twin pairs. Anatomic characteristics of midline structures were also considered. Four twin pairs were male and three were female; their ages ranged from 19 to 47 years (mean age, 36 years). All 14 subjects were volunteers and gave written informed consent to the study.

Zygocity was determined by physical similarity, by findings on 14 genetic typing systems, and/or by analysis of a zygocity questionnaire (10). Information about chorion status was not

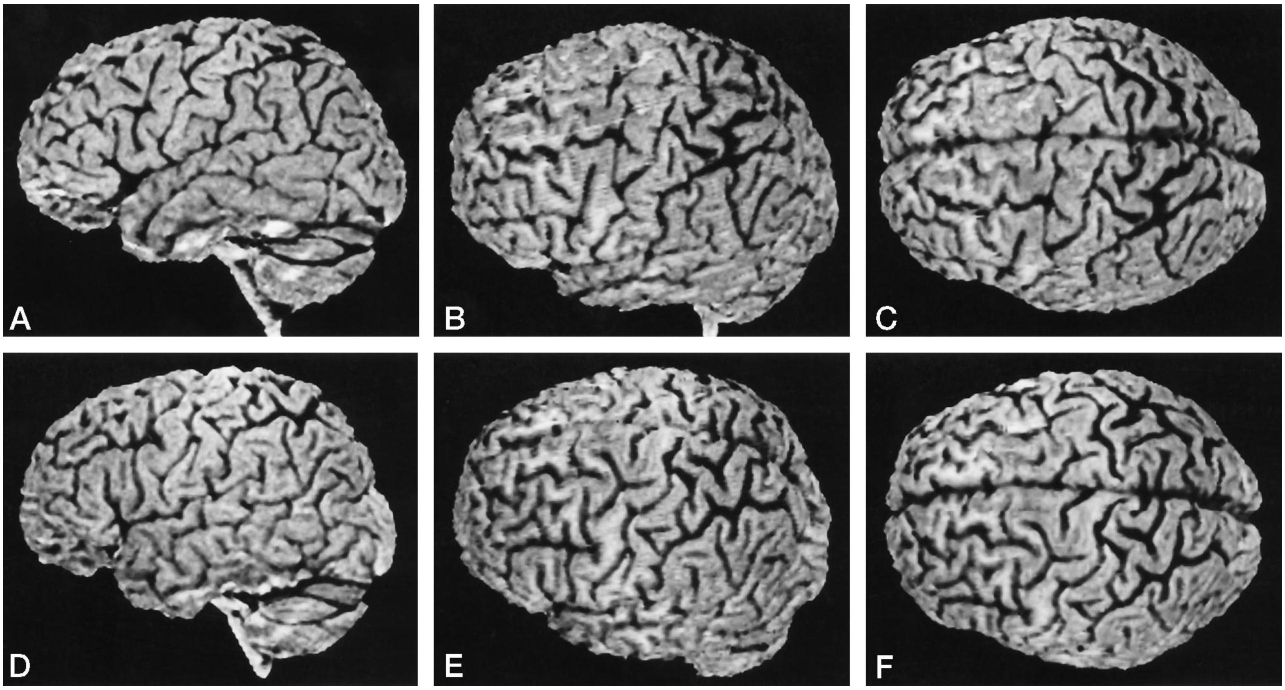

FIG 1. MR images of the 3-D surface-rendering models of the brains of a pair of monozygotic twins. For all 14 twins, the 3-D models of each brain were displayed on two films (24 views in all). The orientation from one view to the next changed by 15°.

A–F, The figures represent three of 12 views of the first film. *A–C* are of the first-born twin and *D–F* are of the second-born twin. In *A* and *D* (first view), the convexity surface of the brain is displayed in a left lateral view; in *B* and *E* (fourth view) and in *C–F* (sixth view, a nearly −15° superior view), the orientation has changed to 45° and 75°, respectively, in relation to the first view. Differences in the cortical anatomy of the two twins are apparent.

available. The seven twin pairs were identified by the letters A through G, and the subscripts $_1$ and $_2$ were used to designate the first- and second-born twin, respectively.

MR imaging was performed on a 1.5-T unit. First, a coronal scout view was obtained, then a 3-D acquisition was obtained in the sagittal plane with a T1-weighted spoiled gradient-recalled acquisition in the steady state (SPGR) sequence. Parameters were 23/5/1 (TR/TE/excitations) with a 35° flip angle; the field of view was 24 cm and the matrix was 256 × 256. One hundred twenty-four contiguous sagittal sections were obtained of the entire head, with a section thickness of 1.5 mm. The 3-D acquisitions were transferred to an Advantage Windows workstation (General Electric, Buc, France) through an Ethernet connection.

A 3-D surface rendering model of the brain was obtained from the 124 sections using Voxtool software (General Electric). In all 3-D models, the horizontal plane was defined as the plane perpendicular to the midline sagittal plane, which included the anterior and posterior commissures. This horizontal plane enabled us to display all the brains with the same orientation. The 3-D surface-rendering model of each brain was displayed on two films (24 views in all). On the first film of 12 views, the convexity surface of the brain was displayed from a left lateral view (first image) to a nearly (−15°) superior view (sixth image) and then from a right lateral view (seventh image) to a nearly (−15°) superior view (12th image). On the second film of 12 views, the convexity surface of the brain was displayed from a superior view with the frontal regions toward the bottom (first image) to a nearly (−15°) anterior view (sixth image) and then from a posterior view (seventh image) to a nearly (−15°) superior view with the frontal regions toward the top (12th image). In all subjects, the orientation from one view to the next changed by 15° (Figs 1–3). In addition, 14 midline sagittal images showing the midline structures of all subjects were obtained (Fig 4). All data enabling subject identification (such as name, sex, age, and examination date and number) were deleted.

The study was organized into three parts, as follows.

Parts 1 and 2: Morphologic Qualitative Analysis

Part 1.—Six observers, who had not previously seen the MR images of the twin pairs, were asked to independently identify each pair of twins. Three of the observers were experienced neuroradiologists, one was in training as a radiologist, one was a genetic biologist, and one was a psychologist. For each of the seven twin pairs, an imaging set that included the 3-D brain renderings of five of the 14 twins (two films for each subject, 10 films in all) was presented simultaneously on the viewing boxes (Figs 2 and 3). Each observer was informed that the first MR study belonged to the "target" twin, and that his (or her) related twin was among the other four subjects presented. There was no other twin pair in the set. Except for the target twin, the presentation order of the other four subjects of a set was randomly assigned for each of the six observers. The distribution of the twins in the set is reported in Table 1.

Part 2.—A set of seven images showing the midline structures of the seven first-born twins was presented, and the six observers (the same as in part 1) were independently asked to find the midline structures of the related twin among another set of seven images. For both sets, the MR images were presented in random order.

Part 3: Morphometric Quantitative Analysis

In all twin pairs, the maximal length, perimeter, and area of the corpus callosum and of the AC-PC distance were established independently by three observers using the 3-D software. The AC-PC distance was determined by tracing a line that joined the center of the anterior and posterior commissures. The measurements obtained by each of the three observers are reported in Table 2.

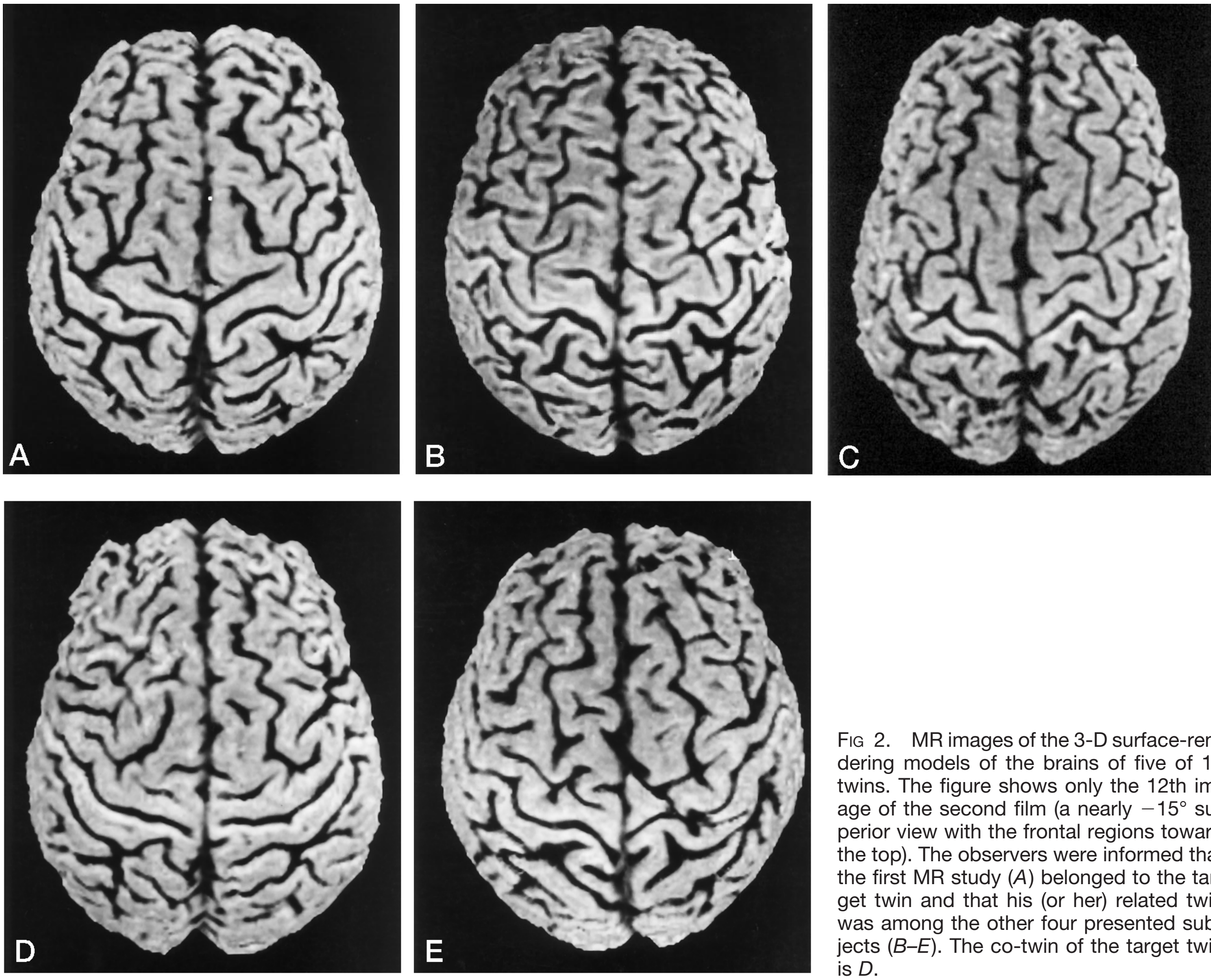

FIG 2. MR images of the 3-D surface-rendering models of the brains of five of 14 twins. The figure shows only the 12th image of the second film (a nearly −15° superior view with the frontal regions toward the top). The observers were informed that the first MR study (*A*) belonged to the target twin and that his (or her) related twin was among the other four presented subjects (*B–E*). The co-twin of the target twin is *D*.

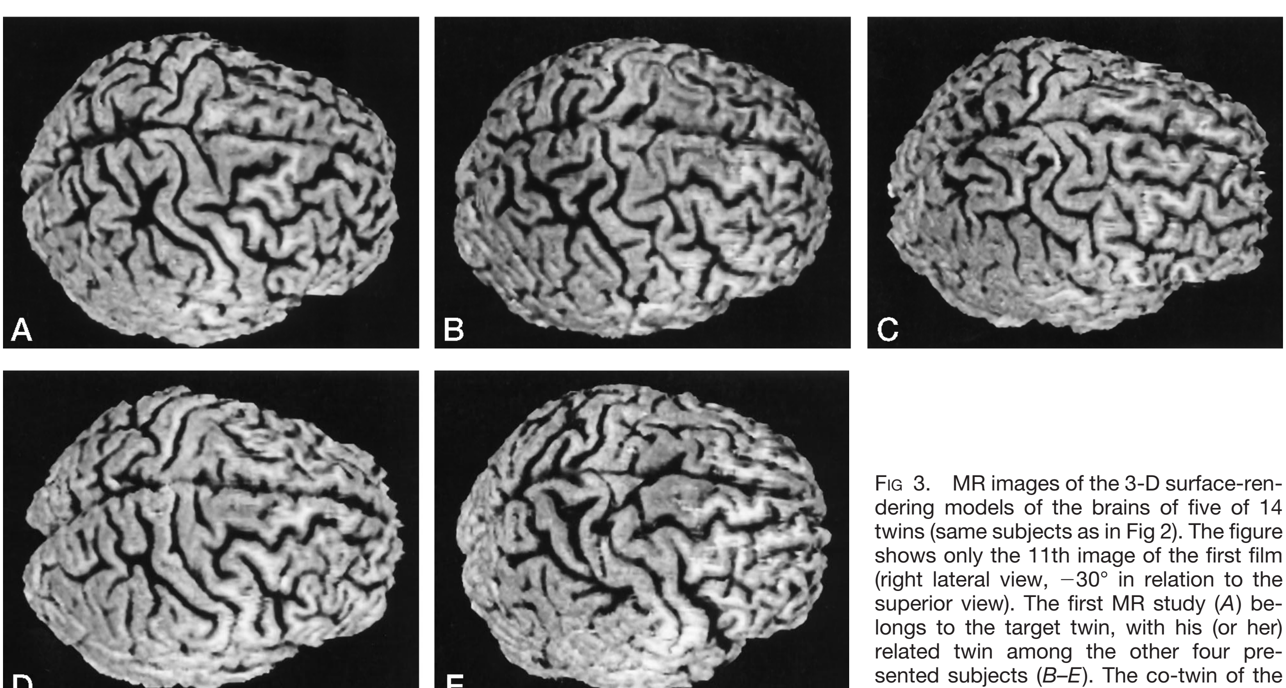

FIG 3. MR images of the 3-D surface-rendering models of the brains of five of 14 twins (same subjects as in Fig 2). The figure shows only the 11th image of the first film (right lateral view, −30° in relation to the superior view). The first MR study (*A*) belongs to the target twin, with his (or her) related twin among the other four presented subjects (*B–E*). The co-twin of the target twin is *D*.

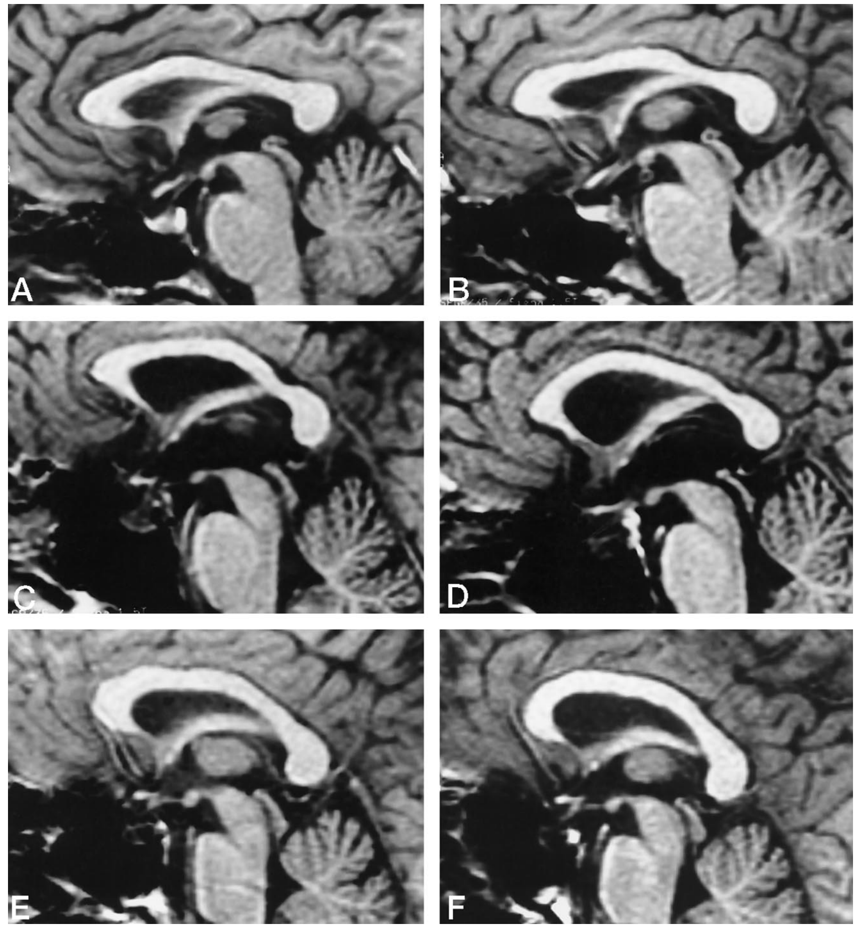

FIG 4. Sagittal MR images (from a 3-D T1-weighted SPGR sequence) of the midline structures of three pairs of monozygotic twins are shown side by side.

A–F, Twin pairs C_1 and C_2 (*A* and *B*), E_1 and E_2 (*C* and *D*), and G_1 and G_2 (*E* and *F*]).

TABLE 1: Distribution of twins in the seven presented sets

Set	Target Twin	Other Twins			
1	A_1	A_2	B_1	C_2	D_1
2	B_1	B_2	E_2	F_1	G_2
3	C_1	C_2	A_1	D_2	G_1
4	D_1	D_2	B_2	E_1	F_2
5	E_1	E_2	C_1	D_1	G_2
6	F_1	F_2	A_2	B_1	E_2
7	G_1	G_2	A_1	C_2	F_2

Note.—1, first-born twin; 2, second-born twin. Each observer was informed that the first MR study belonged to the target twin and that his (or her) related twin was among the other four presented subjects. Except for the target twin, the presentation order of the other four twins in the set was randomly assigned.

Statistical Analysis

For part 1 of the morphologic qualitative data analysis, in which the observers had to identify the co-twin among the 3-D surface rendering brain models of four subjects, the results obtained in performing the correct couplings were compared with the at-random probability (ARP) to choose the correct co-twin (ARP = 0.25).

For part 2 of the morphologic qualitative data analysis, in which the observers were asked to pair up seven MR images of the cerebral midline structures with those of the related twins among another set of seven images, the results obtained by the observers were compared with the ARP. ARP for an observer to correctly pair up the MR images of all seven twin pairs is .0002, and ARP for an observer to correctly pair up the MR images of only five of the seven twin pairs is .004 (Gaillard, P. Probability and forming an equation. Personal communication, Grenoble, France, 1997). Differences between the ARP and the observed rate were calculated by using Quick Probability Calculator (Statistic Software, 1993). The *P* level was determined on the basis of the *t* value for the respective comparison.

For part 3 of the morphometric quantitative analysis, reliability among the observers in measuring the midline structures was tested by using an intraclass coefficient correlation (ICC). The ICC was also used to test the similarity of measurement values of the midline structures within the twin pairs. The ICC was computed before and after adjustment for sex. The adjustment was computed by regression between sex and measurement values of the four study parameters (corpus callosal length, perimeter, and area, and AC-PC distance) (11). The *P* level of ICC for $\alpha = .05$ was determined by following the Bonferroni correction for multiple tests; in the present study, $\alpha = .05/4 = .0125$.

Results

Parts 1 and 2: Morphologic Qualitative Analysis

Part 1.—Visual comparison of the 3-D surface rendering models of the brains showed differences in the gyral and sulcal patterns between the pairs of monozygotic twins (Figs 1–3). Despite these differences in morphologic characteristics, five of six observers were able to identify correctly the brains of all seven twin pairs; the remaining observer (an experienced neuroradiologist) failed to identify the brain of the related twin in only one of seven pairs. In all, the six observers recorded 41 of 42 correct couplings. The

TABLE 2: Quantitative measurements of corpus callosum and bicommissural distance in seven pairs of monozygotic twins

Twins (n = 14)		Corpus Callosum									Distance between Anterior and Posterior Commissures, mm		
		Length, mm			Sagittal Perimeter, mm			Area, mm^2					
Pair (n = 7)	Age, y/Sex	Observer			Observer			Observer			Observer		
		1	2	3	1	2	3	1	2	3	1	2	3
A_1	19/M	78.0	78.2	78.9	197.8	197.3	199.0	633.5	650.4	643.0	26.3	26.1	26.5
A_2	19/M	82.2	82.4	82.0	221.5	221.4	221.4	679.9	680.7	680.5	25.4	25.6	25.7
B_1	35/M	69.0	69.7	69.9	182.7	183.0	183.2	544.6	546.9	557.4	27.6	27.5	27.4
B_2	35/M	67.1	67.3	67.1	179.6	179.8	180.1	572.0	573.1	576.9	27.8	27.8	28.4
C_1	47/F	75.2	75.5	74.9	191.8	191.9	192.2	500.6	605.4	604.8	24.4	24.2	24.2
C_2	47/F	76.7	76.7	76.7	202.3	202.3	202.4	636.4	635.8	640.9	24.3	25.0	25.0
D_1	39/F	72.2	72.0	72.1	195.2	194.4	194.3	699.7	701.1	701.0	24.7	25.0	24.7
D_2	39/F	71.6	71.8	71.2	194.7	195.1	195.1	707.9	708.8	705.9	24.6	24.6	24.1
E_1	36/M	64.4	64.3	64.5	175.5	175.4	175.4	466.8	466.0	466.0	25.8	25.6	25.5
E_2	36/M	66.9	66.6	66.9	183.9	183.9	184.0	490.9	492.6	493.5	25.6	25.4	25.2
F_1	40/F	67.9	68.7	67.7	180.9	180.6	180.5	609.1	607.2	608.0	24.1	24.4	24.5
F_2	40/F	70.6	70.5	70.5	185.2	185.8	185.7	603.2	600.3	602.1	24.2	24.2	24.6
G_1	35/M	70.0	70.4	70.8	193.9	194.2	194.1	622.1	621.4	618.0	27.3	27.7	27.4
G_2	35/M	67.5	68.3	68.0	198.3	194.4	195.3	665.2	660.9	675.1	26.3	26.7	26.3

Note.—1, first-born twin; 2, second-born twin.

difference between the observed rate of correct identification of twin pairs (.976) and the ARP in performing correct pairings (0.25) was significant ($P <$ .00001, one-tailed test).

The observers reported no strictly identical brains in the presented sets, but they were able to identify two similar brains, which they presumed to belong to a pair of twins. The major sulci seemed to be more similar between twins than were secondary and tertiary sulci. Although anatomic similarities were, of course, of great help, the observers reported to be often diverted and misled by the detailed analysis of the size, shape, and direction of the cerebral gyri and sulci. The global aspect of the cortical surface and/or the aspect of some regions of the cortex seemed to play an important role in the identification of brain pairs. In choosing the presumedly related twin, the observers appraised the cortical surfaces faster and more easily during the later presentations of the imaging sets than during the earlier presentations.

Part 2.—The MR studies revealed no identical morphologic characteristics of midline structures between pairs of monozygotic twins. Three of six observers (two experienced neuroradiologists, one radiologist in training) identified the midline sagittal images of the related twin in all seven pairs; the other three observers (one experienced neuroradiologist, one genetic biologist, and one psychologist) identified the related midline sagittal images in five of seven pairs. The incorrect selection of one twin pair necessarily produced two incorrect couplings. The difference between the rate at which observers correctly identified the midline structures of all seven monozygotic twin pairs (0.50) and the ARP for an observer to correctly pair up the MR images of the seven pairs (ARP = .0002) was significant (P = .04, one-tailed test). If we consider the correctly identified midline structures of five of seven monozygotic twin pairs, the difference between the rate at which observers made five of seven correct identifications (1.00) and the ARP for an observer to correctly pair up the MR images of five of seven monozygotic twin pairs (ARP = .004) is significant (P = .003, one-tailed test).

TABLE 3: Statistical analyses of measurements of corpus callosum and distance between anterior and posterior commissures before and after adjustment for sex

Before Adjustment for Sex	*df* Effect	*df* Error	F Test	Intraclass Coefficient Correlation	*P**
CC length	6	7	17.457	.892	.0007
CC perimeter	6	7	4.268	.620	.0394
CC area	6	7	24.566	.922	.0002
AC-PC distance	6	7	19.806	.904	.0005
After Adjustment for Sex	***df* Effect**	***df* Error**	**F Test**	**Intraclass Coefficient Correlation**	***P****
CC length	6	7	17.007	.889	.0007
CC perimeter	6	7	4.268	.620	.0395
CC area	6	7	20.347	.906	.0004
AC-PC distance	6	7	5.786	.705	.0181

Note.—CC, corpus callosum; AC-PC, anterior commisure-posterior commisure

**P* level for multiple tests: $\alpha = .05 / 4 = .012$.

Part 3: Morphometric Quantitative Analysis

The results of the measurements of the midline structures (length, perimeter, and area of the corpus callosum, and AC-PC distance) obtained independently by three observers are shown in Table 2. The values of the AC-PC distance were always lower in women than in men.

The ICC used to test the reliability among the observers in performing the measurements of the midline structures varied from .97 to .99 and is significant ($P < .00001$). The statistical analysis of the results of the measurements of the midline structures within the twin pairs are presented in Table 3. To test the similarity within twin pairs, the ICC was also used. The ICC, computed before and after adjustment for sex, varied from .62 to .92 before adjustment for sex, and from .62 to .91 after adjustment. The ICC scores for corpus callosal length and area were statistically significant ($P < .001$). The ICC scores for corpus callosal perimeter were not significant. The ICC scores for the distance between the AC-PC commissures may be considered significant before ($P < .0005$) and after ($P < .018$) adjustment for sex.

Discussion

The patterns of the gyri and sulci of the mature adult brain have been studied and reported in detail, and the general features and major anatomic variants are well known. Although the advent of MR imaging has made it possible to study brain morphology and its anatomic variances in living subjects (2–5), the mechanisms operative in the development of the gyral and sulcal patterns of the human brain are still poorly understood (1). Monozygotic twin pairs appear to be an excellent subset of subjects by which we can improve our knowledge of the development of the convolutions of the brain. Preliminary observations (6, 7) based on MR images have shown variability in cortical patterns of the brains of monozygotic twin pairs, and these authors have stressed the strong influence of nongenetic factors. Further evidence of the variances found in the brains of monozygotic twin pairs has been reported by Steinmetz et al (12), who conducted a study of human brain laterality. These researchers used MR morphometry to measure cerebral hemispheric asymmetry of the planum temporale in pairs of monozygotic twins concordant or discordant for handedness. They found that right-handed twins showed leftward asymmetry of the planum temporale whereas left-handed co-twins displayed symmetry in this region. Our MR study, based on 3-D surface rendering models of the brains, confirmed that monozygotic twins have many anatomic variations in their cerebral gyral and sulcal patterns.

Although the global shape and size of particular brain regions and large fissures are quite similar within monozygotic twin pairs, the shapes and courses of individual gyri and sulci tend to be dissimilar. Our purpose was to test the hypothesis that the brains of monozygotic twins are alike enough to make identification possible despite these recognized differences. Indeed, our results showed that the morphologic features of the cortices were sufficiently similar to differentiate twin pairs from unrelated subjects. These results were statistically significant.

The global aspect of the cortical surface seemed to play an important role in the identification of twin pairs in our study; however, it was not possible to identify the precise criteria on which the observers based their choices. The fact that the observers became more facile in their analyses seems to suggest a learning curve in the recognition of twins' brains. In the course of one's daily life, one meets many people and becomes accustomed to seeing a multitude of faces; picking out a pair of monozygotic twins on the basis of facial features should not to be difficult, even if they are not as alike as "two peas in a pod." The hypothesis that the mechanisms for identifying the brains of monozygotic twin pairs might be similar to those of recognizing two similar faces is supported by the fact that some observers in our study were not trained to evaluate cerebral MR images.

A search of the literature uncovered no studies based on a qualitative data analysis of cortical patterns in twin pairs; however, quantitative studies in five and 10 monozygotic twin pairs were performed by another team and published in two separate reports, respectively (6, 9). To quantitate the cortical gyral patterns, these authors used a cross-correlation analysis of rendered 2-D images of the lateral and mesial cortical surface, consisting of an automatic analysis of the cortical anatomy by means of an algorithm adapted for comparison of brain images. In their second study (9), in order to test the potential utility of their cross-correlation method as a tool for quantifying gyral pattern similarity, the authors performed a preliminary assay with five monozygotic twin pairs. Ten photographic renderings of the left hemisphere of the 10 twins were distributed to six observers who were asked to classify the images into twin pairs. Only one observer was able to identify all five monozygotic twin pairs correctly and, overall, the six observers averaged a 50% success rate in identifying the five pairs of twins (15 of 30 correct couplings). Our results are discordant with these, probably because our test, which required observers to identify the co-twin among four other subjects, was a less difficult task and because our multiple 3-D images turned every 15° represented a better rendering of the brain than did the one lateral view of the left hemisphere supplied to the observers in the other study. In their first report (6), those authors found that the monozygotic twin pairs had greater cortical pattern similarity than did pairs of unrelated subjects. In their more recent study (9), the authors quantitatively compared brain volume and gyral patterns in a population of 10 pairs of monozygotic twins and nine pairs of same-sex dizygotic twins. Using their approach of cross-correlation analysis on the 2-D images, the authors found that gyral patterns were significantly more alike within monozygotic pairs than within dizygotic pairs; however, no differences were found in comparisons of dizygotic twins and unrelated pairs.

Similar results were obtained by Tramo et al (13), who found that the mean cortical surface areas of the brains of monozygotic twins were significantly more alike than those of unrelated persons.

With the use of a different methodological analysis, our study confirms the results published by Bartley et al (9) concerning cortical patterns in monozygotic twins.

Results of our qualitative study showed that the observers identified the midline structures of the monozygotic twin pairs with a high rate of success despite the difficulty of the task. As for the quantitative study, the ICCs for the length and area of the corpus callosum among twin pairs were always significant ($P < .001$), although the ICCs for the perimeter of the corpus callosum were never significant. This lack of significance seems to suggest that the perimeter of the corpus callosum might be modified in relation to structural changes of the brain, while the area of the corpus callosum, as the cerebral volume, may be more genetically determined. Thus, the area of the corpus callosum may reflect neuronal density, which is probably genetically determined, while the perimeter may be influenced by environmental factors. We found a single report of measurements of the corpus callosum in monozygotic twin pairs (8). In this study, MR images from five pairs of monozygotic twins and five pairs of unrelated control subjects were analyzed. The measurements of size and overlap revealed greater similarity in callosal morphologic characteristics between the twin pairs than between the control pairs. As in our series, callosal area correlated significantly within twin pairs ($r = .9886$, $P < .01$) but not within control pairs. However, unlike our results, these researchers found no significant correlation for callosal length within either group, and concluded that their results were consistent with the view that the anatomy of the corpus callosum, while clearly influenced by nongenetic factors, is under considerable genetic control.

We found that the distance between the anterior and posterior commissures was always shorter in women than in men, and for this reason we evaluated results before and after adjustment for sex. Our findings showed a significant correlation among measurements of AC-PC distance within twin pairs before and after adjustment for sex.

Conclusion

Our study demonstrates that the brains of monozygotic twin pairs contain important similarities despite their apparent differences. These differences are probably due to multiple nongenetic factors acting on a genetically programmed structure. One could speculate that the degree of morphologic similarities in the brains of monozygotic twins changes progressively with cerebral growth from birth (or even from intrauterine life) to adulthood (with the greatest similarity in the newborn period). This may suggest a progressive modeling of the gyral pattern, resulting from such factors as the environment, experience, learning, and chance. Future researchers may seek to address the question of which of the elements that constitute the cerebral pattern are more fixed, and thus more genetically determined, and which are more malleable, and thus more likely to be dependent on environmental or random factors. However, the relationship between morphology and function itself remains speculative, and hence worthy of future investigation.

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Please see the Editorial on page 1185 in this issue.