

It is well established in HNPP that seemingly unaffected individuals or patients with only focal symptoms can show widespread electrophysiological abnormalities that point to a diffuse subclinical polyneuropathy [2–5]. It is not certain whether our patient's histopathological findings were inherited or acquired. Family history was negative for neuropathy, no specific precipitating factor was apparent, and compression seemed unlikely. Thus, we believe that the tomaculous changes in our case were acquired. However, the possibility of a preceding subclinical polyneuropathy cannot be excluded with certainty. Interestingly, similar histological findings have been described in neuropathy associated with benign monoclonal gammopathy, suggesting an acquired basis in some cases [8].

Since exhaustive investigation revealed no other cause for our patient's symptoms, we postulate that tomaculous change is the important association. When tomaculous change first occurred cannot be stated. We believe that this case is unique and broadens the clinical spectrum of TN, which may not always manifest as recurrent hereditary mononeuropathy or brachial plexopathy.

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Magnetic Resonance Imaging Morphology of the Corpus Callosum in Monozygotic Twins

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Recent reports describe wide variations in the size and shape of the human corpus callosum. To investigate genetic influences on this variability, magnetic resonance images from 5 pairs of monozygotic twins and 10 unrelated control subjects were analyzed. Measurements of size and shape revealed greater similarity in twin pairs than in randomly paired controls. The results are consistent with the view that the anatomy of the corpus callosum, while clearly influenced by nongenetic factors, is under considerable genetic control.

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Variability in brain organization may reflect the spectrum of cognitive capacities among individuals. The hemispheres of the human cerebral cortex are uniquely specialized in function. Hemispheric specialization arises from innate and developmental factors and can be associated with specific anatomical asymmetries of the cortex [1, 2]. The corpus callosum, the major neural pathway interconnecting the two cerebral hemispheres, plays a major role in the development of laterality in higher functions and the preservation of cognitive unity [1].

Results of several recent studies have suggested that particular anatomical characteristics of the human corpus callosum may be associated with functional specialization of the hemispheres [3–5]. Although there is no clear consensus regarding the validity of these claims [6–10], one consistent finding has been a variation in the size and shape of the callosum across the population [5, 9, 10]. Such anatomical variation must arise from environmental factors, genetic factors, or a combination of the two. To determine whether or not

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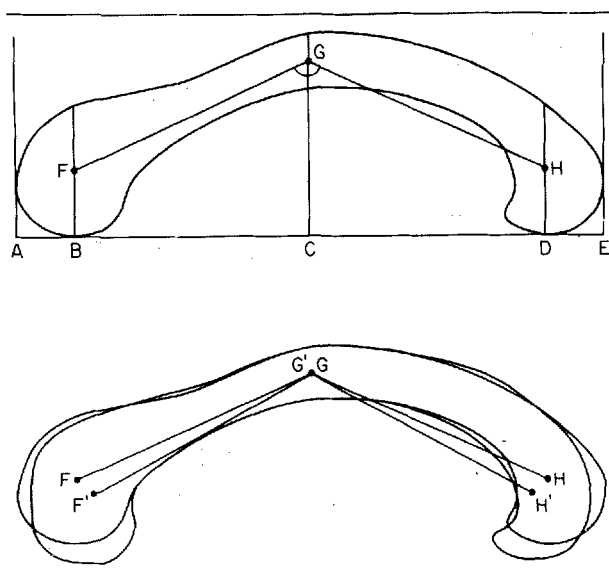


Fig 1. Method of morphological analysis of the corpus callosum. Top: the major callosal angle is determined. Bottom: the method of overlapping is illustrated. See text for description.

variations in callosal size and shape are related to genotype, we measured callosal area, length, and overlap in sagittal magnetic resonance images from pairs of monozygotic twins and unrelated control subjects.

Method

Five pairs of twins and 10 unrelated control subjects were studied. All subjects were recruited from the local community by advertisements and were remunerated for their participation. None of the participants had any history of neurological disease. Informed consent was obtained from each subject.

Four pairs of the twins were female and 1 pair was male. Six control subjects were women and 4 were men. All of the twin pairs were reared together. Twin monozygosity was assessed by blood antigen tests and questionnaires [11]. Blood antigens evaluated included ABO, MNSs, P, Rh, Kell, Duffy, and Kidd. Estimations of dizygotic-monozygotic ratios (DMRs) and probabilities of monozygosity were based on standardized formulas and predetermined DMR values [12]. Analysis of blood antigen DMRs revealed the probability of monozygosity to be greater than 96% for all twin pairs. In addition, analysis of the questionnaires supported monozygosity based on a positive predictive value of 98.6% [11]. Handedness was assessed using the Edinburgh Inventory [13]. All of the control subjects and 9 of the 10 twins were right handed. One twin in Pair 3 was left handed (laterality quotient = -40.7, decile L.2, see [13]). The area and length of her corpus callosum fell within one standard deviation of the group mean. The mean ages of the twin and control groups (25.6 ± 4.5 years and 23.6 ± 2.9 years, respectively) did not differ significantly ($t = 2.32$, $df = 18$, $p > .01$).

Midsagittal brain sections, 0.75 mm in thickness, were scanned using a 0.6-magnetic resonance imaging Tesla (MRI)

Table 1. Quantitative Results for Callosal Length and Area

Callosal Area	Twins (N = 10)	Control Subjects (N = 10)
Length (cm)		
Pair		
1	8.48/8.46	7.81/7.72
2	7.63/7.79	8.58/7.79
3	7.90/7.59	7.79/8.01
4	8.49/8.98	8.07/7.68
5	8.50/8.02	8.44/7.29
Mean	8.18	7.91
Standard deviation	0.46	0.31
Pearson r	0.7264 ($p > .01$)	-0.3742 ($p > .01$)
Area (cm ²)		
Pair		
1	877.6/983.1	628.4/626.2
2	793.9/802.5	877.9/759.8
3	723.1/714.5	793.0/707.5
4	802.3/813.5	899.4/595.2
5	673.6/631.4	852.1/693.3
Mean	781.7	742.8
Standard deviation	102.4	110.3
Pearson r	0.9886 ($p < .01$)	-0.0857 ($p > .01$)

Table 2. Callosal Morphological Results^a

Overlap Measurements	Twins	Control Subjects	Scan-Rescan
Angulation method			
Pair			
1	82.4	48.8	83.8
2	79.3	56.7	88.5
3	65.0	62.6	87.6
4	63.5	43.6	90.5
5	61.2	54.5	90.8
Mean	70.3	53.2	88.2
Standard deviation	9.80	7.31	2.82
Best-fit data			
Mean	72.2	56.5	
Standard deviation	8.83	5.24	

^aValues are expressed as percentage of overlap.

unit at the Cornell University Medical Center. Area, length, and overlap measurements were performed on T1-weighted spin echo sequences. Satisfactory sagittal images clearly delineated the corpus callosum and three midline structures (the vermis cerebelli, the spinal cord, and the infundibulum). Images of the corpus callosum were traced by two independent observers and were enlarged four and one-half times their original size for subsequent planimetry and overlap measurements.

Tracings were measured for maximal callosal length and area using a Zeiss MOP X,Y planimetric digitizer. A correction coefficient, derived from an MRI standard and the tracing enlargement factor, was used to compute in vivo length and area.

To assess similarities in shape, tracings of sex-matched un-

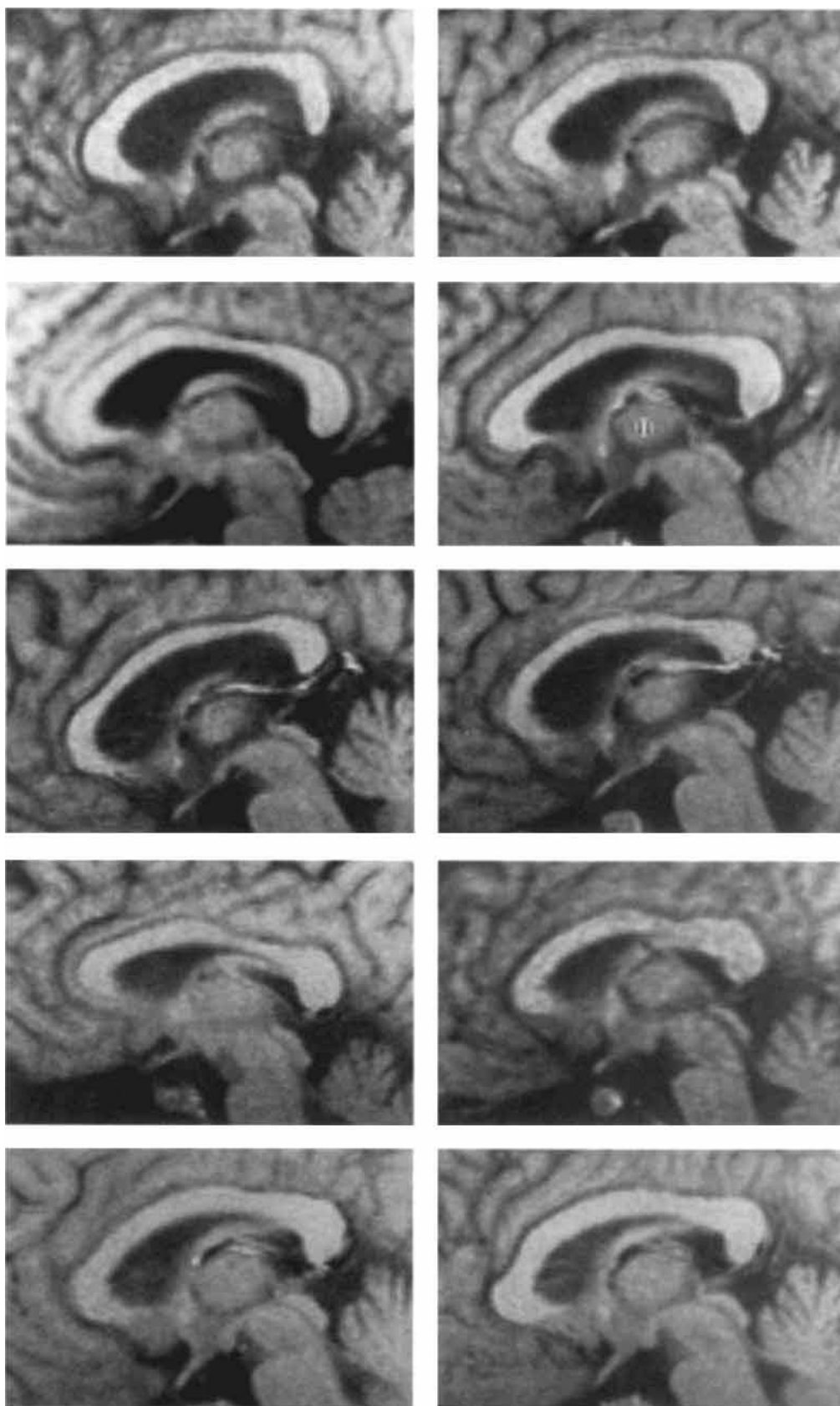


Fig 2. Sagittal magnetic resonance images of 5 pairs of identical twins are shown side by side from top to bottom. (In row 2,

column 2, the signal emanating from the diencephalon is a magnetic resonance imaging artifact.)

related control subjects were randomly paired and their overlap compared with that of the twin pairs. The unrelated pairs were formed in a blind fashion by an observer who pulled from a hat pairs of the names of 6 female and 4 male control subjects separately, so that 3 female pairs and 2 male pairs were created. Although this match was age independent, all of the control subjects were between 20 and 30 years old. Thus, 4 pairs of female twins and 1 pair of male twins were compared with 3 pairs of unrelated women and 2 pairs of unrelated men.

A line was drawn along the bottom of each callosal tracing (Fig 1, top). Perpendiculars were extended from this line at the rostral and splenial edge to define the maximal callosal length (line AE). Perpendiculars were also placed at points 10%, 50%, and 90% along the AE line, defining points B, C, and D, respectively. Midpoints were defined in the intracallosal segments of these perpendiculars (points F, G, and H). An angle was formed from these points (angle FGH). Paired tracings were overlaid at point GG' (see Fig 1, bottom). Tracings were rotated about this point until angle FGF' was equivalent to angle HGH'. This orientation achieves a maximal overlap of the major callosal angles. Planimetric measurements of the overlapping callosal areas were divided by the total area of overlapping and nonoverlapping areas. This yielded a percentage value of callosal overlap for each set. Additionally, a series of overlap measurements was made based on three estimations by each observer of the "best fit" between the two tracings in each pair. Finally, a single observer was asked to sort the 10 twin tracings into pairs.

To test scan-rescan sensitivity, 1 subject was scanned on six separate occasions. One of the six scans was paired with the other five and these five pairs were analyzed by the angulation method.

Results

Callosal area correlated significantly within twin pairs ($r = .9886$, $p < 0.01$) but not within control pairs. There was no significant correlation for callosal length within either group. The group means for callosal length and total area did not differ significantly between the two study populations ($p > 0.1$, Table 1).

Overlap measurements, computed as an average of the two observers' results using the angulation method, are listed in Table 2. The individual results of the two observers were significantly correlated (angulation method: $r = .9603$, $df = 8$, $p < 0.01$; best-fit method: $r = .8610$, $df = 8$, $p < 0.01$) for measurements of both groups. Mean and standard deviations for the observers' averaged results using the best-fit method are also listed.

The original magnetic resonance images showing the corpus callosum are displayed in Figure 2. Mean overlap of the images from the twin group was significantly greater than mean overlap of those from the control group, using both the angulation method ($t = 3.127$, $p < 0.01$) and the best-fit method ($t = 3.43$, $p < 0.01$). In addition, the sorting of twin callosal scans was performed rapidly and without error. Mean overlap in the

scan-rescan series was significantly greater than the mean overlap in the twin group ($t = 3.925$, $p < 0.01$).

Discussion

The measurements of area and overlap reveal greater similarity in callosal morphological characteristics between twin pairs than between control pairs. However, the fact that the overlap in the scan-rescan series was greater than the overlap in the twin series indicates that the callosa of identical twins are not identical.

A genetic basis for the observed similarity in callosal morphological characteristics between twins seems likely, although it is possible that their similar in utero and postnatal environments influenced the results. Conversely, the observed differences in callosal morphological characteristics between twins necessarily reflects nongenetic influences in view of the high probability of monozygosity in our pairs. Whereas little is known about the neurogenesis of the corpus callosum in man, studies in animals have shown that nongenetic factors can influence synaptic adjustments made following "exuberant" growth patterns [14, 15].

The results of the present study indicate that the morphology of a major human brain structure that participates in intellectual functions is subject to both genetic and nongenetic influences. Interestingly, studies of intelligence in twins reveal a significant correlation of intelligence quotients that is subject to a variance caused by environment [16, 17]. This environmental influence may be manifest in the structural and functional plasticity of the human brain.

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