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Sexual Dimorphism of the Anterior Commissure and Massa Intermedia of the Human Brain

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ABSTRACT

Neuroanatomical sex differences were observed in the midsagittal area of both the anterior commissure and the massa intermedia on analysis of postmortem tissue from 100 age-matched male and female individuals. The anterior commissure, a fiber tract whose axons in primates primarily connect the two temporal lobes, was an average of 12%, or 1.17 mm^2 larger in females than in males. The massa intermedia, a structure that crosses the third ventricle between the two thalami, was present in 78% of the females and 68% of the males. Among subjects with a massa intermedia, the structure was an average of 53.3% or 17.5 mm^2 larger in females than in males. Inclusive of subjects with and without a massa intermedia, this structure was a mean of 76% or 16.93 mm^2 greater in females than in males. These sex differences were present despite the fact that the brains of males were larger than those of females. Since a majority of subjects were adults, it is unknown *when* sexual differentiation occurred. Anatomical sex differences in structures that connect the two cerebral hemispheres may, in part, underlie functional sex differences in cognitive function and cerebral lateralization.

Key words: interthalamic adhesion, sexual differentiation

Although it has long been recognized that the brain influences sex differences in animal behavior and reproductive physiology, neuroanatomical sexual dimorphisms have only recently been discovered that may underlie these functional differences. In regions of the brain known to control sexually dimorphic function, there are intracellular and ultrastructural neuroanatomical sex differences in the size of nerve cell nuclei (Pfaff, '66; Dörner and Staudt, '68); dendritic branching patterns of neurons in the preoptic area (POA) in the rat (Hammer and Jacobson, '84), hamster (Greenough et al., '77), and the macaque monkey (Ayoub et al., '83); and synaptic organization of the POA (Raisman and Field, '71), arcuate nucleus (Matsumoto and Arai, '81), and medial amygdala (Nishizuka and Arai, '81) of the rat. In contrast to these intracellular and ultrastructural differences, there are dimorphisms in terms of the volume of nuclei involved in vocal communication in songbirds (Nottebohm and Arnold, '76), in the bed nucleus of the stria terminalis in guinea pigs (Hines et al., '85) and rats (del Abril et al., '87), and in the POA of rats (Gorski et al., '78), gerbils (Yahr and Commins, '82), guinea pigs (Hines et al., '85), ferrets (Tobet et al., '86), and quail (Panzica et al., '87). In addition, scientists have recently identified structural sex differences in regions not directly related to reproductive function: in rats, there may be sexually dimorphic patterns of cortical and hippocampal asymmetries (Diamond et al., '83); and the corpus callosum is sexually dimorphic in terms of midsagittal area (Berrebi et al., '88), the number of axons, and extent of myelination (Juraska and Kopcik, '88).

Although numerous reports now exist on sex differences in laboratory animals, relatively little is known about sex differences in the human brain. In the preoptic-anterior hypothalamic area, a region of the brain implicated in rodents and subhuman primates in gonadotropin release (Gorski, '68; Plant et al., '79; Pohl and Knobil, '82), sexual behavior (Arendash and Gorski, '83; Oomura et al., '83), and maternal behavior (Jacobson et al., '80), there are dramatic sex differences in humans in the volume of several nuclei (Swaab and Fliers, '85; Allen et al., '89); similarly, a region of the bed nuclues of the stria terminalis is larger in men than in women (Allen and Gorski, '90); the shape of the suprachiasmatic nucleus differs between men and women (Swaab et al., '85); and Onuf's nucleus in the spinal cord, which innervates the perineal muscles, contains more motoneurons in men than in women (Forger and Breedlove, '86). In addition, several neurally controlled functions

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not directly related to reproduction are also sexually dimorphic: there are subtle differences in terms of cognitive abilities whereby women generally score better on tests of verbal abilities, and men on exams of mathematical skills (Harris, '78; Kimura, '87); there is a prevalence in boys relative to girls of several language disorders, including dyslexia, delayed speech acquisition, and stuttering (Hier, '79); and there is greater functional asymmetry in the male than in the female brain (McGlone, '80; Beaton, '85; Kimura, '87).

Recent evidence suggests that there may be a neuroanatomical basis for these functional differences. The massa intermedia (MI) of the thalamus is more often present in women than in men (Morel, '48; Rabl, '58; Davie and Baldwin, '67; Samra and Casper, '68), the direction of the asymmetry of the temporal planum differs between male and female fetuses (Wada, '75), and the shape of the splenium of the corpus callosum (CC) may be more bulbous in females (de Lacoste-Utamsing and Holloway, '82; Allen et al., '91). The latter observation has led to speculation that the axonal connectivity between the two hemispheres of the brain differs between the sexes; however, subsequent studies of the CC have produced conflicting results (for review see Allen et al., '91) in part because a specific, regional sex difference in this heterogenous structure may be difficult to isolate by arbitrarily partitioning and measuring parts of the CC based on its shape alone.

Should there be a general sex difference in the connectivity between the two cerebral hemispheres, either in terms of axons and/or other neural components such as glia, myelin, and connective tissue, then other structures present at the midsagittal plane of the brain may also be sexually dimorphic. In contrast to the CC, two smaller structures, the anterior commissure (AC) and the MI, connect relatively specific regions of the brain. Therefore, a sex difference in either structure may become apparent on examination of the total midsagittal area without further arbitrary partitioning.

MATERIALS AND METHODS

The brains used in this study, which were obtained from two Southern California hospitals, had been removed within 24 hours postmortem and placed directly into acetate-buffered 10% formalin for 2 to 4 weeks prior to coronal sectioning performed during routine autopsy. Following autopsies, the present investigators collected approximately 500 samples of brain tissue containing either the midsagittal region of the AC or the medial thalamic nuclei and the MI, if present; however, a note was made if no MI was present. These samples were collected without knowledge of gender. If one of the regions was removed or damaged during autopsy, only the other structure was collected from a given individual. Subsequently, samples were eliminated if they were from an individual whose medical record indicated neuropathology, neuroendocrine disorder, or homosexual orientation. This resulted in 138 ACs and 156 MIs (inclusive of subjects without an MI) whose identification codes were organized into four columns based on structure and gender, and ordered according to age. We age-matched subjects to obtain 50 pairs of males and females for both ACs and MIs. The region of the brain containing the medial area of the AC and the MI were sectioned in the midsagittal plane, and this surface of each structure was placed against a glass, adjacent to a ruler taped at the same plane, photographed, and made into slides (Fig. 1a,b). The slides of the ACs and MIs were projected onto white paper at a magnification of 20× and 12×, respectively.

Without knowledge of age or gender, two individuals traced each image. The area of each outline was determined by using a Bioquant Hipad digitizer, which is adjusted to correct for magnification (Bioquant IBM Program version 2.1; R & M Biometrics). Each measurement of the two investigators was compared, and if there was greater than a 5% difference between the areas of the tracings, the structure was reexamined by a third investigator and the two measurements in closest agreement were averaged.

The paired t-test was used to compare the areas and brain weights of the AC and the MI between male and female subjects. However, when the area of the MI was examined in only subjects with an MI, the independent t-test was used. Sex by age interractions was tested, using the paired paradigm, by regressing the difference in area between each male and female pair with the average age of each pair (Smith and Choi, '82). Pearson's correlation coefficient (Dawson-Saunders and Trapp, '90) was used to test for correlations between the measurements of the two tracers, brain weight and area, age and area, and between areas of the AC and MI when both were examined within a given individual.

Abbreviations

AC	anterior commissure
CC	corpus callosum
MI	massa intermedia
POA	preoptic area

RESULTS

Anterior commissure

There was a highly significant correlation between the two measurements of the two individual tracers ($r = 0.93$; $p < 0.0001$). Three pairs of children ranged from 4 to 14 years of age and 47 pairs of adults ranged from 20 to 84 years, with a maximum of 10 years and an average of 2.2 years between pairs (Table 1, Fig. 2a). The midsagittal surface area of the AC of the female subjects (mean ± S.E.M. = 11.003 ± 0.45 mm^2) was an average of 1.165 mm^2 or 11.8% greater than that of male subjects (9.838 ± 0.41 mm^2) (paired t-test: $p = 0.038$), despite the fact that the male brains (1332.83 ± 16.41 gms) were 6.7% larger than those of the females (1248.7 ± 15.48 gms) ($p = 0.0006$). Similarly, the midsagittal surface area of the AC was greater in women (10.964 mm^2) than in men (9.76 mm^2) ($p = 0.030$); however, there was an insufficient number of children to determine whether there was a sex difference during childhood. There was no significant correlation between brain weight and size of the AC ($r = 0.13$; $p = 0.186$). In adults, the area of the AC did not change with advancing age ($r = 0.04$; $p = 0.69$), for women ($r = 0.05$; $p = 0.718$), or men ($r = 0.15$; $p = 0.31$).

Since visual inspection of Figure 2a suggested that the difference in area between males and females might be greater after the age of about 50, we tested our data for a sex by age interraction by regressing the difference in area between males and females of each pair (in this case, the male value minus the female value) against the average age

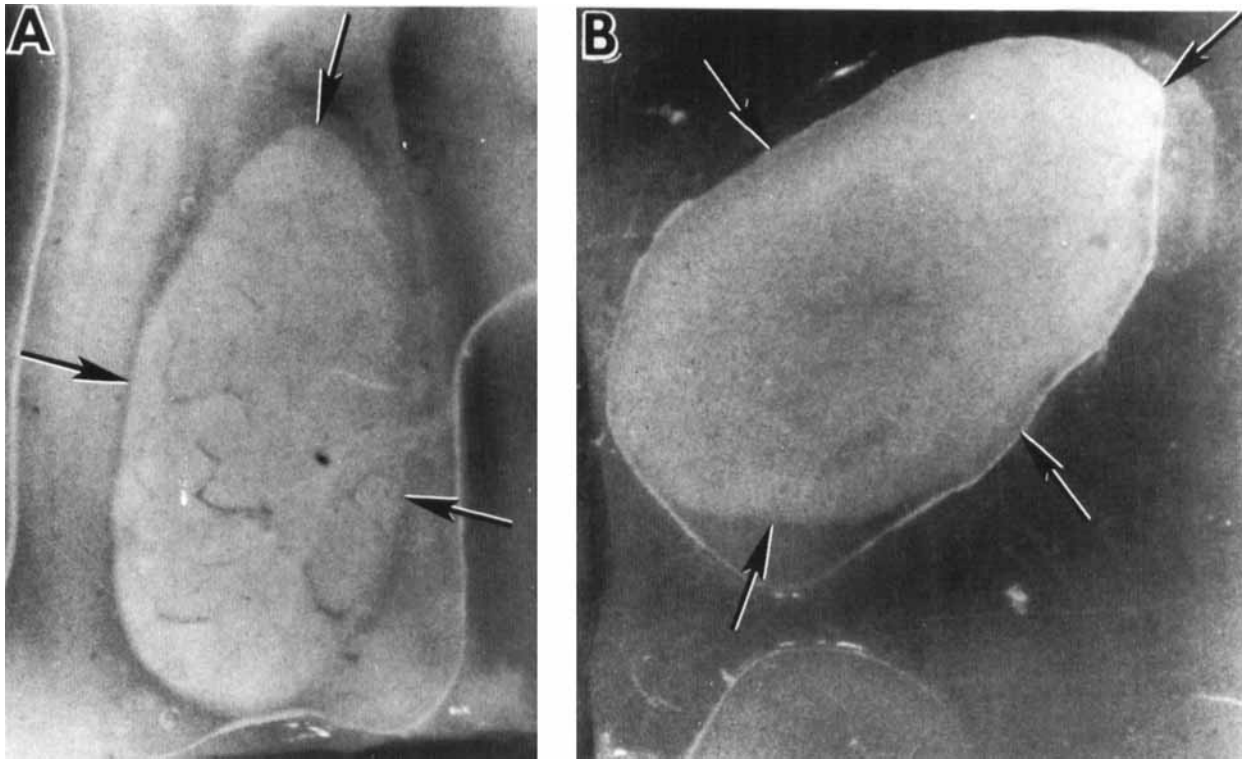

Fig. 1. **A** and **B** are photographs of the midsagittal region of the anterior commissure and the massa intermedia, respectively. The arrows indicate the borders of the anterior commissure and the massa intermedia.

TABLE 1. Mean ± S.E.M. for Age, Brain Weight, and Area of the Anterior Commissure (AC) and Massa Intermedia (MI)

	N	Age (years)	Brain weight (grams)	Area (mm^2)	p
AC—all females	50	58.38 ± 2.7	1,249 ± 15	11.00 ± 0.45	0.038
AC—all males	50	58.52 ± 2.7	1,332 ± 16	09.84 ± 0.41	
AC—adult females	47	61.57 ± 2.14	1,257 ± 15	10.96 ± 0.48	0.030
AC—adult males	47	61.72 ± 2.09	1,334 ± 17	09.68 ± 0.43	
MI—all females w/MI	39	59.35 ± 3.04	1,233 ± 17	50.31 ± 5.8	0.011
MI—all males w/MI	34	58.92 ± 3.55	1,290 ± 36	32.83 ± 3.2	
MI—adult females w/MI	36	63.92 ± 1.76	1,238 ± 16	46.88 ± 5.67	0.023
MI—adult males w/MI	31	64.19 ± 2.15	1,327 ± 22	31.77 ± 3.12	
MI—all females	50	59.53 ± 2.54	1,236 ± 15	39.26 ± 5.4	0.009
MI—all males	50	59.24 ± 2.63	1,307 ± 26	22.33 ± 3.1	
MI—adult females	47	63.04 ± 1.6	1,240 ± 15	35.91 ± 5.2	0.024
MI—adult males	47	62.75 ± 1.8	1,333 ± 17	20.96 ± 3.0	

of each pair ($r = 0.209$; $p = 0.145$) (Smith and Choi, '8 2). However, at the correlation coefficient of $r = 0.209$, a total of 200 pairs would be necessary to detect a significant ($p = 0.05$) sex by age interraction at a power of 0.81.

There was no correlation between the area of the AC and duration in fixative ($r = 0.2$; $p = 0.87$); furthermore, the average duration in fixative was 20.3 months for females and 20.1 months for males ($p = 0.90$).

Massa intermedia

There was a highly significant correlation between the two measurements of the two tracers for only subjects *with* an MI ($r = 0.87$; $p < 0.0001$) and for *all* subjects ($r = 0.91$; $p < 0.0001$). Three pairs of children ranged from 0.2 to 11 years of age; 47 pairs of adults ranged from 28–82 years, with a maximum of 6 years and an average of 1.1 years between pairs (Table 1, Fig. 2b). The MI is more frequently absent in males than in females (Morel, '48; Rabl, '58; Davie and Baldwin, '67; Samra and Cooper, '68). However, in this study, the sex difference in the midsagittal area of the MI was not a result of its greater absence in males than in females (32% of the males and 22% of the females had no MI), since the midsagittal surface area of the MI for subjects with an MI was greater in females (50.33 ± 5.77 mm^2) by an average of 17.5 mm^2 or 53.3% greater than in males (32.83 ± 3.2 mm^2) ($p = 0.011$; independent t-test), despite the fact that the male brain (1,290 ± 36 gms) in these subjects weighed an average of 4.6% more than the female brain (1,233 ± 17 gms) ($p = 0.15$). Among adults *with* an MI the mean midsagittal surface area of the MI of women (46.88 ± 5.7 mm^2) was 15.11 mm^2 or 47.6% greater than that of men (31.77 ± 3.1 mm^2) ($p = 0.023$; independent t-test); however, there were only six children, thereby precluding statistical analysis on these subjects alone.

Among *all* subjects, the mean midsagittal surface area of the MI of females (39.258 ± 5.39 mm^2) was an average of 17.498 mm^2 or 75.8% greater than of males (22.33 ± 3.1 mm^2) (paired t-test: $p = 0.009$) despite the fact that the male brain (1,307 ± 26 gms) weighed an average of 5.7% more than the female brain (1,236 ± 15 gms) ($p = 0.007$). Similarly, among adults the midsagittal surface area of the MI was greater in women (35.911 ± 5.39 mm^2) than in men (20.956 ± 3.10 mm^2) ($p = 0.024$); however, there were only three pairs of children, which precluded statistical analysis of these subjects. There was no significant correlation between brain weight and size of the MI among subjects

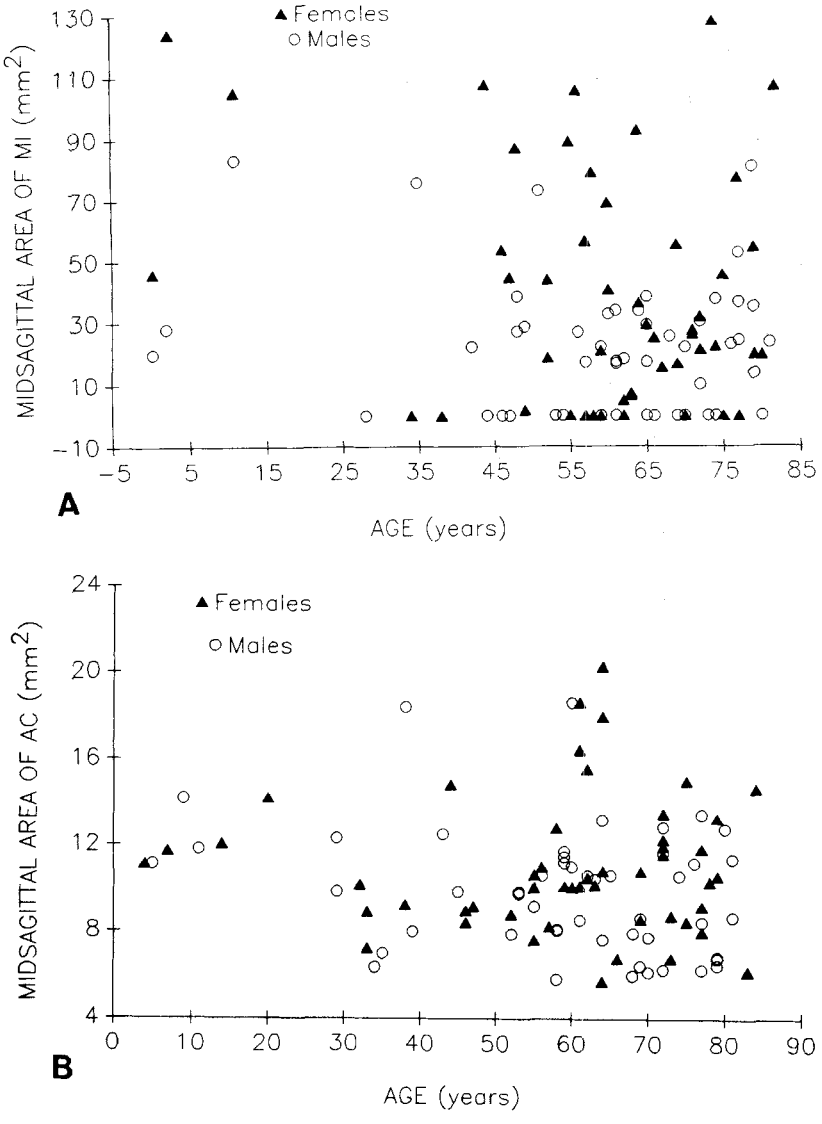

Fig. 2. (**a**) Anterior commissure (AC) midsagittal cross-sectional area as a function of age. In adults, there was no significant change in the area of the AC ($r = 0.04$; $p = 0.692$) in women ($r = 0.054$; $p = 0.717$) or in men ($r = 0.152$; $p = 0.308$). (**b**) Massa intermedia (MI) midsagittal cross-sectional area as a function of age. In adults, there was no significant change in the area of the MI ($r = 0.0196$; $p = 0.851$) in women ($r = 0.007$; $p = 0.962$) or in men ($r = 0.035$; $p = 0.815$).

with an MI ($r = 0.021$; $p = 0.86$) or among all subjects ($r = 0.058$; $p = 0.562$).

In adults *with* an MI, the area did not change with advancing age ($r = 0.116$; $p = 0.352$) in women ($r = 0.107$; $p = 0.535$) or in men ($r = 0.161$; $p = 0.387$). Similarly, among *all* adults, the area of the MI did not change with advancing age ($r = 0.02$; $p = 0.85$) in women ($r = 0.007$; $p = 0.96$) or in men ($r = .04$; $p = 0.815$). There was no sex by age interraction for either pairs where *both subjects had an MI* ($r = 0.018$; $p = 0.905$), or for *all* adults ($r = 0.094$; $p = 0.586$) when we regressed the difference in area between males and females of each pair (in this case, male value minus female value) with the average age of each pair.

The average duration in fixative for subjects with an MI was 18.8 months for females and 19.1 months for males, with no correlation between duration in fixative and area of the MI ($r = 0.107$; $p = 0.334$). For *all* subjects, the average duration in fixative was 18.5 months for females and 18.6 months for males, with no correlation between duration in fixative and area of the MI ($r = 0.11$; $p = 0.51$).

Relation between the anterior commissure and the massa intermedia

In 39 subjects in which both the AC and MI were obtained, there was no correlation between midsagittal surface areas of the AC and the MI ($r = .047$; $p = 0.803$). However, failure to obtain correlations could, in part reflect the great variability in areas of both the ACs and the MIs (Table 1, Fig. 2a,b).

DISCUSSION

The functional significance of sex differences in the AC and the MI is unknown. However, such sexual dimorphisms

may underlie differences between males and females in terms of cognitive skills (Harris, '78; Kimura, '87), developmental language disorders (Hier, '79), and functional asymmetry (McGlone, '80; Beaton, '85; Kimura, '87). It is unclear whether these sex differences are due to differences in the number of axons, thickness of myelination, or, in the case of the MI, the number of cell bodies. However, in the rhesus monkey, the area of the AC does not correlate well with the number of axons (LaMantia and Rakic, '90). The size of the MI at the midsagittal surface may not relate to the interhemispheric axons or the cell bodies at the midsagittal plane; rather, it may underlie a sex difference in the volume, presence, and/or arrangement of nuclei which compose the thalamus.

Methodological considerations

Although we matched our subjects for age, we did not match them for either the postmortem period prior to removing the brains from their skulls and placing them into fixative, or for the duration in fixative prior to histological preparation. Although either of these two variables could influence shrinkage, the postmortem period was less than 24 hours, and there was neither a significant difference in duration of fixation between male and female subjects, nor a significant correlation between duration of fixation and the midsagittal area of either the AC or the MI for either males, females, or for all subjects combined. Furthermore, slight error could be introduced by imprecision of the midsagittal plane; however, all brains were sectioned through the third ventricle as close to the midline as possible. Although either of these variables may have introduced error into our measurements, it is unlikely that they contributed significantly to the sex difference. We believe that the 3.5-fold range in the areas of the ACs among all subjects and the 71.1-fold range in the areas of the MIs among subjects *with* an MI reflects the actual high degree of variation in the area of these structures within the human brain, rather than artifactual or methodological error; therefore, large sample sizes are necessary to demonstrate the presence of sex differences. Similarly, other investigators observed considerable variation in the area of the AC (Tomasch, '57; Demeter et al., '88) and the MI (Morel, '48; Rabl, '58; Davie and Baldwin, '67; Samra and Cooper, '68).

Anatomy

Anterior commissure. The AC of the primate brain is a tract of axons that primarily connects the right and left temporal neocortices (Fox et al., '48; Whitlock and Nauta, '56; Pandya et al., '69; Pandya et al., '73; Rocha-Miranda et al., '75; Gross et al., '77; Jouandet and Gazzaniga, '79; Jouandet, '82). It is unknown whether sex differences in the area of the AC reflect differences in the number of axons, in myelination, connective tissue, or glia. In a small sample of human subjects, differences in the area of the AC reflected differences in the number of axons and not their density (Tomasch, '57). In contrast, in a study of the rhesus monkey, the midsagittal surface area of the AC did not correlate strongly with the number of axons ($r^2 = .473$) (LaMantia and Rakic, '90). Although there may be axonal elimination due to atrophy with advancing age, in humans there is protracted myelination of the AC at least into adulthood (Yakovlev and Lecours, '67). Therefore, the relation between midsagittal area of the AC and the number of axons may actually change over the course of a lifespan, which in part can be accounted for by age-matching subjects should these two processes occur at a similar rate in both sexes.

Massa intermedia. The MI of the primate is composed of neurons and neuropil, as well as loosely organized axons that connect the thalami (Crouch and Thompson, '38; Glees and Wall, '48), and motor, premotor, and prefrontal areas (DeVito, '69; Künzle, '76). In humans, pro-somatostatin-derived-peptide-positive fiber tracts course through the MI (Bouras et al., '87). Neuroanatomists do not agree on which thalamic nuclei constitute the human MI, perhaps because of its considerable variability among individuals. However it may be composed of nucleus rhomboideus (Sheps, '45), nucleus centralis medialis (Sheps, '45; Toncray and Krieg, '46), and/or nucleus renuniens (Rabl, '48). It is unknown whether variation among individuals in the midsagittal area of the MI reflect differences in neurons, glia, neuropil, connective tissue, or axons. In fact, sex differences in the MI may reflect differences in the size and/or presence or absence of the nuclei rhomboideus, centralis medialis, and/or reuniens, which are also present bilaterally.

Sexual differentiation

On the basis of our small sample of children, it is unclear *when* sexual differentiation occurs. However, genomic factors, the environment, and/or gonadal hormone levels may influence sex differences in the AC and/or MI. For example, structures reported to be sexually dimorphic in rats, including the cerebral cortex (Diamond, '88) and the CC (Berrebi et al., '88; Juraska and Kopcik, '88), are influenced by environmental factors both pre- and postnatally in a sexually dimorphic manner. The sexually dimorphic pattern of cerebral cortical asymmetry may be altered by both prenatal stress (Fleming et al., '86) and an enriched postnatal environment (Diamond, '88), and the CC in rats may be influenced prenatally by maternal alcohol consumption (Zimmerberg and Scalzi, '89) and postnatally by handling (Berrebi et al., '88), and each of these environmental factors influences males and females differently. More consistent, however, have been the observations in laboratory animals that all sexually dimorphic structures examined thus far have been shown to be influenced by perinatal gonadal hormone exposure. Therefore, based on animal studies, it is possible that environmental factors may influence the AC and MI in a sexually dimorphic manner, but perinatal gonadal hormones are also likely to be involved.

The mechanism by which environmental factors influence neural structure differently between males and females is unknown, although a gonadal hormone mechanism underlies the effect of prenatal stress in rats (Ward, '84). With respect to gonadal hormones, the elimination of neurons in sexually dimorphic nuclei appears to be determined by the presence or absence of gonadal hormones during a critical period of development (Nordeen et al., '85). Since there is uptake of gonadal hormones in the cerebral cortex of the developing rat (Sheridan et al., '74; MacLusky et al., '79) and rhesus monkey (MacLusky et al., '86) and an elimination of neurons and their axons during development (Berlucchi, '81), it is conceivable that gonadal hormones influence the number of axons and/or neurons of the AC and MI. Similarly, it is possible that (to some extent) sex differences in the AC and MI reflect the different influences of gonadal hormones upon myelination: in rats, *estradiol* increases myelination (Curry and Heim, '66), and during

development, 5-α-reductase, the enzyme that converts testosterone to dihydrotestosterone, is inversely related to myelination (Celotti et al., '87).

It is unknown whether the sex differences in the *presence or absence* of an MI, and in the *midsagittal area* of the MI are similar in terms of the process of sexual differentiation and/or functional significance.

Functional significance

In contrast to the sexually dimorphic nuclei, many of which are believed to underlie sexually dimorphic reproductive functions, sexual dimorphism in the AC, MI, CC, and cerebral hemispheres are less dramatic and more difficult to explain. Whereas the sexually dimorphic nuclei are highly dimorphic as are the functions that they probably underlie, sex differences in regions not directly related to reproductive function are less dimorphic in terms of magnitude and exhibit considerable overlap among individuals of both genders in terms of the midsagittal area of the AC (Fig. 2a), MI (Fig. 2b), CC (Allen et al., '91), and cerebral hemispheres (Wada et al., '75). Although the functional significance of these structural sex differences is unknown, they are present in regions of the brain that control functions such as cerebral lateralization and cognitive skills that also exhibit only subtle sex differences with considerable overlap between male and female individuals. In fact, it is conceivable that differences in the AC and MI are of no functional significance but simply a result of different metabolic influences of estrogen (Curry and Heim, '66) and testosterone (Celotti et al., '87) on myelination. Should sex differences in the AC and/or MI reflect differences in the number of axons coursing through these structures, then these differences in "communication" may, in part, underlie sex differences in neurofunctional asymmetries (McGlone, '80; Beaton, '85; Kimura, '87) and/or cognitive function (Nyborg, '84; Kimura, '87). In fact, there is some indication that both the AC and MI may be involved in both cerebral lateralization and cognitive function.

Anterior commissure. The AC in macaques may play a role in inhibiting the bilateral formation of engrams, thereby increasing both functional asymmetry and pneumonic storage capacity of the brain by preventing redundancy (Doty and Overman, '77). The presence of the AC may be responsible for difficulties in discriminating left-right mirror images, since monkeys with sectioned ACs are able to differentiate more accurately between left-right mirror images (Achim and Corballis, '77). Together with the splenium of the CC, which may also be sexually dimorphic (de Lacoste-Utamsing and Holloway, '82; Allen et al., '91), the AC mediates the interhemispheric transfer of visual discrimination between the hemispheres of nonhuman primates (Black and Myers, '64; Gazzaniga, '66; Noble, '68; Rocha-Miranda et al., '75; Gross et al., '77; Jouandet and Gazzaniga, '79) and in humans, the interhemispheric transfer of visual, auditory, and olfactory information (Risse et al., '78). However, it is unclear whether any of these specific functions is sexually dimorphic or whether the actual number of axons and/or midsagittal surface area of the AC has any bearing upon these functions.

Massa intermedia. In cats, the MI is involved in both the *symmetric* and *asymmetric* release of dopamine in the basal ganglia. With respect to the asymmetric effects, electrical stimulation of the forelimb (Leviel et al., '81) and certain dopaminergic drugs infused into the substantia nigra (Glowinski et al., '84) increase dopamine release from the ipsilateral caudate and decrease it from the contralateral caudate while decreasing it from the ipsilateral substantia nigra and increasing it from the contralateral substantia nigra. Similarly, unilateral infusions of GABA into the thalamic or intralaminar nuclei induce the release of dopamine in the contralateral substantia nigra (Romo et al., '84). The *anterior* part of the MI (interanteromedialis nucleus and nucleus reuniens), but not the nucleus centralis medialis, is involved in the bilateral regulation of dopamine from the nerve terminals and dendrites of the nigro-striatal dopaminergic neurons (Chéramy et al., '81). With respect to the *symmetric* effects upon dopamine release, unilateral electrical stimulation of the nucleus interanteromedialis, and nigral infusions of potassium (Glowinski et al., '84) result in increased *bilateral* release of dopamine from the caudate and substantia nigra (Glowinski et al., '84).

In the cat, the MI plays an important role both for transhemispheric ictal propagation and for the positive transfer effect of amygdaloid kindling (Hiyoshi and Wada, '88). In primates, there is the development of convulsive seizure bilateralization in animals with a sectioned hippocampal commissure, corpus callosum, and AC, probably due to communication between hemispheres through the MI (Wada and Mizoguchi, '84).

The role of the MI in asymmetries in the human brain is unknown; however, in the thalami, between which the MI is a major bridge, there are asymmetries of norepinephrine levels (Oke et al., '78). Furthermore, in humans, there is thalamic lateralization of language function (Riklan and Cooper, '77). Whether these asymmetries are due to axons that course through the MI or whether there are sex differences in thalamic nuclei is unknown; however, there are sex differences in rats in striatal dopamine (Robinson et al., '80) and norepinephrine levels (Dark et al., '84). With respect to cognitive function, pneumoencephalograms demonstrated that men without an MI exhibited higher performance on the nonverbal portion of the Wechsler Bellevue IQ test than men with this structure (Lansdell and Davie, '72).

Future studies

Although it is unknown whether nonhuman animals have a sexually dimorphic AC or MI, animal models may be difficult to utilize for studying sexual dimorphism of the human AC and MI, since both structures change dramatically with advancing evolutionary development. For example, the AC in rodents consists predominantly of the anterior limb, which contains primarily axons from cell bodies of the olfactory system; however, in primates, the anterior limb may be reduced to a few strands and the posterior limb, which contains principally axons from cell bodies of the temporal cortex, is relatively evolved (Fox et al., '48; Klinger and Gloor, '60; Jouandet and Gazzaniga, '79). In contrast, the MI decreases in relative size as cortical evolution progresses (Sheps, '45; Glees and Wall, '48; Malobabíc et al., '87). However, advancements in the resolution of in vivo imaging techniques such as magnetic resonance imaging may enable us to correlate the midsagittal areas of ACs and MIs with neuropsychological function and gonadal hormone exposure, thereby leading to an understanding of how environmental factors and/or the gonadal hormones sexually differentiate both the structure and function of the human brain. Since the AC, the MI, and possibly the splenium of the CC, are on the average larger

at the midsagittal plane of the brain in human females, an interesting question arises: Is there greater connectivity between the cerebral hemispheres of women than in men?

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