Commentary

Analyzing the Corpus Callosum

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The corpus callosum has been recognized and studied for centuries. Although this structure appears to have been mentioned by Galen in the second century AD, the first available anatomic description appears to have been rendered by Vesalius in "De Humani Corporis Fabrica" (1543, translated by Clarke and O'Malley [1]). As reviewed by Njiokiktjien (2), speculation on the function of the corpus callosum began during the 17th century, but it was not until the late 19th century, after it was discovered that the white matter of the brain is composed of separate bundles of axons, that neuroscientists became aware that callosal axons connect homologous areas in the cortices of the cerebral hemispheres. Afterward, in the early years of the 20th century, studies of patients with disconnection syndromes were published (3–6), and the function of the corpus callosum became much better defined. Accurate clues to the embryology of the corpus callosum came much later, with the most important early work done by Abbie (7), Loeser and Alvord (8, 9), and Rakic and Yakovlev (10), as noted in the article by Kier and Truwit (11) in this issue of *AJNR*. More recent work on the mechanisms by which the callosal axons migrate across the midline of the developing brain and navigate through the milieu of the developing brain to reach their final synaptic connections has been largely performed by Silver and coworkers (12–15) and suggests that callosal axons are guided across the midline by molecular clues on the surface of glial cells. These theories have been reviewed recently in the *AJNR* (16).

The article by Kier and Truwit (11) in the present issue of the *AJNR* deals with the appearance of the normal corpus callosum and in particular the location of certain portions of the corpus callosum with respect to the mamillary bodies and the anterior commissure during development. The article has a number of interesting aspects, although this commentary will deal with only a few of them.

As the authors point out, it was established long ago that the initial callosal axons cross in the midline near the region of the foramina of Monro. This is discussed both in the paper by Abbie (7) and in the paper by Rakic and Yakovlev (10), both referenced by the authors. Kier and Truwit have not modified this concept; instead they have focused on the location of the point of initial callosal crossing with respect to what they call the *MAC line*, a line defined by two points, the mamillary bodies and the anterior commissure on a (presumably) midline sagittal magnetic resonance image. Kier and Truwit have defined the callosal genu as the portion of callosal fibers that lies anterior to the MAC line. They do not define the thickness of the midline image that they use, nor do they discuss the portion of the anterior commissure or mamillary bodies (anterior edge, posterior edge, middle) that should be used for drawing the line or the potential effects of averaging the two mamillary bodies. They do not discuss whether the structures chosen as the points for the creation of the MAC line might be important. The authors justify their definition of the genu by its ease of application on sagittal MR images and by their statement that the boundaries of the components of the corpus callosum are not defined in the anatomic literature. Although some definitions of the genu have been presented in the neuroscience (17) and neuropathology (18) literature, the authors have chosen not to use these. In fact, defining the genu by the MAC line seems to be as reasonable as the other definitions that have been proposed.

Kier and Truwit have performed an extraordinary amount of work to complete this project and they are to be commended for that. The mere thought of reviewing 1800 cases of normal corpora callosi is exhausting! Nonetheless,

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I must state that points made by the authors by definition anticipated their results. An example is their statement "In 1800 clinical scans with a normal corpus callosum. . .the genu always projected anterior to the MAC line." This should not be surprising to the authors as they in fact defined the genu as that portion of the corpus callosum anterior to the MAC line. It would have been truly extraordinary had the genu *not* projected anterior to the MAC considering the definition.

A few questions arise in reviewing this work. The first pertains to the consistency of the anatomic relationship of the mamillary bodies to the anterior commissure. Although the consistency of this relationship is the cornerstone of their paper, Kier and Truwit have not proved that the relationship of these structures is unchanged during development. If, in fact, these structures were to move with respect to one another during the formation of the cerebral hemispheres, it would weaken the authors' arguments regarding the relative location of the crossing of the callosal axons during different stages of development. In fact, there seems to be considerably more cerebral hemisphere anterior to the MAC line in their Figures 4B, C, and D (developing brain), for example, than in their Figures 6A and B (mature brain). If the mamillary bodies and the anterior commissure were in a constant relation to one another, one would expect the opposite finding because, as the authors mention, the prefrontal regions develop late in gestation. In addition, their Figures 8 and 9 show very variable relationships between the mamillary bodies and anterior commissures. Finally, in looking at the authors' examples in Figures 8 and 9, it is not at all obvious to this observer how they were able to determine with confidence the location of the anterior commissure in all cases and how they were able to determine which portion of the anterior commissure through which to draw the MAC line in those patients in whom the commissure is large. The point at which the MAC line intersects the corpus will vary considerably depending on the point in the anterior commissure through which the line is drawn.

The key to getting the most out of this is taking home a message that can be used in everyday practice. Proper analysis of the corpus callosum is an easy and extremely important step in the accurate interpretation of pediatric brain MR. The corpus and its precursors develop between the 8th and 20th gestational weeks, a time during which the basal ganglia, cerebral, and cerebellar hemispheres are forming (19). Therefore, the presence of an anomaly of the corpus callosum strongly correlates with anomalous development of other portions of the brain (20). Thinning of the corpus, either focally or diffusely, is suggestive of either brain injury or an abnormality of myelination (20). By drawing attention to the corpus callosum, the article by Kier and Truwit will, I hope, focus attention on this very important structure. Aside from emphasizing the importance of the corpus callosum in the analysis of the pediatric brain, the most important message of this paper seems to be that an anterior bend, which might be called the *genu*, is present in nearly all cases of callosal hypogenesis (partial callosal agenesis). This is apparent both from illustrations in the basic science literature on callosal development (13) and from many cases in the authors' own series. The authors have termed this the *fetal genu* to distinguish the genu seen in the fetal corpus callosum and in callosal hypogenesis from the *normal genu*, which they define as that portion of the corpus anterior to the MAC line. This is an unfortunate choice of terms in that the fetal genu is "normal" for the fetus. Nonetheless, the key concept is to recognize that, no matter when in gestation the axons within it actually cross the midline, a genu (the exact term for which is unimportant) will be present at the anterior end of most hypogenetic corpora callosi.

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