

REVIEW AND UPDATE

Functioning of the corpus callosum in children with early hydrocephalus

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Abstract

The development and organization of the corpus callosum is described as well as the relationship between the timing of insults and the type of partial agenesis of the corpus callosum are discussed. Neuropathology and callosal damage associated with spina bifida meningocele, aqueductal stenosis, and prematurity–IVH are outlined. Relationships between corpus callosum/whole brain ratios and cognitive functioning as well as interhemispheric transfer in children with these disorders are outlined. Shortcomings of current research and future directions are suggested. (*JINS*, 2000, 6, 351–361.)

Keywords: Hydrocephalus, Corpus callosum, Children, Tachistoscopic, Dichotic listening, Tactile naming, ITT

INTRODUCTION

Hydrocephalus generally refers to excessive cerebrospinal fluid (CSF) in the head (Shaw & Alvord, 1995). Hydrocephalus is always secondary to another disorder or disease of the brain. In its acquired form, hydrocephalus can occur at any age. It can be associated with trauma, infection, or tumors in both children and adults and, additionally, with dementia-like conditions in adults (Gascon & Leech, 1991). Early-onset hydrocephalus can be the result of congenital and perinatal disorders such as neural tube defects (e.g., spina bifida meningocele), aqueductal stenosis, and intraventricular hemorrhage associated with prematurity as well as other disorders (Barkovich, 1995). Spina bifida (SB) meningocele occurs at a rate of .5 to 1 per 1,000 live births and the rate is approximately .05 per 1,000 live births for aqueductal stenosis (AS). About 20% of premature births involve prematurity–intraventricular hemorrhage (IVH; Volpe, 1995). Early onset hydrocephalus is often associated with abnormalities of the corpus callosum. Before describing the neuropathology of these disorders and the associated callosal difficulties, the development and organization of the corpus callosum will be discussed in order to provide a context for later comments. The importance of taking a

neurodevelopmental approach to understanding relationships between callosal as well as other dysmorphologies and cognitive dysfunction is emphasized. Research using this approach may produce theoretically important information about callosal functioning as well as clinically relevant information about cognitive deficits in children with hydrocephalus.

DEVELOPMENT AND ORGANIZATION OF THE CORPUS CALLOSUM

The corpus callosum is the largest of the forebrain commissures. At about 7 weeks of gestation, the dorsal part of rostral wall of the forebrain known as the lamina terminalis begins to thicken and form the lamina reuniens or commissural plate. The dorsal part of the lamina reuniens folds into a median groove called the sulcus medianus telencephali medii (SMTM). A glial sling bridges the groove and helps to guide axons across the midline by expressing surface molecules and secreting chemicals (Barkovich, 1995). At 9 weeks of gestation, cells from the lamina reuniens grow into the SMTM. The cell mass in the SMTM eventually becomes the massa commissuralis into which fibers of the corpus callosum grow beginning at 12 weeks (Barkovich, 1995; Barkovich & Norman, 1988). It should be noted that other cerebral commissures have already begun to send fibers across the midline. The anterior commissure begins to develop at about 10 weeks of gestation followed by the hip-

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poampal commissure at 11 weeks. The earlier development of commissures other than the corpus callosum may be important to the interhemispheric transfer of children with complete or partial agenesis of the corpus callosum (Jeeves, 1994). For instance, the anterior commissure normally connects visual and auditory association areas in the temporal lobes and, in some cases of agenesis, may be enlarged to provide a compensatory mechanism (Fischer et al., 1992).

The corpus callosum is basically present by 20 weeks (Barkovich, 1995). Development continues during gestation and after birth with the corpus callosum increasing in thickness as the cortex matures. All parts of the corpus callosum do not develop simultaneously. The genu, the body, and then the splenium develop before the rostrum (Figure 1). Because of the sequence of callosal development, the regions that develop or do not develop give evidence of the timing of the insult and, to some degree, the type of insult (Barkovich, 1995). When there is partial agenesis from congenital disorders, the genu is almost always present since it begins to develop before the body. The body, or part of it, may be present. The rostrum and the splenium are most likely to be small or absent (Barkovich, 1995). Generally, if the rostrum and splenium are present while the genu and body are hypoplastic (thinned) or absent, a destructive lesion such as secondary hydrocephalus is likely to be the cause. This is common in premature infants with IVH who require shunts to control progressive hydrocephalus.

If there is agenesis or partial agenesis of the corpus callosum, the cingulate gyrus or parts of it in the region of the agenesis do not invert as they should. Furthermore, the axons of callosal neurons which would normally run interhemispherically may turn and run parallel to the interhemispheric fissure forming the longitudinal callosal bundles of Probst and producing crescent shaped lateral ventricles

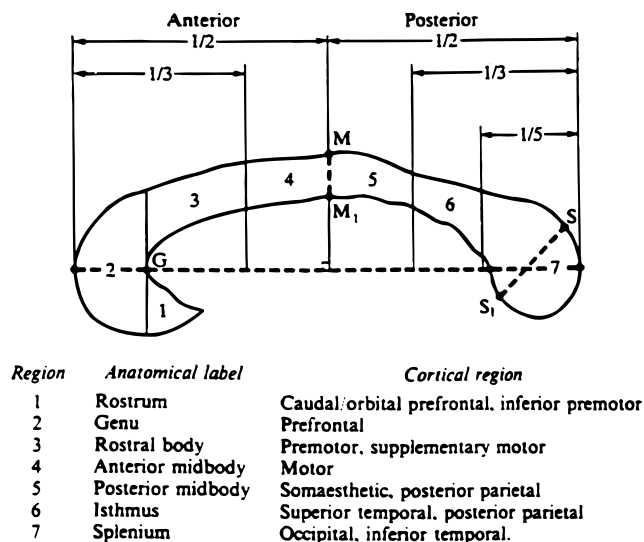


Fig. 1. Anatomy of the corpus callosum with divisions given by Witelson (1989). (Reprinted with permission from Klaas et al., in press).

(Barkovich, 1995; Barkovich & Norman, 1988; Rakic & Yakovlev, 1968; Figure 2).

Not much is known about the Probst bundles. Research with mice having congenital agenesis of the corpus callosum (Ozaki & Walsten, 1993) indicates that not all axons in the Probst bundles stay in the bundles. Some are able to traverse the midline by growing across the dorsal surface of the hippocampal commissure when it is large enough. In fact, patients sometimes have an enlarged hippocampal commissure that may be mistaken for the splenium of the corpus callosum on a sagittal view but can be seen to connect the fornices on a coronal view of the corpus callosum (Barkovich, 1995; Figure 3). Some axons leave the bundle and enter the ipsilateral white matter to form functional ipsilateral cortico-cortical connections (Lefkowitz et al., 1991; Ozaki et al., 1989). Corpus callosum axons have been traced in adult mice with partial agenesis and even a small corpus callosum was reported to include axons from many cortical regions (Olavarria et al., 1988; Ozaki et al., 1987). These findings raise several questions: Are there fibers from many cortical areas in the remaining corpus callosum of children with partial agenesis? If so, are these fibers sufficient to support callosal transfer? Are the anterior commissure and the hippocampal commissure involved in compensatory processes in humans? If so, to what degree and with what pattern of agenesis?

The corpus callosum provides communication between most regions of the cerebral hemispheres. Experimental work with monkeys and clinical research with humans (see Witelson, 1989) have resulted in rough divisions of the corpus callosum. These divisions include the rostrum, genu, body (rostral body, anterior midbody, posterior midbody, isthmus, and splenium), going from anterior to the posterior. The rostrum seems to connect the caudal-orbital prefrontal and inferior premotor cortices. The genu connects the prefrontal

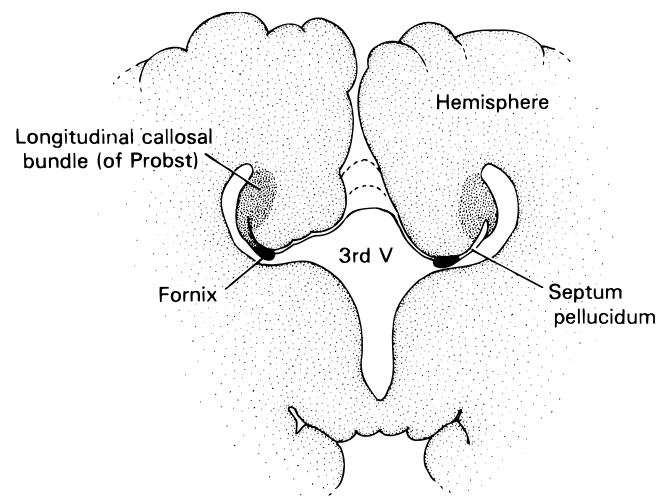


Fig. 2. Illustration of crescent shaped ventricles, longitudinal bundles of Probst, and everted rather than inverted cingulate gyri. (Reprinted with permission from Barkovich, 1995).

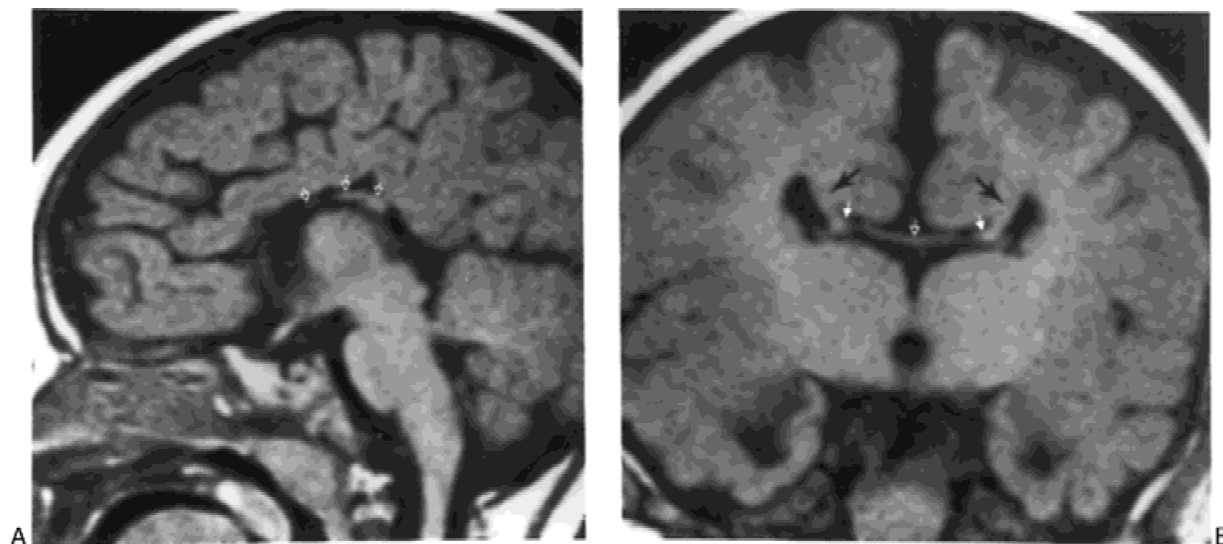


Fig. 3. Enlarged hippocampal commissure mimicking agenesis (outline arrows on both sagittal and coronal views), hippocampal commissure connecting the fornices (white arrows on the coronal view), and longitudinal bundles of Probst (black arrows on coronal view). (Reprinted with permission from Barkovich, 1995).

cortices. The rostral body connects the premotor and supplementary motor cortices. The anterior midbody connects the motor cortices. The posterior midbody connects the somesthetic and posterior parietal cortices. The isthmus connects the superior temporal and posterior parietal cortices. The splenium connects the occipital and inferior temporal cortices. This information is particularly useful in trying to predict which cognitive and motor functions are likely to be affected by primary and secondary insults to the developing brain which result in partial agenesis and/or hypoplasia of parts or all of the corpus callosum.

NEUROPATHOLOGY OF SPINA BIFIDA MENINGOMYELOCELE, AQUEDUCTAL STENOSIS, AND PREMATURETY-IVH

Spina Bifida

SB is the most common neural tube defect producing early onset hydrocephalus. SB produces several spinal dysraphic conditions, malformations of the spine resulting from defective or delayed closure of the embryonic neural tube. In SB occulta there is no herniation of meninges or neural tissue through the cleft. SB meningocele involves herniation of the meninges through the cleft. Children with SB meningocele infrequently show lower limb and bladder difficulties and changes at the level of the brain (e.g., Chiari malformation) that are expected with SB meningocele. The most serious of the SB conditions is SB meningocele and occurs in about 70% of SB cases (Wills, 1993). It is most common at the lumbosacral level but can occur at any level of the spine, secondary to the failure of the caudal end of the neural tube to develop. Some bones of

the vertebral column do not fuse in the posterior midline leaving a bony cleft through which meninges, spinal cord parenchyma, and nerve roots protrude (Menkes et al., 1990). Frequently there are abnormalities of the cervical spinal cord as well. There may be many brain abnormalities, including malformations of the brainstem, ventricular system, cerebellum, and cerebral hemispheres, and agenesis of the corpus callosum (Menkes et al., 1990). Practically all of these children (95%) have the Arnold–Chiari II malformation of the cerebellum and the hindbrain. They may have a small posterior fossa with low attachment of the tentorium (Barkovich, 1995). As a result, an elongated and malformed brainstem and the unrolled vermis of the cerebellum may extend well down into the cervical spinal cord. The fourth ventricle is compressed also and the foramina of Luschka and Magendie are compromised obstructing flow of CSF from the third and fourth ventricles. The superior and inferior colliculi may be fused and stretched posteriorly and inferiorly giving the tectum a beaked appearance (Leech, 1991). The cerebral cortex may be folded into an excessive number of small gyri (polymicrogyri), have only four layers, and there may be grey matter areas in the white matter near the ventricles (heterotopias; Leech, 1991) and there may be interdigitation of the gyri. Hydrocephalus that needs shunting is observed in 80 to 90% of these children (Reigel & Rothstein, 1994). Partial agenesis is present in about 65% of the cases in Houston and an additional 35% of the cases have hypoplasia of the corpus callosum. The fact that the splenium and rostrum are most likely to be missing and the genu is usually present suggests that the partial agenesis results from a disturbance of normal development rather than the secondary destructive hydrocephalus (Barkovich, 1995). Moreover, the presence of agenesis suggests a prolonged disruption of neuroembryogenesis that extends beyond the

first trimester. The variable pattern of agenesis may provide clues to the timing of some of the insults associated with SB meningocele (Barkovich, 1995).

Aqueductal Stenosis

Early onset hydrocephalus is also the result of aqueductal stenosis (congenital narrowing of the cerebral aqueduct). The narrowing generally occurs at the level of the superior colliculi and the intercollicular sulcus. There may be pure aqueductal stenosis or branching of the aqueduct into dorsal and ventral channels (aqueductal forking). Fusion of the inferior and superior colliculi producing beaking of the tectum may be present (Barkovich, 1995; Shaw & Alvord, 1995). The cerebellum is usually normal though pressure effects of the hydrocephalus may produce some downward extension (Robertson et al., 1990). Partial agenesis occurs at a lower rate than with SB meningocele, possibly because aqueductal stenosis occurs later in gestation. Partial agenesis is present in about 35% of our children and 50% have hypoplasia of the corpus callosum.

Prematurity–IVH

Hydrocephalus associated with prematurity–IVH in premature children results from a hemorrhage shortly after birth and is a common sequela of neonatal intracranial hemorrhage (Menkes et al., 1990; Volpe, 1987). In the premature infant, the bleeding starts over the head of the caudate nucleus in the capillaries of the germinal matrix (the area in the ventricle wall from which brain cells are generated). The hemorrhage usually occurs 24 to 48 hr after a major hypoxic–ischemic event at the time of birth or shortly thereafter. Bleeding into the ventricles is evident. The choroid plexus frequently bleeds also. Periventricular hemorrhagic infarctions (periventricular leukomalacia) are common (Barkovich, 1995). There may be blood in the subarachnoid space of the posterior fossa. Since the effects on the corpus callosum are secondary to the hydrocephalus and not the result of a disorder of neuroembryogenesis, hypoplasia is most likely. All of our children are shunted. None have partial agenesis and 100% have hypoplasia.

In general, with early onset hydrocephalus there may be reduced overall brain mass, a thinner cortical mantle, and thinning of some brain areas, particularly in the posterior regions (Dennis et al., 1981). Agenesis and/or hypoplasia of the corpus callosum may be present. White fiber tracts, especially those near the midline connecting the cerebral hemispheres to the diencephalon and more caudal regions, may be damaged. Abnormalities of the tectum, and medulla, compression of the diencephalon, defects of the optic pathways, polymicrogyri, heterotopias, and demyelination of white matter may be present. Cerebellar abnormalities vary across etiologies (Barkovich, 1995; Dennis et al., 1981; Fletcher et al., 1995). There are large individual differences in the pathology within and across etiologies (Fletcher et al., in press).

Midsagittal slices from magnetic resonance imaging (MRI) scans are useful for illustrating dysmorphologies of the brains of hydrocephalic children. Figure 4 includes a midsagittal slice from a normal child (upper left panel), and children with SB meningocele and shunted hydrocephalus (lower left panel), AS shunted hydrocephalus (upper right panel), and prematurity–IVH (lower right panel; Fletcher et al., 1995). The child with SB meningocele has a beaked tectum, compression of the cerebral aqueduct, dilation of the third ventricle, and partial agenesis of the corpus callosum in which the splenium and rostrum are missing. The child with AS has an enlarged third ventricle and thinning of the corpus callosum. The child with prematurity–IVH has very noticeable hydrocephalus of the third and fourth ventricles. Figure 5 depicts midsagittal slices of four children with SB meningocele (Hannay et al., 1999). Dilation of the third ventricle and the Arnold–Chiari II formation are particularly evident. Different types of partial agenesis of the corpus callosum as well as hypoplasia and a normal corpus callosum are illustrated.

EARLY HYDROCEPHALUS AND CALLOSAL FUNCTIONING

The investigations of callosal functioning with early hydrocephalus in Houston began with the work of Fletcher and his colleagues (Fletcher et al., 1992, 1996). The size of the remaining corpus callosum was correlated with cognitive and motor functions. More recently Klaas et al. (in press) developed a battery of experimental tests of callosal transfer and we are on our second generation of tests. First, the results of correlational studies and an experimental investigation will be reviewed. Then limitations of current callosal research will be described. Finally current and future directions will be discussed.

Correlational Investigations

In the first study (Fletcher et al., 1992), children with SB meningocele ($N = 17$), SB meningocele ($N = 6$), aqueductal stenosis ($N = 9$), and normal children ($N = 12$) of comparable age, SES, and race were given the Wechsler Intelligence Scale for Children–Revised (WISC–R; Wechsler, 1974), and the McCarthy Scales of Children’s Abilities (McCarthy, 1972). Tests of verbal and nonverbal ability including the Auditory Analysis Test (Rosner & Simon, 1971), Rapid Naming (Denckla & Rudel, 1974), Word Fluency (Benton et al., 1983), Word-Finding Test (Dennis et al., 1987), the Beery Visual–Motor Integration Test (Beery, 1982), and Judgment of Line Orientation (Benton et al., 1983) were administered additionally. The corpus callosum/whole brain ratio (using cross-sectional area from a midsagittal MRI slice) correlated significantly with WISC–R and McCarthy verbal and performance scale measures. The ratio also correlated with additional visual–spatial but not language measures.

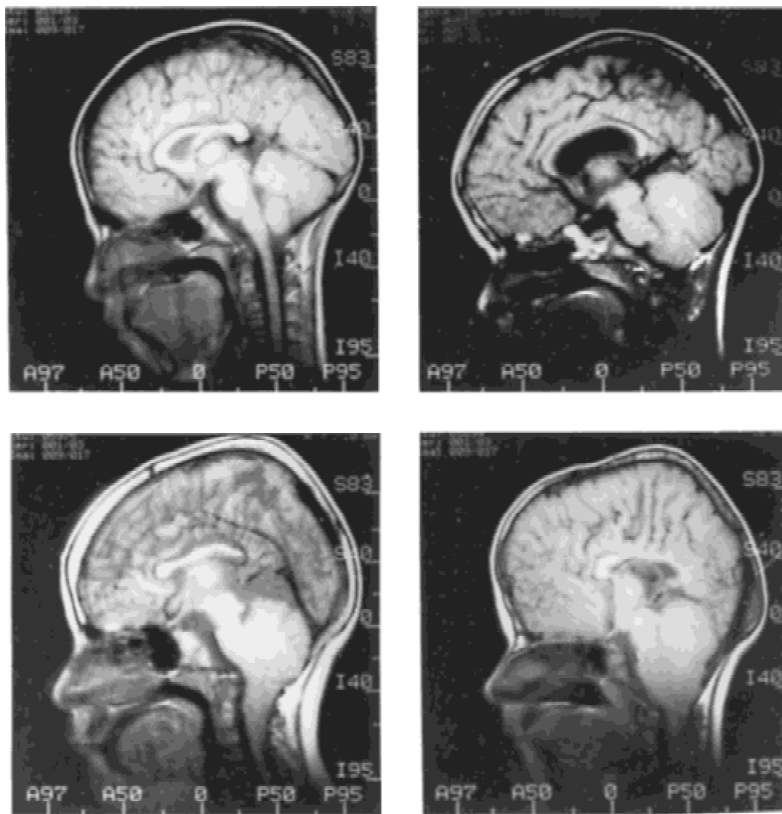


Fig. 4. Midsagittal slice from MRI of a normal child (upper left panel), and children with shunted hydrocephalus having spina bifida meningocele (lower left panel), aqueductal stenosis (upper right panel), and prematurity intraventricular hemorrhage (lower right panel). (Reprinted with permission from Fletcher et al., 1995.)

These findings were replicated with a larger sample (Fletcher et al., 1996). The sample included children with shunted hydrocephalus ($N = 42$), arrested hydrocephalus ($N = 19$), patient controls with no hydrocephalus ($N = 23$), and normal children ($N = 15$). The same cognitive measures were administered. Tests of motor function, the Grooved Pegboard (Knights & Moule, 1968), and executive function, the Tower of London (Shallice, 1982), and the Wisconsin Card Sorting Test (Heaton, 1981) were added. Corpus callosum/whole brain ratios were strongly correlated with various nonverbal measures and also fine motor coordination and weakly correlated with various verbal measures. They were not correlated with measures of executive function. The lateral ventricle/hemispheric and internal capsule/hemispheric ratio correlations were generally weaker or nonsignificant as they had been in the previous study. The shunted hydrocephalic group provided the greatest contribution to the correlation for performance IQ. These findings suggest that the corpus callosum plays a particularly important role in nonverbal, perceptual-spatial-constructional and motor skills. These findings could be construed as providing support for a facilitatory model of callosal functioning in which interhemispheric transfer of information is important in hemispheric activation and specialization and presumably for the reorganization of posterior right hemisphere function after insult (Fletcher et al., 1992, 1996).

Initial Experimental Investigation

Klaas et al. (in press) investigated interhemispheric transfer of information in children with hydrocephalus having partial agenesis and/or hypoplasia of the corpus callosum. A review of experimental studies of acallosals was useful for generating hypotheses about the effects of partial agenesis but not hypoplasia since there were no experimental studies that they knew of examining the effects of hypoplasia. It should be kept in mind that the striking disconnection effects seen in commissurotomy patients are not expected in individuals with partial agenesis.

Children with hydrocephalus from spina bifida meningocele ($N = 8$) or aqueductal stenosis ($N = 5$) who were missing a splenium and had partial agenesis/hypoplasia of the body as determined by sagittal MRI were studied. It was thought that this group would be most likely to differ from normal children on the tasks. Normal controls ($N = 13$) of similar age, race, sex, and socioeconomic status were tested also. All were right-handed. There were 7 boys and 6 girls in each group. The age range was 10 to 17 years for the children with hydrocephalus and 9 to 15 years for the normal controls. Children with prior histories of head injury, neurological disorders not associated with shunting, or severe psychiatric disorders were excluded from the study. The WISC-R Verbal or Performance IQ was 70 or greater for

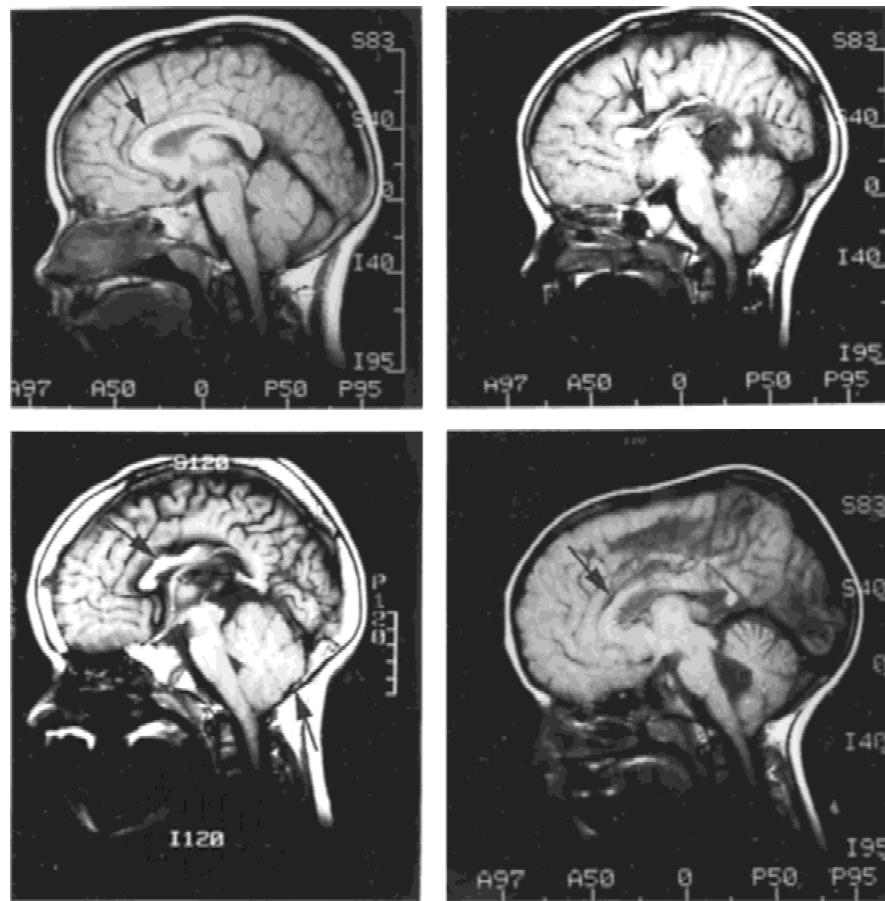


Fig. 5. Midsagittal slice from MRI of 4 children with spina bifida meningocele. Variability in the structure of the corpus callosum (arrows) is demonstrated and include a normal corpus callosum (upper left panel), a hypoplastic corpus callosum (upper right panel), and partial agenesis of the corpus callosum (lower left and right panels). (Reprinted with permission from Hannay et al., in press.)

each child to avoid the effects of mental deficiency. All of the children with hydrocephalus had posterior parietal shunts, 11 in the right hemisphere and 2 in the left hemisphere.

All of the children were given a battery of interhemispheric visual, auditory, tactile, and visuomotor interhemispheric transfer tasks. Additionally, sensory-perceptual tasks were administered in order to determine whether difficulties in receiving and interpreting stimuli that did not have to cross the corpus callosum was responsible for any unusual interhemispheric transfer task performance.

Visual information

Callosal transfer of visual information was accomplished with a tachistoscopic laterality task (Fontenot, 1973; Hannay et al., 1981). High complexity-low association forms were presented unilaterally 2° in either the left or right visual field and are expected to produce a left visual field superiority in normal adults indicative as greater right hemisphere involvement. Given that all of the children with hydrocephalus were missing the splenium, it was hypothesized that some neural reorganization would have taken place. For the most

part, visual field effects for acallosal children are similar to those of normal children (Ettlinger et al., 1974; Karnath et al., 1991; Lassonde et al., 1988; Lehmann & Lampe, 1970). However, Klaas et al. (in press) hypothesized that transfer of visual information by other pathways such as the anterior commissure should produce slower and more degraded transfer of the information. It was predicted that the hydrocephalic children would be able to correctly identify visual stimuli presented in either visual field but would show a larger left visual field superiority for recognition of high complexity-low association value forms. That is, children with hydrocephalus were expected to identify fewer of the forms presented in the right visual field since the forms initially went to the left hemisphere and then were transferred to the right hemisphere to be processed. The children with hydrocephalus showed a significant left visual field superiority for the forms, primarily because they made more errors when the forms were presented in the right visual field. The controls actually obtained a small nonsignificant right visual superiority.

The pattern of performance for the children with hydrocephalus can be viewed as an exaggeration of normal per-

formance related to poorer transfer of right visual field information from the left hemisphere to the right hemisphere for processing. There did appear to be transfer of visual information, however. At the time that this study was completed, the size of the anterior commissure was not being measured. This will be done in future research. It would be very interesting to see if some of the children in Klaas et al. (in press) had a hyperplastic anterior commissure and/or a hyperplastic hippocampal commissure to determine if visual field effects are related to commissural size.

There is study of children with total agenesis of the corpus callosum that does just this (Fischer et al., 1992). Unfortunately, only 2 children were examined and one of them was left-handed, making interpretation of the results more difficult. A right-handed boy with an absent or very small anterior commissure showed an exaggerated right visual field superiority in reaction time for naming drawings of common objects and words because of a much reduced ability to name the stimuli quickly when presented in the left visual field. The stimuli may have been degraded in their transfer from the right hemisphere to the language-dominant left hemisphere. Alternatively, the left-handed boy with an enlarged anterior commissure had a slight left visual field superiority in reaction time for the same task. While his hyperplastic anterior commissure might have been transferring the verbal information successfully from the right to left hemisphere, it is possible that his language was more bilaterally represented anyway since he was left-handed. It needs to be kept in mind that approximately 10% of acallosals have an enlarged anterior commissure (Rauch & Jinkins, 1994), and so other compensatory mechanisms for interhemispheric transfer of visual information need to be considered as well.

Klaas et al. (in press) assessed visual acuity with Clark's Eye Chart. Acuity was 20/25 for the children with hydrocephalus and 20/20 for the normal children. The threshold duration for identifying two of three letters of a trigram in central vision had been assessed in order to obtain stimulus exposure duration for the laterality task for each child. This duration was only slightly higher for the children with hydrocephalus. The relationship of acuity and the threshold duration to laterality task performance was determined. The longer the threshold duration for the children with hydrocephalus, the fewer correct responses they made when the forms were presented in the right visual field and thus initially went to the left hemisphere. The interpretation of this finding is not entirely clear.

Auditory information

A fused word dichotic listening task (Halwes, 1991) was used by Klaas et al. (in press) to examine callosal transfer of auditory information. In this task different three-to-five-letter common words were presented simultaneously to each ear on each trial but the child was supposed to hear only one word that, in the Klaas et al. (in press) modification of the Halwes (1991) procedure, was reported verbally. Nor-

mal individuals usually obtain a right ear advantage for dichotic words. The findings for acallosals have been contradictory (see Chiarello, 1980, for a review). Researchers have reported no ear advantage, a right ear advantage, and a left ear advantage (Chiarello, 1980; Lassonde et al., 1990). While most of these children do show a right ear advantage, there does appear to be a greater incidence of a left ear advantage (Chiarello, 1980; Lassonde et al., 1990). Strengthening of the ipsilateral and/or subcortical pathways has been suggested as the compensatory mechanism although the anterior commissure is also a possible candidate (Risse et al., 1978). In children with hydrocephalus studied by Klaas et al. (in press), the body of the corpus callosum was primarily hypoplastic rather than missing. It was hypothesized that there would be greater use of ipsilateral and/or subcortical pathways since the remaining callosal auditory fibers might not be fully capable of transferring auditory information. Specifically, it was predicted that some reorganization would result in either a reduction in the normal right ear advantage for fused dichotic words or even a left ear advantage. No significant ear effects were found for either group of children. The children with hydrocephalus had a slight left ear advantage for the dichotic words while the controls had a slight right ear advantage. Interestingly, ear effect and group were related because more normal children showed a right ear advantage than a left ear advantage and more children with hydrocephalus showed a left ear advantage rather than a right ear advantage. This provided weak support for the idea that the children with hydrocephalus and a hypoplastic body have stronger ipsilateral and/or subcortical projections. Since Klaas et al. (in press) had concerns about the dichotic listening task not producing significant ear effects with either group, we have replaced it with a more sensitive task in our current research program. Both groups of children correctly identified a similar number of words presented monotonically to each ear. Thus there were no group differences in speech perception, at least for the words presented.

Tactile information

A tactile naming task required naming of objects felt out of sight with the right or left hand served as the tactile interhemispheric transfer test. Tactile matching of objects in each hand was used as a control task for determining if the children could make appropriate tactile discriminations with each hand since it does not involve the callosal transfer of information. Normal individuals should not show a reliable difference between the hands in tactile naming or matching and should rarely make an error with either hand. Tactile naming of objects appears to be intact in both hands of acallosals even though naming of objects felt by the left hand normally requires callosal transfer of information from the right to the left hemisphere (Ettlinger et al., 1974; Lassonde et al., 1991; Reynolds & Jeeves, 1977). Tactile naming may be longer in acallosals, however. Greater use of ipsilateral and/or subcortical pathways has again been pro-

posed (Dennis, 1976; Ettlenger et al., 1974; Jeeves, 1979; Lassonde et al., 1991). The children with hydrocephalus in Klaas et al. (in press) had hypoplasia of the body of the corpus callosum. It was thought possible that hypoplasia might necessitate some neural reorganization involving greater use of ipsilateral and/or subcortical pathways. Increased use of ipsilateral and/or subcortical pathways could produce equally good naming in both hands similar to that of normals or only somewhat reduced left-hand naming. Since it would take longer to transfer stimuli from one side of the brain to the other using ipsilateral and/or subcortical pathways, the children with hydrocephalus were expected to have longer response times for left-hand naming. Both groups of children named objects presented to their left and right hands equally well but the children with hydrocephalus had longer response times with both hands not just the left hand. This finding suggests that hypoplasia did not affect callosal transfer. Perhaps there was no need for reorganization of tactile information or there was increased use of ipsilateral and subcortical pathways. The children with hydrocephalus matched significantly fewer objects than normal children with each hand, which indicated overall poorer tactile perception. These children also had significantly smaller two-point discrimination thresholds. However, two-point discrimination thresholds were not related to the number of objects correctly named or naming time with each hand.

Visuomotor information

An interhemispheric transmission time (ITT) task was based on studies reviewed by Bashore (1981). In ITT tasks, a visual stimulus such as a small white square is presented in the left or right visual field and the respondent must note detection of its presence by responding as quickly as possible with the right or left hand as specified for a set of trials. Reaction time is determined for crossed trials, ones in which information must cross the body of the corpus callosum for a motor response to be made. These are RVF-left-hand and LVF-right-hand trials. Reaction time is determined for uncrossed trials, ones in which information does not have to cross the corpus callosum for a motor response to be made. These are RVF-right-hand and LVF-left-hand trials. The crossed-uncrossed trial difference (CUD) in RT provides an estimate of the ITT.

In normal individuals, the CUD is usually about 2 to 6 ms (Bashore, 1981). The CUD is usually much longer for acallosals (Clarke & Zaidel, 1989; Di Stefano et al., 1992; Jeeves, 1969; Milner et al., 1985). Again, Klaas et al. (in press) hypothesized that hypoplasia of the body of the corpus callosum in the hydrocephalic children would result in greater dependence on ipsilateral and/or subcortical pathways that would produce a longer CUD. The CUD was longer for the children with hydrocephalus (7.45 ms) than the normal children (3.28 ms) but not significantly so. All of the children had very large standard deviations in their reaction time that may have obscured the group difference. In an attempt to

avoid fatigue in the children, a relatively small number of practice and test sessions were included, below that traditionally given to normal adults. Longer practice and test sessions with distributed practice have been instituted now in an effort to stabilize the reaction times of individual children. It should be noted that reaction time on our task was, in general, significantly longer for the children with hydrocephalus, reflecting their motor slowness.

Our thinking on the pathways by which information is transferred interhemispherically on visuomotor tasks such as the ITT task has changed since Klaas et al. (in press). Variation in the CUD has been reported for acallosals with a variation in stimulus luminance (the higher the luminance, the lower the CUD) as might be expected if the information was coded visually for interhemispheric transfer (Milner, 1994). However, Lassonde (1994) reported similar CUDs for acallosals (51.3 ms) and a callosotomized patient with sparing of the splenium of the corpus callosum (58.3 ms) that were much longer than the CUDs for the normal controls (3 ms). These findings support the idea that the ITT task is a visuomotor task that relies upon transfer by the motor pathways and not the splenium and that the performance of the acallosals on such tasks involves strengthening of ipsilateral and/or subcortical pathways.

Summary

The Klaas et al. (in press) study has been useful to our research program in two ways. First, we gained information about the effects of partial agenesis of the corpus callosum when the splenium was missing and the body was hypoplastic. Children with these callosal anomalies seem to have more difficulty transferring patterned visual information from one hemisphere to another. Auditory and tactile transfer of information was essentially similar to that reported for normal children. There was a slowing of ability to name tactile stimuli with either hand as well as larger two-point discrimination thresholds. A longer interhemispheric transmission time was suggested but the large trial to trial variability in RT may have been, in part, responsible for a nonsignificant group difference. It is unlikely that performance on the tachistoscopic form perception and ITT tasks was affected by posterior parietal shunts in the hydrocephalic children. Even on the tactile matching and naming tasks, the children with hydrocephalus performed similarly to controls. Secondly, this research has led us to reconsider the characteristics of some interhemispheric transfer tasks. Poorly chosen or poorly designed tasks can lead to negative findings. Since this study we have refined our ITT methodology. The dichotic listening task has been replaced and several measures have been added to the battery, including a verbal tachistoscopic laterality task and measures of bimanual coordination and tactile localization.

Practically all studies of callosal functioning document the handedness, sex, and age of the individuals with complete and partial agenesis of the corpus callosum. With some exceptions these studies include both right-handers and left-

handers and male and female participants, of various ages. Performance on cerebral dominance tasks (e.g., tachistoscopic perception, dichotic listening) may be affected by such variables (McKeever, 1986; Springer, 1986), yet the data often are not examined as a function of these variables. Including handedness-, sex-, and age-matched controls does not really address this issue unless these variables are included in the analyses and the sample sizes are generally too small to do so. Klaas et al. (in press) addressed the problem by studying only right-handers in a restricted age range. Both male and female children were included and sex proved not to be a factor in any of the analyses. Whether their results can be generalized to all left-handers with similar abnormalities of the corpus callosum remains to be answered. We are collecting data on a large number of children with various dysmorphologies of the corpus callosum and other structures in order to address issues such as this.

CONCLUSIONS AND FUTURE RESEARCH

More than one mechanism is probably involved in the reorganization of the developing nervous system in order to compensate for partial agenesis and/or hypoplasia of the corpus callosum. For some children with hydrocephalus who are missing the splenium, the anterior commissure or hippocampal commissure may be enlarged and serve as the pathway for interhemispheric transfer of visual information (Fischer et al., 1992). A significant correlation between the size of the anterior commissure or possibly the hippocampal commissure and performance on the visual interhemispheric transfer tasks would provide further evidence for this interpretation of the data (Hannay et al., in press). Another mechanism for functional reorganization is the strengthening of ipsilateral and/or subcortical pathways (Dennis, 1976). This mechanism is a likely candidate for the interhemispheric transfer of auditory, tactile, and visuomotor information. Less lateralized or reversed ear, tactile, and motor performances and a relationship between these effects and the size of particular callosal regions transferring this information would provide evidence for this mechanism (Hannay et al., in press). Bilateral representation of function seems to be a less likely compensatory mechanism (Jeeves, 1994). In some cases, more than one mechanism may be responsible for the functional reorganization that permits interhemispheric transfer of information in a given child.

As mentioned earlier, we reviewed experimental studies of children and adults with complete or partial agenesis of the corpus callosum in order to derive predictions for our research on callosal functioning in hydrocephalic children. These studies provided us with very useful information but clearly have limitations which we expect to avoid in research that we currently have underway (Hannay et al., in press):

1. Many of the studies are really case studies involving only 1 or 2 individuals (Bryden & Zurif, 1970; Dennis, 1976; Lassonde et al, 1981) and only occasionally does the sample size approach 10 or more (Klaas et al., in press; Lehmann & Lampe, 1970). The sample sizes are usually not large enough to examine handedness, sex, and age effects.
2. Some studies have included both patients with complete and partial agenesis of the corpus callosum without considering possible differences in their functioning (Lehmann & Lampe, 1970).
3. Few studies of callosal functioning (Fischer et al., 1992; Geffen et al., 1994) have documented the nature of the callosal dysmorphologies with a MRI because this methodology has been available only in recent years.
4. A variety of callosal transfer tasks have been used across studies, making it difficult to compare and interpret findings.

In order to fully understand the effects of various dysmorphologies of the corpus callosum and to determine the mechanisms involved in functional reorganization in children with early hydrocephalus, a large sample of children with hydrocephalus and normal children needs to be studied. The children need to be given a single set of interhemispheric transfer tasks and a broadly based psychometric examination. The sample should be divided into subgroups on the basis of callosal dysmorphology as determined by sagittal MRI. Qualitative and quantitative measures of the corpus callosum and its various regions should be made to the extent that it is possible. Additionally, the size of the anterior commissure and other structures need to be determined. Interhemispheric transfer task performance as well as sensory-perceptual performance should be related to psychometric task performance, handedness, sex, age, and to MRI findings. Ideally, we would like to be able to determine whether and where stimuli cross from one hemisphere to another to be processed but that awaits further developments in methodology and imaging techniques.

Intellectual, academic, cognitive, and motor difficulties as well as psychosocial problems have been reported in early hydrocephalus (see Baron et al., 1995; Fletcher et al., 1995, in press; Wills, 1993; for reviews of this literature). We do not question the major role of the primary brain malformations in the difficulties displayed by hydrocephalic children. However, the role of abnormalities in interhemispheric transfer in the long-term outcome of these children and their ability to succeed in academic endeavors, in leisure pursuits, and in the workplace need to be determined. As we have said previously, the key to such a research program is having a sufficiently large number of participants in the various groups with callosal dysmorphology to have the power to assess some rather complex relations (Hannay et al., 1999). We have embarked on just such a program.

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