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SHORT COMMUNICATION

Callosotopy: leg motor connections illustrated by fiber dissection

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Abstract Precise anatomical knowledge of the structure of the corpus callosum is important in split-brain research and during neurosurgical procedures sectioning the callosum. According to the classic literature, commissural fibers connecting the motor cortex are situated in the anterior part of the corpus callosum. On the other hand, more recent imaging studies using diffusion tensor imaging indicate a more posterior topography of callosal fibers connecting motor areas. Topographical knowledge is especially critical when performing disconnective callosotomies in epilepsy patients who experience sudden loss of leg motor control, so-called epileptic drop attacks. In the current study, we aim to precisely delineate the topography of the leg motor connections of the corpus callosum. Of 20 hemispheres obtained at autopsy, 16 were dissected according to Klingler's fiber dissection technique to study the course and topography of callosal fibers connecting the most medial part of the precentral gyrus. Fibers originating from the anterior bank of the central sulcus were invariably found to be located in the isthmus of the corpus callosum, and no leg motor fibers were found in the anterior part of the callosum. The current results suggest that the disconnection of the pre-splenial fibers, located in the posterior one-third of the corpus callosum, is paramount in obtaining a good outcome after callosotomy.

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Introduction

Anatomically, three major commissures interconnect the human hemispheres, thereby integrating and equalizing the activity between homologous brain areas: the corpus callosum (CC), the anterior commissure and the hippocampal commissure. The callosal fibers with their more than 200 million axons comprise by far the most prominent and widespread interhemispheric pathway, connecting about 80 % of the cerebral cortex, mostly via homotopic connections (Aboitiz et al. 1992). In an anterior (rostral) to posterior (caudal) direction, the corpus callosum consists of five anatomical subregions without clear boundaries: the rostrum, the genu, the body (truncus), the isthmus and the splenium (Velut et al. 1998). This topography is linked to a functional anterior-to-posterior gradient with prefrontal fibers running in the anterior part of the corpus callosum, and posterior cortical areas connecting through the splenium. Anatomical studies in non-human primates located commissural fibers connecting motor areas in the rostral part of the corpus callosum (Karol and Pandya 1971; Pandya et al. 1971; Sunderland 1940). Based on these findings and anatomical cadaver studies from the early 1900's (Van Valkenburg 1913), the following topography was postulated: higher cognitive information was transferred through the rostrum, auditory and visual information through the isthmus and splenium of the corpus callosum; accordingly, the anterior part of the callosal midbody was believed to transfer motor information, whereas somatosensory information was thought to be transferred in the posterior midbody (Funnell et al. 2000).

Seventy-five years ago the first reports on callosotomy in primates appeared (van Wagenen and Herren 1940; Erickson 1940; Wada 2005). The corpus callosum was shown to be the pathway for bilateral spread of epileptic discharges (Erickson 1940) and seizure synchronization (Ottino et al. 1971). Corpus callosotomy is now regarded as a successful palliative measure to treat a wide variety of epilepsy syndromes, with a good efficacy and a relatively low morbidity. The procedure proved very efficient in the treatment of epilepsies associated with so-called drop attacks. This seizure type consists of abrupt falls and is very disabling, producing a constant traumatic injury risk with a subsequent need for a protective helmet or a wheelchair. Callosotomy for drop attacks can either be incomplete, usually aimed at the anterior part of the corpus callosum, or complete in which the full length of the corpus callosum is transected. The rationale behind an anterior-only disconnection is the prevention of the feared disconnection syndrome (Gordon et al. 1971; Bogen 1993). When insufficient seizure control is obtained after anterior section, a completion of the callosal disconnection can be performed. Arrest of drop attacks is typically observed in 67 % after anterior two-third callosotomy and in up to 91 % after total callosotomy (Shimizu 2005; Asadi-Pooya et al. 2008).

In this anatomical fiber dissection study, we aimed to further investigate the topography of the corpus callosum, with a special emphasis on the precise location of the commissural fibers connecting the leg motor areas. If we assume these fibers play an important role in generating drop attacks, disconnecting them is essential in obtaining optimal results after epilepsy surgery.

Methods

Twenty hemispheres were obtained from 20 necropsy specimens. Brain specimens with macroscopic lesions or agenesis of the corpus callosum were excluded. Similar to previous studies (Peuskens et al. 2004), we used the fiber dissection technique described by Klingler (Klingler 1935). First, the brain was fixed in 10 % formalin for at least 8 weeks. After removal of the meningeal membranes and blood vessels, specimens were frozen at a temperature of −10° for at least 4 weeks. The brains were then immersed in running tap water at room temperature to allow thawing.

The dissection was performed under magnification with the aid of metal blunt spatulas and forceps of various sizes. Dissection was started from the mesial surface of the brain: after blunt removal of the gray matter, the cingulum and surrounding short U-fibers were exposed. In a second phase, we turned to the lateral surface and removed the cortex at the level of the precentral gyrus exposing the U-fibers. In the next stage, the cingulum was removed. At the end of the dissection, we removed the indusium griseum and the superficial layer of the corpus callosum, exposing the underlying callosal fibers running directly into the most medial part of the precentral gyrus.

Segmentation of the corpus callosum was performed according to Witelson's division (Witelson 1989). From the rostral tip of the genu to the posterior-most point of the splenium and along straight lines perpendicular to the bicommissural line, the corpus callosum was partitioned into halves and thirds, resulting in five different portions. After delineating the posterior one-fifth, seven segments can be distinguished: the rostrum, the genu, the rostral body, the anterior midbody, the posterior midbody, the isthmus and the splenium of the corpus callosum. The first three segments are all part of the anterior one-third of the corpus callosum. The splenium was defined as the posterior one-fifth of the corpus callosum, whereas the isthmus involves the pre-splenial part of the posterior one-third (Fig. 1).

Since motor fibers arise from the anterior bank of the central sulcus, the most medial and deep point of the central sulcus was determined and the exact point where the fibers originating from this spot crossed the corpus callosum was marked as Xpost. Accordingly, the point where the fibers from the depth of the precentral sulcus crossed the midline was marked as Xant. An index between 0 and 1 was computed (by dividing Xpost and Xant by the total length of the callosum ($length_{CC)}$), with an index above 0.67 indicating a location in the posterior third of the corpus callosum and an index above 0.8 representing a position in the splenium.

Results

Macroscopic appearance

The brain had a normal macroscopic appearance in 16 of 20 cases. Four subjects showed macroscopic evidence of previous intracerebral hemorrhage, and therefore these specimens were excluded. In all specimens, we were able to macroscopically discern the anterior and posterior commissure. After partitioning according to Witelson's division (Witelson 1989), we could identify the rostrum, genu, body, isthmus and splenium. The average length of the corpus callosum ($length_{CC}$, as measured from the rostral tip of the genu to the posterior-most point of the splenium along straight lines perpendicular to the bicommissural line) was 67.6 mm (±5.1).

Mesial dissection

Dissection was started from the mesial surface of the brain, the most important landmarks being the corpus callosum,

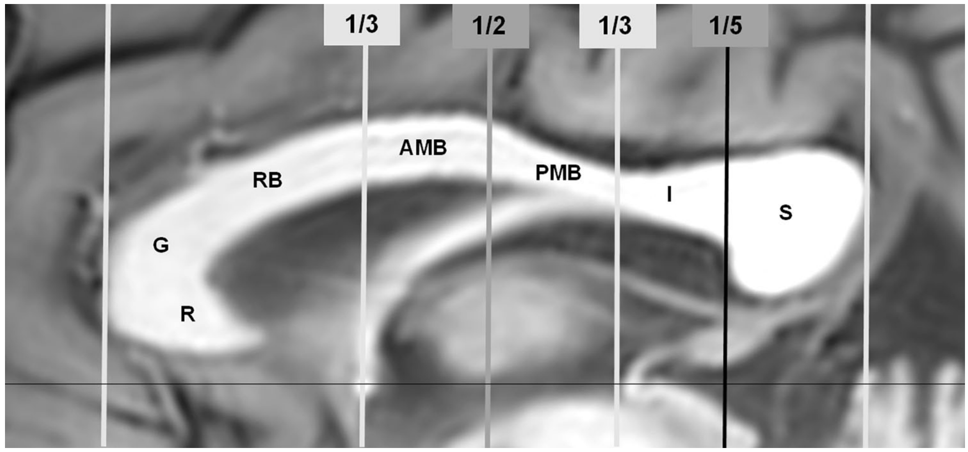

Fig. 1 Sagittal MRI image. The corpus callosum is divided according to Witelson's classification. 7 segments can be distinguished at the level of the midsagittal plane, from anterior to posterior: *R* rostrum, *G* genu, *RB* rostral body, *AMB* anterior midbody, *PMB* posterior midbody, *I* isthmus and *S* splenium

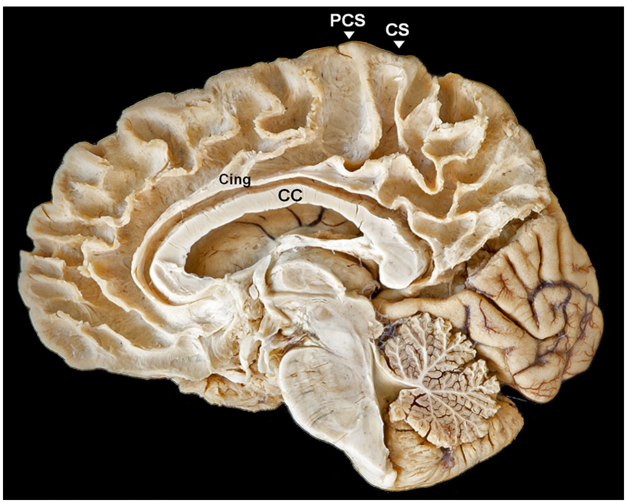

Fig. 2 Anatomy of the mesial brain surface after removal of the gray matter. The *CC* corpus callosum, *PCS* precentral sulcus, *CS* central sulcus and *Cing* cingulum have been labeled

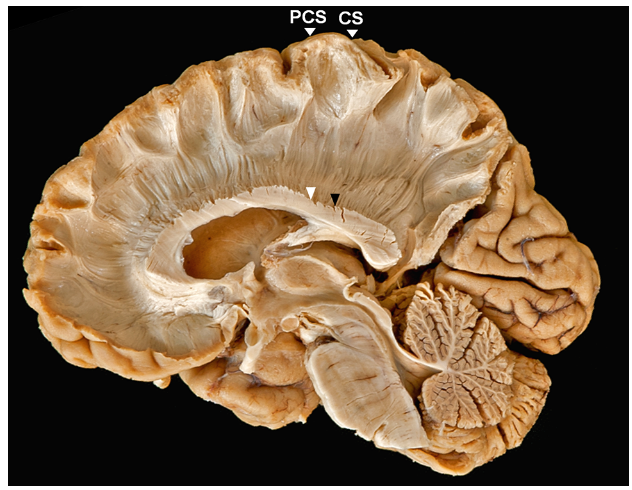

Fig. 3 Fiber dissection of the mesial paracentral region. After removal of the cingulum and the arcuate fibers, the connecting fibers of the corpus callosum are visualized. The *PCS* precentral sulcus, *CS* the central sulcus as well as *Xant* (*white* arrowhead) and *Xpost* (*black* arrowhead) are indicated

the cingulate gyrus and the paracentral lobule. First, we performed a blunt removal of all gray matter. The mesial part of the dorsal surface of the corpus callosum, the entire cingulum and surrounding arcuate fibers (or U-fibers), as well as the arcuate fibers of the mesial part of the central sulcus were then exposed, as illustrated in Fig. 2. The cingulum was removed in a stepwise fashion in an anteroposterior direction thereby exposing the dorsal surface and the radiation of the corpus callosum. Several structures take their course on the callosal surface including the indusium griseum and the lateral longitudinal striae; the latter structures were removed to expose the mesial radiation of the callosal fibers (Fig. 3). The callosal radiation could then be tracked into the cerebral cortex. When following these fibers in a mesial to lateral direction, one can appreciate the fact that they get intermingled with the fibers of the corticospinal tract (Fig. 4). At the point where the commissural fibers intersect and interconnect with the corticospinal tract fibers, the density of the latter white matter tract becomes far greater than that of the commissural tract, as illustrated in Fig. 5. Tracking callosal fibers beyond this junction is technically impossible because upon removal of the arcuate fibers and the most mesial superficial part of the corticospinal tract, the commissural fibers start tearing at the intersection with the corona radiata. Note that Figs. 2, 3, 4 and 5 represent different brain specimens.

Lateral exposure

After performing the mesial dissection, we turned to the lateral aspect of the brain, where the most important landmarks were the central and the precentral sulcus

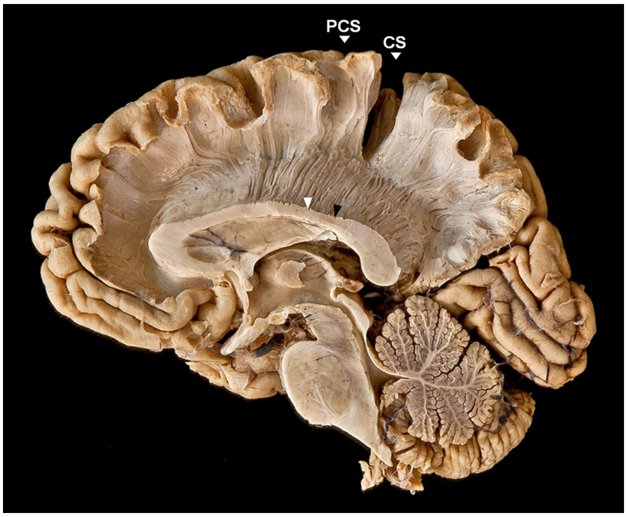

Fig. 4 Leg motor connections of the corpus callosum. Commissural leg motor fibers crossing immediately anterior to *Xpost* consistently ran through the posterior corpus callosum. The *PCS* precentral sulcus, *CS* the central sulcus, *Xant* (*white* arrowhead) and *Xpost* (*black* arrowhead) are indicated

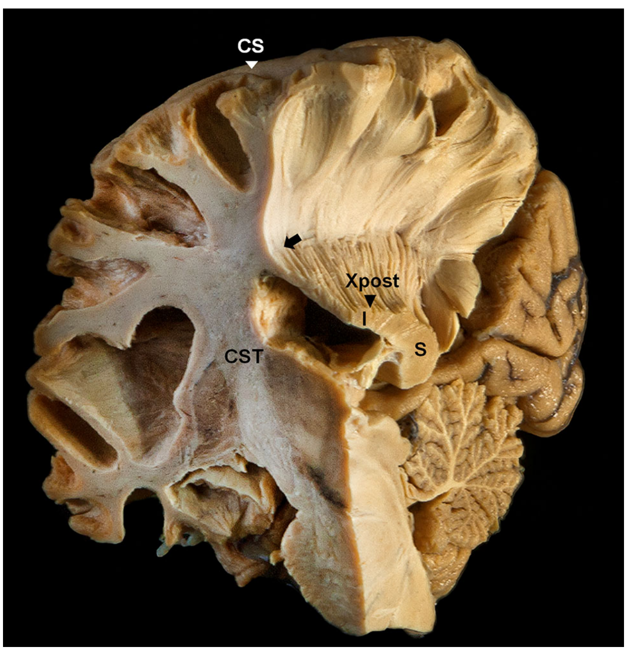

Fig. 5 Coronal section at the level of the precentral gyrus and the isthmus of the corpus callosum. An oblique coronal section illustrates the course of the corticospinal tract (*CST*) from the precentral gyrus through the internal capsule into the brainstem. The commissural fibers of the leg motor area through the corpus callosum have been dissected. The intersection of the commissural fibers with the corticospinal tract fibers is marked (*black arrow*). The central sulcus (*CS*, *white* arrowhead), the posterior part of the isthmus (*I*), the splenium (*S*) and *Xpost* (*black* arrowhead) are labeled

bordering the precentral gyrus, our region of interest. The most mesial part of the central sulcus can be identified immediately anterior to the marginal ramus of the cingulate sulcus. The central sulcus typically does not enter the interhemispheric fissure. The motor area innervating the leg is known to be located in the most medial part of the precentral gyrus and the anterior part of the paracentral lobule (Penfield and Boldrey 1937). After landmark identification, the overlying gray matter, which appeared remarkably thick in this region, was removed from the central sulcus (Fig. 4).

Identification of leg motor fibers

After completely exposing the radiation of the corpus callosum and the U-fibers of the central sulcus, the interconnecting fibers from the leg motor areas could be identified. First, the most medial and deepest point of the central sulcus was determined. The anatomy of the central sulcus, which represents a primary sulcus, was very constant and clearly visible. Under magnification with an operating microscope, the most posterior fibers were tracked on their course from the depth of the central sulcus to and through the CC. These fibers took the shortest route and went almost straight from the central sulcus to the underlying part of the CC. The exact point where the commissural fibers originating from the central sulcus crossed the midline in the CC was labeled Xpost (Fig. 4). Next, the point where the fibers from the depth of the precentral sulcus crossed the midline was determined in a similar fashion and marked Xant. This point was more difficult to define because the precentral sulcus had a more variable anatomical course. The fibers situated between these two points are connecting the precentral gyrus and the anterior part of the paracentral lobule of both hemispheres. Table 1 lists measurements of all specimens indicating the length of the corpus callosum ($\text{length}_{\text{CC}}$), the location of Xpost and the (estimated) projection of the precentral sulcus (Xant).

All 16 specimens harbored motor fibers crossing the midline in the posterior one-third of the corpus callosum, and none of the samples had leg motor fibers coursing in the anterior half of the corpus callosum. In 80 % of cases both Xant and Xpost were located in the posterior third of the corpus callosum. In the remaining cases ($N = 4$), Xant was found in the posterior midbody. In five samples, Xpost was located in the splenium (according to Witelson's division).

Discussion

This study provides insights in the anatomical course and topography of callosal leg motor fibers. Using Klingler's dissection technique, we illustrate that commissural fibers connecting the leg motor areas of both hemispheres are

Table 1 Measurements of CC reference points

Length$_{CC}$ (mm)	Xpost (mm)	Xpost/length$_{CC}$	Xant (mm)	Xant/length$_{CC}$
70	51	0.73	46	0.66
69	53	0.77	47	0.68
74	56	0.76	52	0.7
63	49	0.78	44	0.7
56	37	0.66	32	0.57
69	57	0.83	51	0.74
71	64	0.8	51	0.72
59	48	0.81	41	0.69
68	49	0.72	40	0.59
68	52	0.76	48	0.71
75	59	0.79	52	0.69
67	55	0.82	51	0.76
68	46	0.68	39	0.57
67	52	0.78	46	0.67
65	56	0.86	49	0.75
73	53	0.73	47	0.64

CC corpus callosum, *Xpost* distance from the rostral tip of the genu to the point where fibers from the depth of the central sulcus cross the midline, *Xant* distance from the rostral tip of the genu to the point where fibers from the depth of the precentral sulcus cross the midline

found in the isthmus of the corpus callosum. Callosotomy of these pre-splenial fibers might be important in the treatment of epilepsy.

Until recently, there was a consensus that motor fibers run through the anterior midbody of the CC (Funnell et al. 2000), a belief largely based on monkey research (Pandya and Vignolo 1971; Pandya et al. 1971; Sunderland 1940), lesion studies (de Lacoste et al. 1985) and cadaver studies. Furthermore, in primates, sectioning the corpus callosum was shown to be a successful method to control the spread of epilepsy (Wada and Komai 1985; Wada 2005; Erickson 1940) and anterior two-thirds callosotomy could lead to seizure control in epileptic baboons (Wada and Komai 1985). Consequently, it was assumed that the most effective way to reduce drop attacks in humans was sectioning the anterior part of the corpus callosum (Wada and Komai 1985).

Recent diffusion tensor imaging (DTI) studies, however, provide evidence that the commissural sensorimotor connections are localized far more posteriorly than previously assumed (Hofer and Frahm 2006; Zarei et al. 2006; Wahl et al. 2007; Raybaud 2010). These imaging studies revealed a different topographical organization with prefrontal connections in the anterior part of the corpus callosum, premotor (and cingulate) fibers in the body, central area (precentral and postcentral cortex) and auditory fibers in the isthmus and more posterior cortical areas connecting through the splenium. One possible explanation for the difference with non-human primate topography might be related to the significant increase in prefrontal cortex volume in humans, resulting in a posterior shift of motor fibers. In one study, it was shown that the motor corpus callosum has a somatotopic organization on its own, where fibers originating from the leg area of the motor cortex run more posteriorly than those from the hand and face area (Wahl et al. 2007). The same study has illustrated that callosal leg motor fibers are running more dorsally in the corpus callosum.

No consensus exists on the exact origin or mechanism of drop attacks (Tinuper et al. 1998). Bilateral synchrony which is possible through commissural tracts between homotopic areas in both hemispheres is believed to play an important role. Anterior callosal fibers were believed to play an essential role in motoric bihemispheric synchronization in tonic, atonic and tonic/clonic seizures, and therefore anterior callosotomy was the mainstay of treatment for drop attacks for decades. The posterior part of the CC, especially the splenium, was mostly spared to prevent the feared disconnection syndrome. Although conflicting results exist on the extent of callosal section (Mamelak et al. 1993; Spencer et al. 1993), anterior callosotomy does not always lead to satisfying outcomes and therefore upfront total callosotomy is sometimes advocated, especially in children.(Shim et al. 2008; Rathore et al. 2007; Maehara and Shimizu 2001).

Considering the hypothesis that bilateral synchronization of leg motor areas plays a crucial role in drop attacks, the pathway that allows for this synchronization must be transected for good seizure control. Therefore, the current findings in humans could undermine the rationale behind a restricted anterior callosotomy for drop attacks. Our results show that these motor fibers run through the posterior part of the CC, in a region not always (completely) transected after anterior callosotomy.

In conclusion, our data complement earlier DTI studies providing evidence that leg motor fibers are found in the posterior part of the corpus callosum, more specific in the isthmus of the callosum. These fibers are not tackled during a classic anterior two-third callosotomy, sparing the isthmus.

These results could substantially influence epilepsy surgery for drop attacks where a total or a posterior callosotomy might be preferable to the classic anterior callosotomy.

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Compliance with ethical standards

Conflict of interest The authors declare no conflicts of interest.

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