Transcallosal inhibition in patients with callosal infarction

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Submitted 14 November 2011; accepted in final form 1 November 2012

Li J-Y, Lai P-H, Chen R. Transcallosal inhibition in patients with callosal infarction. J Neurophysiol 109: 659–665, 2013. First published November 7, 2012; doi:10.1152/jn.01044.2011.—Recent studies in normal subjects suggested that callosal motor fibers pass through the posterior body of the corpus callosum (CC), but this has not been tested in patients with callosal infarction. The objective of this study is to define the pathways involved in transcallosal inhibition by examining patients with infarctions in different subregions of the CC. We hypothesized that patients with lesions in the posterior one-half of the CC would have greater reduction in transcallosal inhibition between the motor cortices. Twenty-six patients with callosal infarction and 14 healthy subjects were studied. The callosal lesions were localized on sagittal MRI and were attributed to one of five segments of the CC. Transcranial magnetic stimulation was used to assess ipsilateral silent period (iSP) areas and durations were lower in patients with lesions of the CC producing disturbances of higher brain function. Lesion burden in the posterior one-half of the CC negatively correlated transcallosal inhibition measured with iSP and SIHI. Our study suggests that callosal infarction led to reduced transcallosal inhibition, as measured by iSP, SIHI, and LIHI. Fibers mediating transcallosal inhibition cross the CC mainly in the posterior one-half. Transcallosal inhibition refers to suppression of one hemisphere by the opposite hemisphere, which may help to maintain hemispheric dominance in cognitive and motor tasks. There are two established TMS methods to evaluate transcallosal inhibition in human M1. The first is ipsilateral silent period (isP) (Meyer et al. 1999), which involves the interruption of voluntary muscle activities following stimulation of the ipsilateral M1. The second method is interhemispheric inhibition (IHI) and involves a conditioning stimulus given over one M1, followed by the test stimulus over the opposite M1, 8–50 ms later. IHI can be divided into short-interval IHI [SIHI; interstimulus interval (ISI) ~10 ms] and long-interval IHI (LIHI; ISI ~50 ms) with different physiological properties (Chen et al. 2003; Ni et al. 2009). Pharmacological studies suggest that LIHI likely involves GABAergic-mediated inhibition, whereas the receptor mediating SIHI remains unknown (Irlbacher et al. 2007). Although TMS is widely used to study neurological and psychiatric diseases, IHI has not been explored in patients with callosal infarction.

The topographical organization of the CC has been the focus of several previous studies. Anatomical studies in humans showed that the fibers connecting the M1 pass through the anterior midbody of the CC (de Lacoste et al. 1985; van Valkenburgh 1913; Witelson 1989). Recently, diffusion tensor imaging (DTI), in conjunction with tractography, has been used to visualize major fiber tracts in the human CC in vivo to identify its detailed topographical organization (Abe et al. 2004). These DTI studies and a TMS study suggested a different topographical arrangement of callosal connectivity with the callosal motor fibers crossing more posteriorly in the posterior body of the CC (Fling et al. 2011; Hofer and Frahm 2006; Meyer et al. 1998; Wahl et al. 2007; Zarei et al. 2006). The aims of this study are to examine how callosal infarction affects transcallosal inhibition and to define the pathways involved in the transcallosal inhibition measured by TMS by examining patients with infarction of different subregions of the CC. We hypothesized that the posterior one-half of the CC plays a greater role than the anterior one-half in generating...
transcallosal inhibition to the motor cortex. The reduction of iSP and IHI should be greater in patients with callosal infarction involving the posterior one-half of the CC.

MATERIALS AND METHODS

Subjects. We studied 26 patients (19 men, aged 62.9 ± 11.1 yr) with anterior cerebral artery territory infarcts with callosal involvement and 14 age-matched normal subjects (eight men, aged 56.6 ± 8.9 yr). There was no involvement of the middle cerebral artery territory in all patients. Intermanual conflict was seen in five patients, apraxia in 13, tactile anomia in six, and agraphia in 14. All of the patients and normal subjects were right handed. Handedness of the subjects was evaluated by a modified version of the Edinburgh Handedness Inventory (Oldfield 1971). Figure 1 shows the clinical features of the patients. The study was approved by the Institutional Review Board of Kaohsiung Veterans General Hospital. Written, informed consent was obtained from all subjects.

MRI. All MRI was performed with a clinical 1.5-T system (GE Healthcare, Waukesha, WI). The routine imaging studies included axial and coronal T1-weighted spin-echo (500/30/2 ms [repetition time/echo time/excitations, respectively], T2-weighted fast spin-echo (4,000/100/2 ms) with echo train length 8, axial fast fluid-attenuated inversion recovery (9,000/2,200/133/1 ms [repetition time/inversion time/echo time/number of excitations, respectively]) sequences, and sagittal T2-weighted and diffusion-weighted imaging (DWI). The imaging sequence for DWI was a single-shot spin-echo echo-planar imaging (10,000/93 ms [repetition time/echo time, respectively]) with diffusion sensitivities, $b = 0 \text{ s/mm}^2$ and $b = 1,000 \text{ s/mm}^2$. An apparent diffusion coefficient map was calculated. Sections (5 mm thick) with 2.5 mm interslice gaps, 24 cm field of view, and $256 \times 192$ matrix were used for all scans. The callosal lesions were localized on sagittal MRI (Fig. 2A) and then attributed to one of five segments of the CC, numbered from anterior to posterior, according to the

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Fig. 1. Clinical and MRI features of patients with callosal infarction. D, days; M, months.

Fig. 2. Illustration of the scheme for localization of lesions in the corpus callosum (CC). The sagittal diffusion-weighted MRI shows acute infarction of the CC (A), and the lesions were located at segments 1 and 2 on sagittal T2-weighted imaging, according to the segmentation scheme by Hofer and Frahm (2006).
scheme (Fig. 2B) proposed by Hofer and Frahm (2006). A baseline was drawn through the most inferior borders of the splenium and rostrum of the CC. From this line, perpendicular lines were drawn at the anterior edge of the genu and the posterior edge of the splenium, and then baseline was divided into five segments. Segment 1 covered the first one-sixth of the CC. Segment 2 was the rest of the anterior one-half of the CC. Segment 3 was the posterior one-half minus the posterior one-third, segment 4 was the posterior one-third minus posterior one-fourth, and segment 5 was the posterior one-fourth.

Electromyography recording. Electromyography (EMG) was monitored on a computer screen and via loudspeakers at high gain to provide feedback on the state of muscle relaxation. Visual feedback was provided by passing the EMG signal through a leaky integrator, and the EMG level was displayed on an oscilloscope. The signal was amplified (Digitimer D360, Welwyn Garden City, UK), filtered (band pass, 20 Hz–2.5 kHz), digitized at 5 kHz (CED Power1401, Cambridge Electronic Design, Cambridge, UK), and stored in a laboratory computer for offline analysis.

TMS studies. Two 70-mm figure-of-eight coils and two Magstim 200 stimulators (Whitland, UK) were used. Both M1 were tested in patients with callosal infarction and in normal subjects. The lesioned side refers to the side with infarction. Surface EMG was recorded from both first dorsal interosseous (FDI) muscles. The optimal coil position over the left M1 for eliciting the motor-evoked potential (MEP) from the right FDI muscle was established with the handle of the coil held 45° to the midsagittal line (approximately perpendicular to the presumed direction of the central sulcus). The optimal position was marked on the scalp to ensure identical placement of the coil throughout the experiment. This procedure was then repeated for the right M1 and the left FDI muscle. Resting motor threshold (MT) was the minimum stimulus intensity that produced MEPs of ≥50 μV in at least five out of 10 trials. Active MT was the minimum stimulator output that produced MEPs of ≥100 μV in at least five out of 10 trials, with a constant background contraction of 20% of the maximum integrated EMG.

Contralateral MEP and iSP. TMS at 50%, 75%, and 100% of the stimulator output was applied in random order to the M1, with the subject maintaining a 50% maximum contraction of the ipsilateral FDI muscle with visual and auditory feedback (Chen et al. 2003). Subjects took breaks whenever necessary to avoid muscle fatigue. Each stimulus intensity was repeated 10 times, and the stimuli were presented 5 s apart. Surface EMG was recorded from both FDI muscles by Ferbert et al. (1992). The subjects relaxed both FDI muscles. The conditioning stimuli were applied to the M1 at 75% of the stimulator output with the induced current flowing in the posterior-medial direction (handle of the coil pointed forward and laterally). This stimulus intensity and orientation were chosen, because in some subjects, it was not possible to place both coils at the optimal positions with the handle pointed backward and laterally, due to the size of the coil. A previous study found no difference in the IHI between 75% and 90% of the stimulator output and between four coil orientations 90° apart (Chen et al. 2003). The test stimuli were applied to the opposite M1 with the induced current in the anterior-medial direction (handle pointed backward and laterally) and were adjusted to evoke ~1 mV MEP in the contralateral FDI muscle. Test pulse alone and the ISIs of 6, 8, 10, 20, and 50 ms were tested. Each run consisted of 10 trials of the test pulse alone and 10 trials of each ISI delivered in random order (60 trials).

Data analysis. All patients were included in the analysis. Segments 1 and 2 were the anterior one-half, and segments 3–5 were the posterior one-half of the CC. Segment 2 was defined as the anterior midbody and segment 3 as the posterior midbody. For MRI, each CC segment was considered affected if the lesion occupied more than one-half of the area and was considered unaffected if the lesion occupied less than one-half of the area. Since the size of each segment is different with size ratios of 2:4:2:1:3 from segments 1 to 5, we assigned lesion burden in proportion to the size of each segment. Therefore, the lesion burden score was assigned a 2 if segment 1 were affected, 4 for segment 2, 2 for segment 3, 1 for segment 4, and 3 for segment 5. Lesion burden for the anterior one-half of the CC was the sum of scores for segments 1 and 2. Lesion burden for the posterior one-half of the CC was the sum of each score for segments 3–5. For example, a patient with lesions in segments 3 and 4 will have a lesion burden of 3 (2 + 1) for the posterior one-half of the CC. The assessor for MRI was blinded to the TMS results.

For TMS studies, the peak-to-peak MEP amplitude for each trial was measured. The unconditioned MEP amplitudes and the conditioned MEP amplitudes at each ISI were averaged. The inhibition or facilitation was calculated as a ratio of the conditioned/unconditioned (test pulse alone) MEP amplitude for each subject. Ratios less than one indicate inhibition, and ratios greater than one indicate facilitation. Values are expressed as mean ± SD.

Because iSP may be small, and their determination may be subjective, the occurrence, onset latencies, areas, and durations of iSP were analyzed using automated statistical methods to define their presence (Chen et al. 2003). For each stimulus intensity, surface EMG from the FDI muscle was rectified and averaged. iSP was deemed significant if the poststimulus EMG fell below the prestimulus mean by at least 1 SD for >5 ms (25 consecutive data points based on a 5-KHz sampling rate). iSP onset was defined as the last crossing of the mean baseline EMG level and iSP offset as the first crossing of the mean baseline EMG level. iSP area was calculated between the iSP onset and offset. The iSP duration was the time between the onset and offset values. The details of the method were described in a previous report (Chen et al. 2003).

Statistical analysis. The effects of different stimulus intensities on contralateral MEP, iSP area, iSP duration, and IHI were evaluated by two-way repeated measures ANOVA. For contralateral MEP, iSP area, and iSP duration, we performed two-way repeated measures ANOVA with side (lesioned/nondominant vs. nonlesioned/dominant) and stimulus intensity (50%, 75%, and 100%) as within-subject factors and group (patients and normal subjects) as between-subject factor. For IHI, we performed two-way repeated measures ANOVA with side (lesioned/nondominant vs. nonlesioned/dominant) and ISI (6, 8, 10, 20, and 50 ms) as within-subject factors and group (patients and normal subjects) as between-subject factor. The effects of lesion compared with no lesion in each callosal segment on iSP area, iSP duration, and LIHI (ISI of 50 ms) were analyzed with the unpaired t-test. The effects of lesion in each callosal segment on SIHI (ISI of 8 and 10 ms) were analyzed with repeated measures ANOVA with lesion (presence/absence) as the between-subject factor and ISI as the within-subject factor. Fisher’s protected least significant difference test was used for post hoc testing. Linear regression and multiple regression analyses were used to evaluate the relationship between callosal lesion burden for the anterior one-half and posterior one-half of the CC and measures of transcaldoscal inhibition. For iSP area and iSP duration, the results for stimulation at 100% stimulator output were used for the correlation.

RESULTS

MRI. MRI revealed an isolated infarction of CC in seven patients and CC infarction associated with infarctions in other locations (parasagittal frontal regions, cingulate gyrus, or anterior portions of basal ganglia) in 19 patients. The infarcts were in the dominant hemisphere in 18 patients and in the nondominant hemisphere in eight patients. Most patients had more than one segment of the CC affected, and the affected segments in each patient were shown in Fig. 1. Infarction in segment 1 was seen in 18 patients, segment 2 in 19 patients, segment 3 in 19 patients, segment 4 in 14 patients, and segment 5 in four patients (Fig. 1).

Contralateral MEPs. The contralateral MEP amplitude increased with higher stimulus intensity [F(2, 35) = 45.13, P < 0.0001], and the values tended to be lower for the lesioned (2.30 ± 2.85 mV for 50%, 3.44 ± 2.55 mV for 75%, and 3.86 ± 2.16 mV for 100% stimulus intensity). Linear regression analyses were used to evaluate the relationship between callosal lesion burden for the anterior one-half and posterior one-half of the CC and measures of transcaldoscal inhibition. For iSP area and iSP duration, the results for stimulation at 100% stimulator output were used for the correlation.
for 100% of stimulator output) and nonlesioned (1.99 ± 2.51 mV for 50%, 3.51 ± 2.75 mV for 75%, and 4.16 ± 2.82 mV for 100% of stimulator output) sides in patients and the nondominant side (1.74 ± 2.73 mV for 50%, 3.30 ± 2.06 mV for 75%, and 3.95 ± 1.83 mV for 100% of stimulator output) in normal subjects compared with the dominant side (1.99 ± 2.58 mV for 50%, 4.23 ± 2.15 mV for 75%, and 4.88 ± 2.24 mV for 100% of stimulator output) in normal subjects, but there was no significant effect of side (lesioned/non-dominant vs. nonlesioned/dominant) or group (patients vs. normal subjects) on MEP amplitude.

**iSP.** iSP was detected in all patients and normal subjects. The results for iSP area are shown in Fig. 3, A and B. Two-way repeated measures ANOVA showed significant effects of group [F(1, 37) = 11.74, P = 0.0015; reduced iSP area in patients; mean difference = 2.87 mV·ms] and stimulus intensity [F(2, 37) = 41.29, P < 0.0001] on iSP area, but the effect of side (lesioned/nondominant vs. nonlesioned/dominant) was not significant. iSP area was significantly lower for stimulus intensity of 50% compared with 75% (P < 0.0001; mean difference = −1.66 mV·ms) and 100% (P < 0.0001; mean difference = −3.00 mV·ms) stimulator output. The results for iSP duration are shown in Fig. 3, A and C. Two-way repeated measures ANOVA showed significant effects of group [F(1, 37) = 12.59, P = 0.0011; lower iSP area in patients; mean difference = 22.14 ms] and stimulus intensity [F(2, 37) = 41.87, P < 0.0001] on iSP duration, and there was no effect of side (lesioned/nondominant vs. nonlesioned/dominant). iSP duration was significantly lower for 50% compared with 75% (P < 0.0001; mean difference = 16.37 ms) and 100% (P < 0.0001; mean difference = 28.14 ms) stimulator output. These findings showed that iSP was markedly reduced in patients compared with controls.

**IHI.** The results are shown in Fig. 4. Two-way repeated measures ANOVA showed a significant effect of group [F(1, 37) = 10.22, P = 0.0018; lower iSP area in patients; mean difference = −22.65 ms] and stimulus intensity [F(2, 37) = 41.79, P < 0.0001] on IHI duration, and there was no effect of side (lesioned/nondominant vs. nonlesioned/dominant). IHI duration was significantly lower for 50% compared with 75% (P < 0.0001; mean difference = −16.37 ms) and 100% (P < 0.0001; mean difference = −28.14 ms) stimulator output. These findings showed that iSP was markedly reduced in patients compared with controls.

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**Fig. 3.** Findings for ipsilateral silent period (iSP). **A:** examples of iSP in a normal subject and on the lesioned side and the nonlesioned side in a patient. Recordings were from the 1st dorsal interosseous (FDI) muscle with 50% maximum voluntary contraction, and electromyography (EMG) was rectified and averaged from 10 trials. The primary motor cortex (M1) was stimulated at 100 ms at 100% of stimulator output. MEP, motor-evoked potential; TMS, transcranial magnetic stimulation. **B** and **C:** effects of stimulus intensities on iSP area and iSP duration, respectively. There were significant differences between patients and normal subjects. *P < 0.0001* significant differences. Error bars represent SE.
36) = 25.63, *P* < 0.0001; reduced in patients; mean difference = 0.32] and ISI [F(4, 36) = 3.90, *P* = 0.0049] on IHI with no significant effect of side (lesioned/nondominant vs. nonlesioned/dominant).

Relationship between transcallosal inhibition and locations of callosal lesions. Unpaired *t*-test showed that patients with lesions in segment 3 had a significantly smaller iSP area [t(48) = 4.35, *P* < 0.0001; difference between groups = 4.14 ± 1.31] and duration [t(48) = 3.93, *P* = 0.0003; difference between groups = 34.73 ± 9.98] than patients without lesions in this segment. However, iSP area and iSP duration were similar for patients with and without lesions involving segment 1, 2, 4, or 5. For SIHI and LIHI, there was no significant effect of the presence of lesions in all segments of the CC.

Linear regression showed that iSP area (*P* = 0.0073, r = 0.38; Fig. 5B) and iSP duration (*P* = 0.010, r = 0.36; Fig. 5D) negatively correlated with lesion burden in the posterior but not in the anterior one-half of the CC (Fig. 5, A and C). SIHI also correlated with lesion burden in the posterior (*P* = 0.0004, r = 0.35; Fig. 5F) but not in the anterior one-half of the CC (Fig. 5E). To further analyze the effects of lesion locations within the posterior one-half of the CC, which consists of segments 3–5, we performed multiple regression analysis with lesion burdens in segments 3–5 as three independent variables. Both iSP area and iSP duration significantly correlated with the presence of lesion in segment 3 (*P* = 0.0005 and 0.002, respectively) but not with the presence of lesion in segment 4 or 5. However, no significant correlation was found between SIHI and the presence of lesions in segment 3, 4, or 5. There was no correlation between lesion burden and LIHI.

SIHI correlated with iSP area (*P* = 0.0001, r = 0.49) and iSP duration (*P* = 0.0002, r = 0.48). LIHI correlated with iSP area (*P* = 0.041, r = 0.28) and showed a trend of correlation with iSP duration (*P* = 0.053).

**DISCUSSION**

iSP, iSP and IHI in patients with callosal infarction have not been reported previously. In patients with partial agenesis (Meyer et al. 1995) or with circumscribed surgical lesions in
different parts of the CC (Meyer et al. 1998), iSP was reduced or absent, suggesting that it is mediated through a transcallosal pathway. iSP was also found to be delayed or prolonged in neurological disorders, such as amyotrophic lateral sclerosis (Wittstock et al. 2007), multiple sclerosis (Schmierer et al. 2000), and writer’s cramp (Nieuhaus et al. 2001). Patients with corticobasal degeneration or progressive supranuclear palsy had either absent iSP or reduced iSP duration (Wolters et al. 2004). The marked reduction in iSP, which we observed in patients with callosal infarction, further indicates that the iSP is mediated through the CC.

**IHI.** IHI is thought to be mediated by excitatory transcallosal fibers that originate from the hand area of the conditioning M1 and project onto local inhibitory interneurons in the homologous area of the contralateral hemisphere (Di Lazzaro et al. 1999; Ferbert et al. 1992). Reduced IHI has been reported in several neurological and psychiatric conditions, including schizophrenia (Daskalakis et al. 2002a), corticobasal degeneration (Pal et al. 2008; Trompetto et al. 2003), and writer’s cramp (Nelson et al. 2010). IHI may help to maintain hemispheric dominance in cognitive and motor tasks by suppressing undesired activities of the opposite hemisphere. An inverse correlation between SIHI and physiological mirror activities during unilateral phasic movements has been reported (Habers et al. 2008). Moreover, the neural mechanisms underlying iSP may also be involved in the lateralization of voluntary movements (Giovannelli et al. 2009). Reduced LIHI and its effect on intracortical inhibitory circuits have also been reported in Parkinson disease patients with mirror movements (Li et al. 2007).

Several previous studies suggested that IHI is due to transcallosal inhibition (Brooojerdi et al. 1996; Daskalakis et al. 2002b; Di Lazzaro et al. 1999; Ferbert et al. 1992) based on indirect evidence using transcranial electrical stimulation (Ferbert et al. 1992) and recordings of TMS-evoked descending corticospinal waves in patients with cervical epidural electrodes (Di Lazzaro et al. 1999). They tested SIHI, but LIHI was not examined. One report suggested that SIHI may be mediated partly by subcortical circuits (Gerloff et al. 1998). We found marked impairment of SIHI and LIHI in patients with callosal infarctions in the absence of significant impairment in corticospinal projection, as measured by MEP amplitudes and recruitment curves. These results provide direct evidence that SIHI and LIHI are measures of transcallosal inhibition.

**Reduced transcallosal inhibition and lesion locations in the CC.** The CC is usually divided into the rostrum, genu, body, isthmus, and splenium. Since there are no clear anatomical landmarks to delineate distinct, functional subregions, several approaches have been used for CC segmentation (Wahl and Ziemann 2008). Most studies rely on Witelson’s scheme (1989), which defines five vertical callosal segments based on geometric fractions of the anterior-posterior extent. According to studies in monkeys (Pandy et al. 1971) and postmortem studies in humans (Witelson 1989), the callosal fibers connecting the M1 are located in the anterior midbody, defined as the anterior one-half minus the anterior one-third of the CC. The posterior midbody, defined as the posterior one-half minus the posterior one-third region, contains fibers connecting the somatosensory cortex and the posterior parietal area of the two hemispheres. However, recent studies suggested that the human callosal motor fibers are found in the posterior body of the CC. Meyer et al. (1998) studied the iSP in one split-brain patient and 13 patients with circumscribed surgical lesions in different parts of the CC. They suggested that the fibers mediating transcallosal inhibition (iSP) predominantly pass through the posterior one-half of the trunk of CC. In line with this, DTI tractography studies found that human callosal motor fibers cross the CC at a more posterior location than indicated previously (Fling et al. 2011; Hofer and Frahm 2006; Wahl et al. 2007; Zarei et al. 2006). Because of the discrepancies between the DTI-based topography in healthy human CC and Witelson’s classification (1989) based on postmortem studies, Hofer and Frahm (2006) suggested subdividing the CC into five segments, similar to Witelson’s scheme (1989), but with modified proportions of the segments and a different scheme of fiber attribution. For example, callosal motor fibers cross in region 3 in Hofer and Frahm’s scheme (2006) instead of region 2 in Witelson’s scheme (1989). We applied Hofer and Frahm’s scheme (2006) and found that reduced iSP area and duration were mainly due to lesions in segment 3. Thus our findings suggest that the callosal motor fibers cross the CC through the posterior one-half of the CC, mainly in segment 3 (posterior midbody). This is in agreement with studies of patients with surgical callosal lesion (Meyer et al. 1998) and DTI tractography studies (Hofer and Frahm 2006; Wahl et al. 2007; Zarei et al. 2006). A recent DTI study provided coordinates in a midsagittal callosal atlas in normalized Montreal Neurological Institute (MNI) space (Fling et al. 2011). Future studies examining callosal lesions mapped to MNI space may provide further information on the locations of sensorimotor fibers within the CC.

In our study, the lesion burden of the posterior one-half of the CC also correlated with SIHI but not with LIHI. Previous studies suggest that iSP and LIHI may be mediated by overlapping circuits (Chen et al. 2003). A different neuronal population in ipsilateral M1 may mediate iSP and IHI, perhaps through different sets of callosal fibers. The lack of correlation between lesion burden of the posterior one-half of the CC and LIHI may be due to involvement of different callosal fibers or because most patients have mixed lesions of anterior and posterior one-half of the CC. Studies with a larger number of patients and patients with more discrete lesions of the CC will be needed to demonstrate the callosal locations that mediate iSP, SIHI, and LIHI.

There are limitations to this study. First, most patients have lesions affecting multiple segments rather than lesions restricted to one segment. Second, very few patients had lesions involving segment 5. These factors affect our ability to precisely correlate lesion location and measures of transcallosal inhibition. Moreover, Fig. 5 shows that some patients with no lesion in the posterior one-half of the CC also had little or no iSP. One possible explanation is that areas other than segment 3 may also mediate transcallosal inhibition. For example, Meyer et al. (1995) reported an absent iSP in patients with abnormalities in the anterior one-half of the CC. In a subsequent study in patients with surgical lesions of the CC, Meyer et al. (1998) found reduced iSP predominately in the posterior trunk of the CC, but they also reported abnormally weak iSP in one patient with a lesion in the anterior trunk of the CC (second segment). Therefore, there may be individual variations in the CC segment that mediate iSP, SIHI, and LIHI. Other possible explanations include that: areas other than segment 3 may also mediate transcallosal inhibition; some lesions in segment 3 might not be adequately visualized on MRI; and infarction of less than one-half of segment 3, which would be scored as no lesion, was...
sufficient to disrupt transcallosal inhibition. A larger study sample, especially involving patients with more restricted lesions of the CC, will be needed for further evaluation.

The present study shows that cerebral infarction of the CC led to reduced transcallosal inhibition as measured by iSP, SIHI, and LIHI. Fibers mediating transcallosal inhibition mainly pass through the posterior midbody of the CC.

**AUTHOR CONTRIBUTIONS**

Author contributions: J-Y.L. and R.C. conception and design of research; J-Y.L. and R.C. performed experiments; J-Y.L. and R.C. analyzed data; J-Y.L. and R.C. interpreted results of experiments; J-Y.L. and P-H.L. prepared figures; J-Y.L. drafted manuscript; R.C. edited and revised manuscript; J-Y.L., P-H.L., and R.C. prepared final version of manuscript.

**DISCLOSURES**

The authors report no relevant disclosures.

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