Transcallosal inhibition in patients with callosal infarction

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Dr. J-Y Li: Conception and design of research, performed experiments, analyzed data, interpreted results of experiments, prepared figures, drafted and approved final version of manuscript.
Dr. P-H Lai: Performed experiments, prepared figures, approved final version of manuscript.
Dr. R. Chen: Conception and design of research, analyzed data, interpreted results of experiments, edited and revised manuscript, approved final version of manuscript.
ABSTRACT

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 the study is to define the pathways involved in transcallosal inhibition by examining patients with infarctions in different sub-regions of the CC. We hypothesized that patients with lesions in the posterior 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), short (SIHI) and long latency (LIHI) interhemispheric inhibition originating from both motor cortices. The results showed that the iSP areas and durations were markedly reduced bilaterally in patients with callosal infarction compared to normal subjects. Patients with callosal infarctions also had less IHI bidirectionally compared to normal subjects. iSP areas and durations were lower in patients with lesions than in patients without lesions in segments 3 (posterior midbody) of the CC. Lesion burden in the posterior 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 half.

Keywords: TMS, Interhemispheric inhibition, Ipsilateral silent period, Callosal infarction
INTRODUCTION

The corpus callosum (CC) is the major white matter tract connecting the cerebral hemispheres. It is considered the most important structure for interhemispheric communication of sensory, motor and higher-order information between the hemispheres. The CC is also important for the coordination of bimanual movements. Bimanual coordination deficit can be seen in patients with lesions of the CC or partial callosotomy (Caille et al. 2005; Jeeves et al. 1988). Infarcts of the CC are rare and this is most likely due to the rich blood supply from the main arterial systems, specifically the anterior cerebral, anterior communicating, and posterior cerebral arteries. Lesions of the CC producing disturbances of higher brain functions are often recognized as disconnection syndrome, in which unilateral left hand apraxia, agraphia and tactile anomia are most commonly encountered (Giroud and Dumas 1995; Watson and Heilman 1983; Yamadori et al. 1980). In addition, specific syndromes such as alien hand syndrome (Aboitiz et al. 2003; Feinberg et al. 1992) and an isolated gait disorder (Giroud and Dumas 1995) had been described in relation to lacunas in the anterior portion of the CC. Therefore, patients with callosal infarction may serve as a clinical model to investigate interhemispheric connections. The transcallosal connection between motor cortices (M1) has been studied in human
with transcranial magnetic stimulation (TMS), including transcallosal inhibition and facilitation. 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 intervals ~ 10 ms) and long interval IHI (LIHI, ~ 50 ms) with different physiologic properties (Chen et al. 2003a; Ni et al. 2009). Pharmacological studies suggest that LIHI likely involves GABA\textsubscript{B}-mediated inhibition, while 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 the fibers connecting the M1 pass through the anterior midbody of the CC (de Lacoste et al. 1985; van Valkenburg C.T. 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 sub-regions of the CC. We
hypothesized that the posterior half of the CC plays a greater role than the anterior 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 half of the CC.
MATERIALS AND METHODS

Subjects

We studied 26 patients (19 men, aged 62.9 ± 11.1 years) with anterior cerebral artery territory infarcts with callosal involvement and 14 age-matched normal subjects (8 men, aged 56.6 ± 8.9 years). There was no involvement of the middle cerebral artery territory in all patients. Intermmanual conflict was seen in 5 patients, apraxia in 13, tactile anomia in 6 and agraphia in 14. All 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). Table 1 shows the clinical features of the patients. The study was approved by Institutional Review Board-Kaohsiung Veterans General Hospital. Written informed consent was obtained from all subjects.

Magnetic Resonance Imaging

All MR imaging were performed with a clinical 1.5 T system (General Electric Medical System, Milwaukee, WI). The routine imaging studies included axial and coronal T1-weighted spin-echo (500/30/2 ms [repetition time/echo time/excitations]), T2-weighted fast spin-echo (4000/100/2 ms) with echo train length 8, and axial fast fluid-attenuated inversion recovery (9000/2200/133/1 ms [repetition time/inversion time/echo time/number of excitations]) sequences and sagittal T2-weighted and diffusion-weighted Imaging
The imaging sequence for DWI was a single-shot spin-echo echo-planar imaging (10000/93 ms [repetition time/echo time]) with diffusion sensitivities \( b=0 \) s/mm\(^2\) and \( b=1000 \) s/mm\(^2\). An apparent diffusion coefficient (ADC) map was calculated. Sections (5 mm thick) with 2.5 mm interslice gaps, 24 cm field of view, and 256 x 192 matrix were used for all scans. The callosal lesions were localized on sagittal MRI (Fig. 1A) and then attributed to one of five segments of the CC numbered from anterior to posterior according to the scheme (Fig. 1B) proposed by Hofer et al. (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 sixth of the CC. Segment 2 was the rest of the anterior half of the CC. Segment 3 was the posterior half minus the posterior third, segment 4 was the posterior one-third minus posterior one-fourth and segment 5 was the posterior one fourth.

**EMG recording**

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, Letchworth Garden, UK),
filtered (band pass 20 Hz to 2.5 kHz), digitized at 5 kHz (Power 1401, Cambridge Electronics Design, Cambridge, UK) and stored in a laboratory computer for off-line analysis.

**TMS studies**

Two 70 mm figure-of-eight coils and two Magstim 200 Stimulators (Magstim Company, Whitland, UK) were used. Both M1 were tested in patients with callosal infarction and in normal subjects. Lesioned side refers to the side with infarction. Surface EMG was recorded from both first dorsal interosseous (FDI) muscles. The optimal coil position over left M1 for eliciting the motor evoked potential (MEP) from the right FDI muscle was established with the handle of the coil held about 45 degrees 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 stimulator output that produced MEPs of $\geq 50\mu V$ in at least 5 out of 10 trials. Active MT was the minimum stimulator output that produced MEPs of $\geq 100\mu V$ in at least 5 out of 10 trials with a constant background contraction of 20% of the maximum integrated EMG.
Contralateral motor evoked potential and ipsilateral silent period

TMS at 50, 75 and 100% of the stimulator output were 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. 2003b). Subjects took breaks whenever necessary to avoid muscle fatigue. Each stimulus intensity was repeated 10 times and the stimuli were presented 5 seconds apart.

Interhemispheric inhibition (IHI)

The protocol was similar to that described by Ferbert et al. (Ferbert et al. 1992a). 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 backwards 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 degrees apart (Chen et al. 2003b). 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 about 1 mV MEP in the contralateral FDI muscle. Test pulse alone and the
interstimulus intervals (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 half and segments 3, 4 and 5 were the posterior half of the CC. Segment 2 was defined as the anterior midbody and segment 3 as the posterior midbody. For MR images, each CC segment was considered affected if the lesion occupied more than half of the area and was considered unaffected if the lesion occupied less than 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 as 2 if segment 1 was affected, 4 for segment 2, 2 for segment 3, 1 for segment 4 and 3 for segment 5. Lesion burden for the anterior half of the CC was the sum of scores for segments 1 and 2. Lesion burden for the posterior half of the CC was the sum of each score for segments 3, 4 and 5. For example, a patient with lesions in segments 3 and 4 will have a lesion burden of 3 (2 + 1) for the posterior 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 were calculated as a ratio of the conditioned to 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 ± standard deviation (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. 2003b). For each stimulus intensity, surface EMG from the FDI muscle was rectified and averaged. iSP was deemed significant if the post-stimulus EMG fell below the pre-stimulus mean by at least 1 standard deviation for more than 5 ms (25 consecutive data points based on a 5 KHz sampling rate). iSP onset was defined as last crossing of the mean baseline EMG level and iSP offset 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. 2003b).

Statistical analysis

The effects of different stimulus intensities on contralateral MEP, iSP area, iSP duration and IHI were evaluated by two-way repeated measures analysis of variance.
(ANOVA). For contralateral MEP, iSP area and iSP duration, we performed two-way repeated measures ANOVA with \textit{side} (lesioned/non-dominant vs. non-lesioned/dominant) and \textit{stimulus intensity} (50\%, 75\% and 100\%) as within subject factors and \textit{group} (patients and normal subjects) as between subject factor. For IHI, we performed two-way repeated measures ANOVA with \textit{side} (lesioned/non-dominant vs. non-lesioned/dominant) and \textit{ISI} (6, 8, 10, 20 and 50 ms) as within subject factors and \textit{group} (patients and normal subjects) as between subject factor. The effects of lesion compared to 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 & 10 ms) were analyzed with repeated measures ANOVA with lesion (presence/absence) as the between subject factor and interstimulus interval as the within subject factor. Fisher’s Protected Least Significant Difference (PLSD) test was used for \textit{post hoc} testing. Linear regression and multiple regression analyses were used to evaluate the relationship between callosal lesion burden for the anterior half and posterior half of the CC and measures of transcallosal inhibition. For iSP area and iSP duration, the results for stimulation at 100\% stimulator output were used for the correlation.
RESULTS

*Magnetic Resonance Imaging*

MRI revealed isolated infarction of CC in 7 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 non-dominant hemisphere in 8 patients. Most patients had more than one segment of the CC affected and the affected segments in each patient were shown in Table 1. Infarction in the segment 1 was seen in 18 patients, segment 2 in 19, segment 3 in 19, segment 4 in 14 and segment 5 in 4 patients (Table 1).

*Contralateral motor evoked potentials*

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% of stimulator output) and non-lesioned sides (1.99±2.51 mV for 50%, 3.51±2.75 mV for 75% and 4.16±2.82 mV for 100%) in patients and the non-dominant side (1.74±2.73 mV for 50%, 3.30±2.06 mV for 75% and 3.95±1.83 mV for 100%) in normal subjects compared to 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%) in normal subjects, but there was no significant effect of side (lesioned/non-dominant vs.
non-lesioned/dominant) or group (patients vs. normal subjects) on MEP amplitude.

**Ipsilateral silent period**

iSP was detected in all patients and normal subjects. The results for iSP area are shown in Fig. 2A & B. Two-way repeated measures ANOVA showed a 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/non-dominant vs. non-lesioned/dominant) was not significant. iSP area was significantly lower for stimulus intensity of 50% compared to 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. 2A & C. Two-way repeated measures ANOVA showed a 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/non-dominant vs. non-lesioned/dominant). iSP duration was significantly lower for 50% compared to 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 to controls.

**Interhemispheric inhibition (IHI)**
The results are shown in Fig. 3. Two-way repeated measures ANOVA showed a significant effect of group \((F(1, 36)=25.63, p<0.0001, \text{reduced in patients, mean difference}=0.32)\) and ISI \((F(4, 36)=3.90, p=0.0049)\) on IHI with no significant effect of side (lesioned/non-dominant vs. non-lesioned/dominant).

Relationship between transcallosal inhibition and locations of callosal lesions

Unpaired t-test showed that patients with lesions in segment 3 had significantly smaller iSP area \((t(48)=4.35, p<0.0001, \text{difference between groups}=4.14±1.31)\) and duration \((t(48)=3.93, p=0.0003, \text{difference between groups}=34.73±9.98)\) than patients without lesion 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 lesion in all segments of the CC.

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

*Ipsilateral silent period*

iSP and IHI in patients with callosal infarction have not been previously reported. 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 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 (Niehaus 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 we observed in patients with callosal infarction further indicates that the iSP is mediated through the corpus callosum.

*Interhemispheric inhibition*

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. 1992b). Reduced IHI has been reported in several neurological and psychiatric conditions including schizophrenia (Daskalakis et al. 2002a), corticobasal degeneration (Pal et al. 2004).
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 unimanual phasic movements has been reported (Hubers 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 has 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 (Boroojerdi et al. 1996; Daskalakis et al. 2002b; Di Lazzaro et al. 1999; Ferbert et al. 1992b) based on indirect evidence using transcranial electrical stimulation (Ferbert et al. 1992b) 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 partly be mediated 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 is no clear anatomical landmarks to delineate distinct functional sub-regions, several approaches have been used for CC segmentation (Wahl and Ziemann 2008). Most studies rely on Witelson’s scheme (Witelson 1989), which defines five vertical callosal segments based on arithmetic fractions of the anterior-posterior extent. According to studies in monkeys (Pandya 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 half minus the anterior one-third of the CC. The posterior midbody, defined as the posterior half minus the posterior 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. studied the iSP in one split-brain patient and 13 patients with circumscribed surgical lesions in different parts of the CC (Meyer et al. 1998). They suggested the fibers mediating transcallosal inhibition (iSP) predominantly pass through the posterior half of the trunk of CC. In line with this, DTI tractography studies found that human callosal motor fibers cross the CC at more posterior location than previously indicated (Fling et al. 2011; Hofer and Frahm 2006; Wahl et al. 2007; Zarei et al. 2006).
Because of the discrepancies between the DTI-based topology in healthy human CC and Witelson’s classification based on post-mortem studies (Witelson 1989), Hofer and Frahm (Hofer and Frahm 2006) suggested subdividing the CC into five segments similar to Witelson’s scheme 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 instead of region 2 in Witelson’s scheme. We applied Hofer and Frahm’s scheme and found reduced iSP area and duration was mainly due to lesion in segment 3. Thus, our findings suggest that the callosal motor fibers cross the CC through posterior 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 mid-sagittal 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 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. 2003a). 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 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 half of the CC. Studies with 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. 4 shows that some
patients with no lesion in the posterior half of the CC also had little or no iSP. One possible
explanation is areas other than segment 3 may also mediate transcallosal inhibition. For
example, Meyer et al. reported absent iSP in patients with abnormalities in the anterior half
of the CC (Meyer et al. 1995). In a subsequent study in patients with surgical lesions of the
CC, Meyer et al. 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) (Meyer et al. 1998). Therefore, there may be individual

variations in the CC segment that mediates iSP, SIHI and LIHI. Other possible
explanations include 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 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 posterior midbody of the CC.

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Disclosure

Dr. J-Y Li reports no disclosures.

Dr. P-H Lai reports no disclosures.

Dr. R. Chen reports no relevant disclosures.
Figure 1. Illustration of the scheme for localization of lesions in the corpus callosum. The sagittal diffusion-weighted MRI shows acute infarction of the corpus callosum (A) and the lesions were located at segments 1 and 2 on sagittal T2-weighted imaging according to segmentation scheme by Hofer.

Figure 2. Findings for ipsilateral silent period (iSP). (A) Examples of iSP in a normal subject and on the lesioned side and the non-lesioned side in a patient. Recordings were from the first dorsal interosseous muscle with 50% maximum voluntary contraction and EMG was rectified and averaged from 10 trials. The M1 was stimulated at 100 ms at 100% of stimulator output. (B & C) Effects of stimulus intensities on iSP area and iSP duration. There were significant differences between patients and normal subjects. Significant differences are shown by asterisks. Error bars represent standard errors.

Figure 3. Interhemispheric inhibition in patients and normal subjects. The conditioning stimuli were applied to the M1 at various ISIs before the test stimuli to the opposite M1. MEP amplitudes from the FDI muscle contralateral to the test stimuli were measured.
Ratios < 1 represent inhibition and ratios > 1 represent facilitation. Error bars represent standard errors. There was less IHI in patients compared to controls.

Figure 4. Correlation between transcallosal inhibition and lesion burden of the anterior and posterior half of the corpus callosum. No correlation was found between lesion burden of the anterior half of the corpus callosum and iSP area (A), iSP duration (C) and SIHI (E). There were significant negative correlations between lesion burden of the posterior half of the corpus callosum and iSP area (B), iSP duration (D) and SIHI (F).


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Table 1. Clinical and MRI features of patients with callosal infarction

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Age</th>
<th>Sex</th>
<th>Duration</th>
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D: days, M: months
Figure 1

A

B
Figure 2

A. Normal subject

B. Ipsilateral silent period

C. iSP duration
Figure 3

- From non-lesioned to lesioned side
- From lesioned to non-lesioned side
- Normal, from dominant to non-dominant
- Normal, from non-dominant to dominant

**MEP Amplitude (ratio to control)**

* Interstimulus Interval (ms): 6, 8, 10, 20, 50
Figure 4

A

B

C

D

E

F