

The Role of the Corpus Callosum in the Coupling of Bimanual Isometric Force Pulses

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Diedrichsen, Jörn, Eliot Hazeltine, Wesley K. Nurss, and Richard B. Ivry The role of the corpus callosum in the coupling of bimanual isometric force pulses. *J Neurophysiol* 90: 2409–2418, 2003; 10.1152/jn.00250.2003. Two split-brain patients, a patient with callosal agenesis, and 6 age-matched control participants were tested on a bimanual force production task. The participants produced isometric responses with their index fingers, attempting to match the target force specified by a visual stimulus. On unimanual trials, the stimuli were presented in either the left or right visual field and the response was made with the ipsilateral hand. On bimanual trials, two stimuli were presented, one on each side, and the target forces could be either identical or different. Bimanual responses of the control subjects showed strong evidence of coupling. Forces produced by one hand were influenced by the forces produced by the other hand with positive correlations observed for all target force combinations. These assimilation effects and correlations were greatly attenuated in the acallosal group, with similar results observed for the split-brain patients and participant with callosal agenesis. Furthermore, the processes involved in selecting and planning the two responses occurred independently in the acallosal group; in contrast to the controls, the three acallosal participants exhibited no differences in reaction times or accuracy between bimanual trials in which the two target forces were the same or different. We also found a striking temporal desynchronization of the responses in the split-brain patients, indicating that in this context, temporal coupling is impaired after callosotomy. These results are congruent with the hypothesis that interference related to response selection and planning of bimanual force pulses arises from callosal interactions.

INTRODUCTION

Human and nonhuman primates possess an extraordinary ability to use both hands simultaneously to manipulate objects. For example, when we open a jar, the timing, force, and direction of each movement must be carefully coordinated between the two limbs. The task becomes more difficult when performed by two people, each using only one hand. Presumably, the advantage arises because, when a single individual performs the task, bimanual control is mediated by a common coordinating structure or synergy (Schmidt et al. 1998; Scholz and Latash 1998).

It has been suggested that the coordination of different aspects of bimanual movements arise at distinguishable levels of the control hierarchy (Heuer 1993). For example, bimanual

reaching movements are closely coupled in their initiation and duration (Boessenkool et al. 1998; Kelso et al. 1979; Kelso et al. 1983; Marteniuk et al. 1984), indicating that the temporal features of the movements are specified by a common underlying mechanism.

Interactions can also be seen in the spatial properties of bimanual movements. Such limitations are demonstrated best in situations when we use our two hands to achieve different goals. For example, when rubbing our stomach and patting our head simultaneously, coupling between the hands can be detrimental. In contrast to temporal coupling, interactions between spatial properties of bimanual movements are strongly influenced by the time given to the participant to prepare and plan the movement (Heuer et al. 2001; Spijkers and Heuer 1995; Spijkers et al. 1997, 2000). Furthermore, spatial interactions depend on the way the bimanual movements are cued and conceptualized (Diedrichsen et al. 2001, 2003; Franz et al. 2001; Hazeltine et al. 2003; Mechsner et al. 2001). These findings indicate that interactions between spatial properties of bimanual movements may arise at the level of the response selection or the specification of movement parameters, rather than reflecting interactions between execution-related signals, as is often assumed to underlie temporal coupling.

Studies with callosotomy patients provide confirmatory evidence for a dissociation between the mechanisms associated with spatial and temporal coupling. Franz and colleagues (1996) reported that when split-brain patients produce bimanual trajectories, spatial coupling is abolished whereas temporal coupling is preserved. When drawing mirror symmetric or asymmetric shapes with both hands, the patients performed similarly in both conditions in terms of reaction times, movement times, and measures of spatial accuracy. In contrast, control subjects exhibited interference on all of these measures when producing asymmetric shapes. These results indicate that interference based on the spatial characteristics of the movements arises through callosally mediated interactions, consistent with the notion that the spatial goals are established at a cortical level (see also Eliassen et al. 1999; Kennerley et al. 2002).

Although callosotomy patients show strongly reduced spatial coupling in bimanual tasks (Franz et al. 1996; Ivry et al.

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1998), they continue to exhibit coupling in the temporal domain. As was true of normal controls (Kelso et al. 1979; Kelso et al. 1983; Marteniuk et al. 1984), the patients initiated and terminated the drawing movements simultaneously (Franz et al. 1996). Tuller and Kelso (1989) observed that callosotomy patients, when paced by lateralized visual metronomes, were strongly biased to produce in-phase movements during a repetitive finger-tapping task. Similarly, Ivry and Hazeltine (1999) reported frequency and phase coupling in a callosotomy patient during repetitive tapping, although the SD of the tap asynchronies was slightly higher for the patient than for age-matched controls (see also Eliassen et al. 2000). Thus temporal coordination does not require the integrity of the corpus callosum, suggesting that the temporal coupling can arise at a subcortical level or is dependent on interhemispheric interactions that do not involve callosal fibers.

The coordination of forces is another important aspect of bimanual action, especially in many tasks in which the two hands are used to manipulate objects. To return to our introductory example, the two hands apply opposing yet equal forces when removing the lid from a jar. Furthermore, to prevent the jar from slipping, the grip forces of both hands have to be adjusted according to the properties of the object and the actions of the other hand (Flanagan and Wing 1995; Johansson and Westling 1988a,b).

Force control during bimanual action has recently been investigated in normal healthy individuals. Steglich et al. (1999) observed extensive coupling when the two hands were required to produce simultaneous force pulses of different magnitude: the produced mean peak forces became more similar to each other. Moreover, when the pulses were examined on a trial-by-trial basis, high correlations were observed between the peak forces produced by the two hands. These phenomena likely reflect interactions between processes involved in planning the force output for each hand rather than from hard-wired interactions associated with response execution. When participants received sufficient time to prepare their responses, they were able to produce different target forces with the two hands and the correlation between the produced forces was attenuated (see also Rinkenauer et al. 2001).

Coupling between the grip forces of the two hands can also be observed in more naturalistic actions. For example, when opening a drawer with one hand, an involuntary increase in grip force can be measured when the other hand is holding an object (Serrien and Wiesendanger 2001b). Similarly, when one hand reacts to an unexpected perturbation to an object that is stabilized with the index finger, a short and transient increase in force is observed in the other hand (Ohki and Johansson 1999; see also Serrien and Wiesendanger 2001a).

To examine the neural locus of force coupling, we tested three patients lacking the corpus callosum on a task similar to that employed by Steglich et al. (1999). On each trial, the participants produced isometric responses on a force key, either with one hand or simultaneously with both hands. The target force for each hand was indicated by the vertical position of a short horizontal bar presented to the left and/or right of fixation, with the side of the stimulus indicating the hand to be used in making the response(s). We expected to observe strong force coupling on bimanual trials among control participants, manifest as an assimilation effect between the forces produced by each hand.

Concerning the performance of the acallosal group, we considered two hypotheses. First, force coupling could arise at a cortical level, resulting from transcallosal exchange of information between the two cerebral hemispheres. By this hypothesis, the specification of isometric force would be similar to the specification of movement direction. Indeed, neurophysiological evidence indicates that force is coded in primary motor cortex (Evarts et al. 1983; Fetz 1992; for a review see Ashe 1997), and that these cells code force in conjunction with movement direction (Georgopoulos et al. 1992; Taira et al. 1996). Given the attenuation of spatial coupling during bimanual movements in split-brain patients (Franz et al. 1996), we would predict the absence of force coupling in the acallosal group.

Alternatively, the interaction of force-related signals during bimanual movements might involve subcortical structures. This hypothesis would predict substantial interactions between the forces produced by the two hands even for participants without a corpus callosum, similar to what is observed with certain temporal features of bimanual actions. This prediction would be congruent with the hypotheses that the timing and the initial force of an action are controlled conjointly (Bullock and Grossberg 1988).

The force production task also allows us to directly assess temporal interactions between the two hands in an isometric task. In normal individuals, the timing of bimanual force pulses, measured at movement onset and time to peak force, is highly correlated, even when the amplitude of the two pulses differs (Rinkenauer et al. 2001). Given the strength of this coupling in normal participants and the tappinglike (Kennerley et al. 2002) nature of the isometric contractions, we expect that the coupling of the onsets and peak forces will be relatively well preserved in individuals without a corpus callosum. However, temporal coupling in callosotomy patients is not universally preserved (Eliassen et al. 2000; Kennerley et al. 2002) and the production of bimanual isometric force pulses has so far not been studied in callosotomy patients.

METHODS

Participants

Two callosotomy patients and one participant with callosal agenesis were tested on the tasks. Both callosotomy patients underwent surgical resection of the corpus callosum for intractable epilepsy in 1979 and their cases are extensively described in the literature (Sidtis et al. 1981). JW is a 47-yr-old male and VP is a 48-yr-old female. Structural MRIs indicate that the callosotomy operation was complete for JW. For VP, the MRIs show some remaining fibers in the ventrorostral portion of the corpus callosum. These fibers provide interhemispheric connection for the ventral striatum, cingulate, and other prefrontal areas (Corballis et al. 2001). RU is a 58-yr-old male. Agenesis of the corpus callosum was detected at age 57 when he was given a precautionary MRI after a headache episode. He reports no difficulty with bimanual coordination in everyday life. In all patients the anterior and posterior commissures are intact.

The age-matched control group was composed of 6 right-handed healthy individuals (3 males, 3 females), selected because their ages (mean = 48 yr) roughly spanned that of the 3 acallosal participants. All the participants gave informed consent adhering to standards of the Committee for the Protection of Human Subjects (CPHS) at the University of California, Berkeley.

Apparatus and stimuli

Participants sat approximately 60 cm in front of the computer monitor. At this distance, the screen subtended a visual angle of approximately 20°. Two force keys were placed on a table in front of the participant. Each force key was composed of an immobile circular button (radius of 1.0 cm) attached to a metal plate (10.4 × 10.4 × 2.1 cm). Pressure on the button was measured by a strain gauge capable of recording forces ≤8.2 N with a resolution of approximately 0.002 N. Participants rested their left index finger on the force key to the left of the midline plane and their right index finger on the one to the right of the midline plane. Force pulses were produced by isometric contractions of the index finger flexors. The strain gauges were sampled at 200 Hz, with all data stored on an IBM-compatible PC.

A fixation cross (“+”) was presented in the center of the computer screen. The imperative stimuli were small, red horizontal lines (7 cm, 6.7° in length), presented at a lateral distance of 5.5 cm (5.3°) from the fixation cross. The vertical position of the lines indicated the target force for the corresponding hand. Target forces of 0.6, 1.2, and 2.4 N were specified by horizontal lines appearing 2.8, 5.6, and 11.2 cm above a base position, indicated by another line. After the completion of each response, a lateralized vertical bar appeared, with the upward extent indicating the peak force produced with that hand. On bimanual trials, 2 vertical bars appeared, one for each hand. These vertical bars provided feedback on a trial-by-trial basis. The left vertical bar was green and the right vertical bar was blue. Concurrent with the vertical bars, the screen displayed 2 dotted lines 0.8 cm above and below the target force. These dotted lines defined a target zone for determining whether the response on that trial met the criterion required for a bonus.

Design and procedure

Participants were required to keep their index fingers (left, right, or both depending on the condition) on the appropriate force keys for the entire duration of a block. Verbal instructions were given, indicating that the participant’s task was to match the target force by pressing on the force key(s) with an appropriately scaled isometric response(s). The instructions emphasized that the responses should be generated as quickly and accurately as possible, and made in a synchronized fashion.

Before the experimental blocks, 3 practice blocks were given, one in which the force pulses were produced only with the left hand (L), one in which force pulses were produced only with the right hand (R), and one bimanual block (B). Each block consisted of 45 trials. For the left and right hand blocks, each force level was presented 15 times in random order. For the bimanual blocks, the 3 force levels were combined in factorial fashion for 9 conditions, and each condition occurred 5 times. The main experiment consisted of 10 blocks in a fixed order (B–L–B–R–B–B–R–B–L–B) and lasted about 1 h.

A trial started with the central presentation of the fixation cross. After 500 ms, the stimulus (on unimanual blocks) or stimuli (on bimanual blocks) appeared. When the response was completed, the vertical feedback bar(s) appeared along with the 2 dotted horizontal lines to indicate the produced force and acceptable target range. This display remained visible for 1,500 ms. After a blank interval of 1,000 ms the next trial began. The exposure duration of the lateralized stimuli was not limited. The acallosal participants are well practiced at maintaining fixation and the experimenter emphasized this requirement throughout the testing session.

Feedback regarding 3 types of temporal errors was provided online. First, if the reaction time was >1,000 ms, the message “Right Hand Too Slow” or “Left Hand Too Slow” was displayed. Second, if the duration of the isometric response was 2,000 ms, the message “Unfinished Pulse” was displayed. Third, the message “Nonsynchronous” was displayed on bimanual trials if the reaction times for the 2

hands were more than 150 ms apart. Error trials were excluded from the analysis.

A point system was devised to engage and motivate the participants. In the bimanual condition, a 10-point bonus was given if both responses fell within the target ranges. If the response for only one hand met the criterion, or if the produced force fell within the target range on a unimanual trial, 2 points were awarded. The point total was displayed at the end of each block and the participants were encouraged to maximize the total.

Data analysis

To determine reaction time, the first time point at which the first derivative of the produced force exceeded 0.8 N/s for an interval longer than 50 ms was identified. Peak force was defined as the highest force produced during the trial.

We calculated statistical measures (e.g., reaction time, mean, SD, and correlation of peak forces) for each participant in the 6 unimanual conditions (3 force targets tested separately for the left and right hands) and 9 bimanual conditions (3 force targets factorially combined). We averaged across these conditions to obtain summary measures for unimanual, bimanual same-target, and bimanual different-target trials. We then conducted an ANOVA with the group as a between-subject and the experimental condition as the within-subject variable and *t*-test on contrasts of interest within the groups. Because of the small sample size for our patient group, we additionally tested the significance of a result for each person for critical comparisons. To indicate the differences between the acallosal participants, the figures present the data for each individual separately.

RESULTS

Mean peak force

Trials in which a temporal error occurred were excluded from the primary analysis. Almost all of these errors were observed on bimanual trials, associated with a failure to initiate the two responses within 150 ms of each other. These occurred on a total of 4.1% of the trials for the control participants and 7.3% of the trials for the acallosal group (see *Temporal coupling at response initiation* below on onset asynchrony). The other types of errors were recorded on only 0.4% of the trials, with no discernable difference between the control and acallosal participants.

Figure 1 shows predicted results for the peak force data given different levels of coupling. The actual force values are arbitrary; the emphasis is to depict predicted patterns for comparison with the observed results. For the bimanual condition, the peak forces for the left hand are plotted on the ordinate and the peak force for the right hand on the abscissa. If the two hands performed independently—that is, if the force produced by one hand were uninfluenced by the force produced by the other—the plot of the 9 bimanual conditions would form a rectangular grid with sides parallel to the axes (see Fig. 1*a*). If the two hands were perfectly coupled such that they always produced identical forces, then the data points for the bimanual condition would all lie along a diagonal line defining the identity function (Fig. 1*c*). It is also possible for the coupling to be asymmetric. Figure 1*b* shows an example in which the force produced by the left hand is affected by the force produced by the right hand, although the right hand is unaffected by the left. With this form of coupling, the line formed by the

peak forces produced by the right hand for each level of left-hand force would be parallel to the y-axis.

Figure 2a shows the mean forces produced by the age-matched control participants. The data for the unimanual condition (triangles) show that participants' responses were appropriately scaled to the target forces. In general, participants tended to overshoot the low-force target and undershoot the high-force target. There was a strong bias to produce identical forces with the two hands. For example, when the left-hand target was 0.6 N and the right hand target was 2.4 N, the mean produced forces were 1.51 and 1.58 N for the left and right hand, respectively. This pattern indicates that each hand exerted a strong influence on the peak force produced by the other hand, a result that is consistent with previous studies (Steglich et al. 1999).

Figure 2, b-d, shows the mean peak forces for 3 acallosal participants. Overall, the patients performed accurately with both hands on unimanual trials, although VP showed a somewhat restricted range in the produced forces especially with her right hand. In the bimanual condition, the results for all three acallosal participants were strikingly different from those observed in the age-matched controls. With the one exception of VP's right hand, the forces produced were not influenced by the forces produced by the other hand.

To quantify the degree of force coupling during bimanual trials, we computed separate linear regressions for the forces produced by the left and right hand. In the regression for the left hand, the observed force in the 9 bimanual conditions (Y_L),

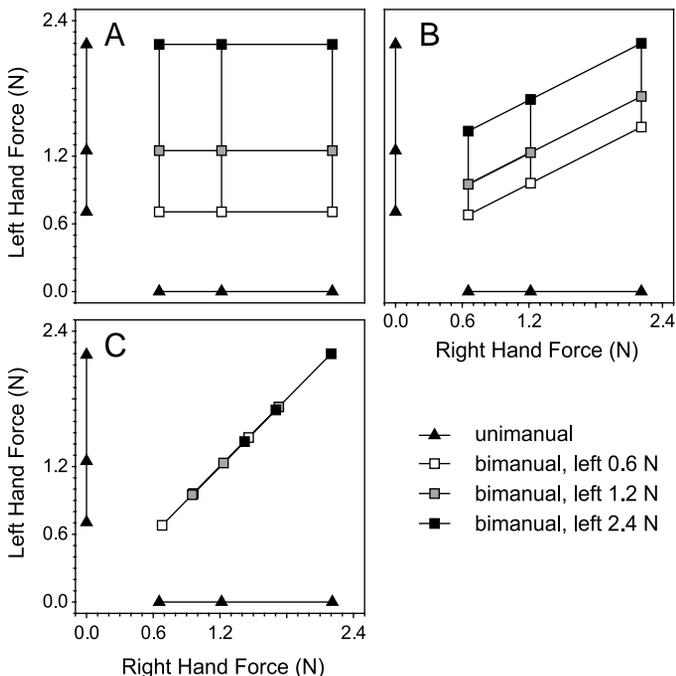


FIG. 1. Predicted peak forces for left (y-axis) and right hands (x-axis) based on different assumptions regarding coupling. Triangles indicate assumed unimanual performance for respective hand. Squares indicate peak forces in 9 bimanual conditions, shaded accordingly to target force required for left hand. a: no coupling between hands yields rectangular grid. Conditions that have same target force for right hand are connected with vertical lines; conditions that have same target force for left hand are connected with horizontal lines. b: right hand influences force produced on left, but left hand does not influence force produced by right hand. c: complete coupling, with each hand producing equal influence on performance of other hand. This causes the two hands to produce the same force on each trial with the produced force a function of the two target forces.

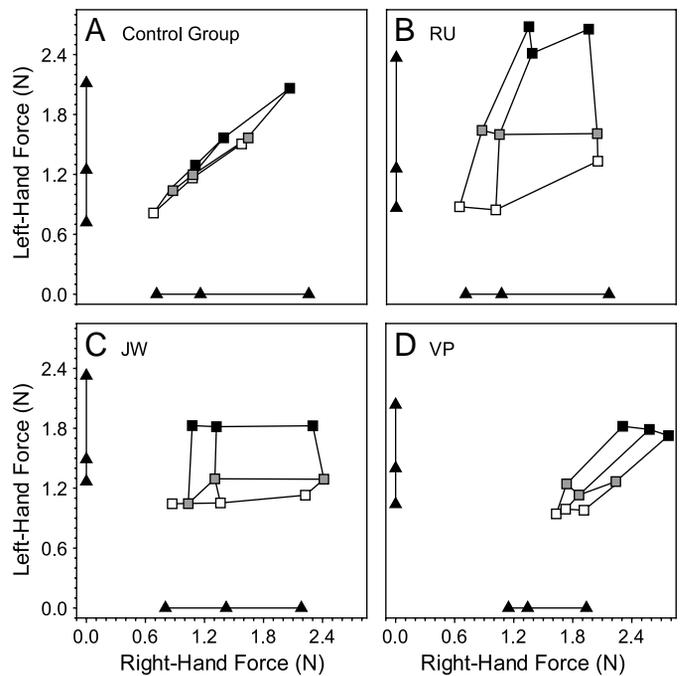


FIG. 2. Average peak force for left (y-axis) and right hands (x-axis). Conventions are as in Fig. 1. Target forces were 0.6, 1.2, and 2.4 N. a: average results for age-matched controls. b: individual results for participant with callosal agenesis patient RU. c and d: results for callosotomy patients JW and VP.

was hypothesized to be a function of the target force for the left hand (X_L) and the difference between the target forces of the right and left hand ($X_R - X_L$)¹

$$Y_L = w_{LL}X_L + w_{RL}(X_R - X_L) + a_L \tag{1}$$

For this equation the regression weights w_{LL} , w_{RL} , and the intercept a_L were estimated. The term w_{LL} refers to how strongly the mean force varied as a function of the instruction; any value smaller than one indicated an undershoot of large and an overshoot of small target forces. a_L is an intercept value referring to an overall bias across the three target forces. Of primary interest is w_{RL} , a weight referring to the influence of the right-hand target on the force produced by the left hand. If the target force for the right hand was larger than that for the left hand, a positive weight would cause the left hand to produce a larger force than specified. To reflect possible asymmetries between the hands in the coupling, the corresponding regression equation was used for the right hand

$$Y_R = w_{RR}X_R + w_{LR}(X_L - X_R) + a_R \tag{2}$$

Figure 3 shows the values for the weights for each group. For the age-matched controls the model resulted in substantial coupling weights, significantly different from zero for both intermanual directions. Furthermore, the influence from the dominant right hand onto the nondominant left hand was stronger than the influence in the reverse direction [$t(1,5) = 3.17$, $P = 0.025$; compare with Semjen et al. 1995]. Indeed,

¹ This regression model is essentially equivalent to the simpler form in which the target force for the left hand (X_L) and the target force for the right hand (X_R) are used as separate regressors. We preferred the current form because in this formulation the regression coefficient w_{LL} represents an interpretable quantity (see text).

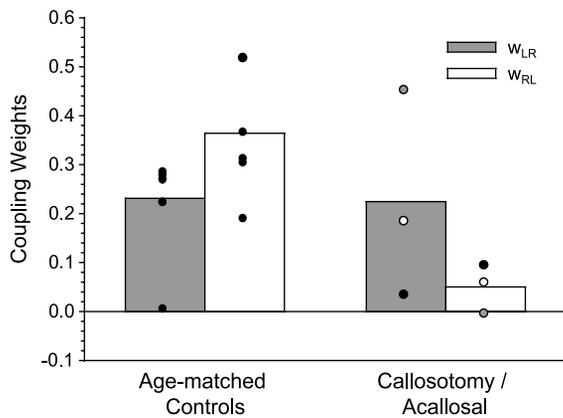


FIG. 3. Estimates of coupling strength from left hand on right hand (w_{LR}), and from right on left hand (w_{RL}). Bars indicate mean; circles indicate values for each individual participant. For the acallosal group, VP's values are displayed in gray, JW's in black, and RU's in white circles.

one of the age-matched controls showed a completely asymmetric coupling profile, with a positive weight found only for w_{RL} .

For the acallosal participants the estimates of the coupling weights were considerably smaller, with the exception of the coupling weight w_{LR} in patient VP. Because of this outlying observation and the small sample size, the difference between the groups just failed significance [$F(1,7) = 4.86, P = 0.063$]. Because there was no consistent asymmetry of the coupling strength evident in these three individuals, the group by coupling direction interaction was significant [$F(1,7) = 8.23, P = 0.024$].

Correlation of peak forces

As a second measure of force coupling, we calculated the between-hand correlation of the produced peak forces. Whereas the prior analysis looked at the influence of coupling on the mean force output, this approach allowed us to determine whether trial-by-trial variability in peak force was correlated for the two hands. Separate correlations were computed for each of the 9 bimanual conditions; thus this measure is statistically independent from the results we reported on the mean of the peak forces. The correlations assess how, for a given target force combination, variability in the force produced by one hand is related to variability in the force produced by the other hand. Even if the mean force values become assimilated as a consequence of coupling, the variability around these mean forces need not be coupled.

Correlation coefficients were Fisher-Z transformed and averaged separately for the same- and different-force conditions. Statistical tests were performed on Fisher-Z transformed correlation coefficients to satisfy the assumption of normally distributed data. For the control participants substantial correlations were observed in all conditions (Fig. 4), providing independent verification of strong force coupling. The correlations tended to be stronger when the left and right target forces were the same compared with when they were different, although this effect was not statistically reliable [$t(5) = 2.00, P = 0.102$]. For the acallosal group the correlations were significantly smaller [$F(1,7) = 10.58, P = 0.014$].

The correlations corroborate the results from the assimila-

tion effects: coupling of isometric forces is significantly reduced when the corpus callosum is absent. The difference between the control and acallosal group is especially marked on trials in which the same target force is required for the two hands. Under this condition, the controls showed the strongest correlation between the two responses. In contrast, the acallosal participants showed no difference between the same- and different-target conditions.

Peak force variability

Given that the variability increases with the mean level of the produced force (Carlton and Newell 1993; Newell and Carlton 1988; Sherwood and Schmidt 1980; Slifkin and Newell 1999), the coefficient of variation (CV; the SD of the peak force divided by the mean) provides a standardized variability measure commonly used in this context. Because target force levels were equivalent in the unimanual, same-target, and different-target conditions, we compared the CVs in an ANOVA with hand and condition as within-subject factors and group as a between-subject factor, averaged over all possible force-level combinations. For the age-matched controls, the variability in the different-force condition was significantly higher than in the same-force [$t(5) = 2.94, P = 0.032$] and unimanual conditions [$t(5) = 2.88, P = 0.034$]. This difference was not present in the acallosal group (Fig. 5), indicated by the significant Group \times Condition interaction [$F(2,14) = 5.13, P = 0.021$]. Thus in terms of force variability, the control participants exhibited increased difficulty when the two target forces were different compared with when they were the same. The performance of the acallosal participants was insensitive to this variable. Overall, there was no difference between the groups [$F(1,7) < 1$] and no significant effect of hand [$F(1,7) < 1$].

Reaction times

The time it takes to initiate the force pulses based on the symbolic stimuli reflects processes associated with response selection and planning. Both groups exhibited faster reaction

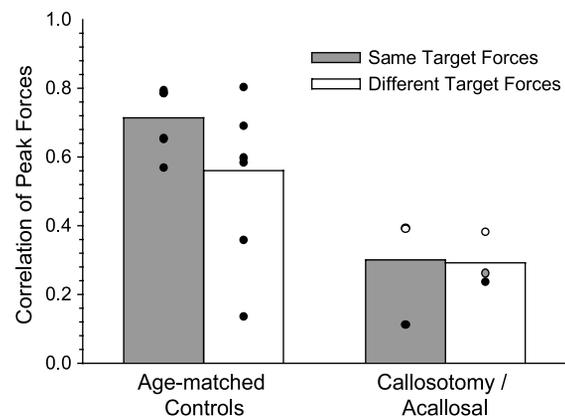


FIG. 4. Correlation coefficients between produced forces for the two hands, shown for conditions in which the target forces were same or different. Bars indicate mean; circles indicate values for each individual participant. Acallosal participants are color-coded as in Fig. 3. Correlation coefficients were calculated within each of 9 bimanual conditions, Fisher-Z transformed, averaged for same- and different-target conditions, and finally, inversely transformed into correlations.

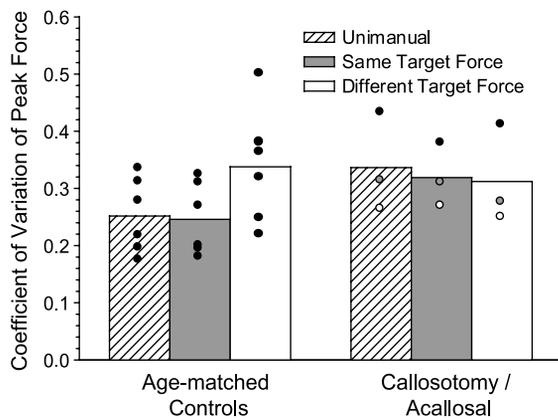


FIG. 5. Coefficient of variation (SD/mean) of peak forces in unimanual trials, bimanual trials involving targets of same target forces, and bimanual trials involving different target forces. Results are averaged over left and right hands. Bars indicate mean values; circles indicate individual participants (see Fig. 3).

times (RTs) in the unimanual condition compared with the bimanual condition (Fig. 6). The difference for the age-matched control participants was 82 ms; the difference for the acallosal group was 49 ms.

Focusing on the bimanual trials, we compared the trials in which the target forces were identical with those in which the target forces were different. An ANOVA revealed no overall difference between the groups [$F(1,7) < 1$]. The control participants initiated their responses 47 ms faster on the same-force trials than on different force trials, whereas the acallosal participants' RTs were identical for the 2 conditions, resulting in a significant Group \times Condition interaction [$F(1,7) = 6.19$, $P = 0.042$]. These results indicate that the cost observed in normal participants when executing bimanual isometric response of unequal force is also evident before response initiation. As with the effects on the variability of the peak forces, these costs are absent in participants lacking a corpus callosum.

Temporal coupling at response initiation

We now turn to the temporal coordination between the two responses. Onset asynchrony is defined as the difference in reaction time for the left and right hands, with positive values

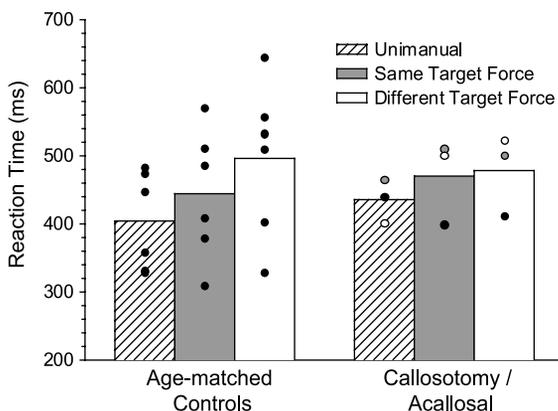


FIG. 6. Reaction times (RTs) for age-matched control and callosotomy groups on unimanual trials, bimanual same-target trials, and bimanual different-target trials. Results are averaged over left and right hands. Bars indicate mean values; circles indicate individual participants (see Fig. 3).

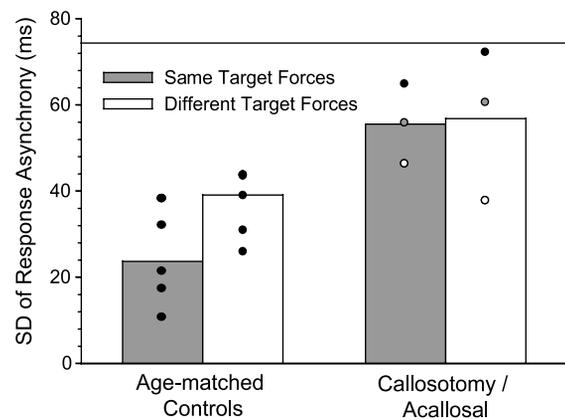


FIG. 7. SD of onset asynchrony of 2 force pulses in bimanual trials with same (gray bars) and different (white bars) target forces. Circles indicate values from individual participants, color-coded as in Fig. 3. Line indicates average expected value of SD, if responses were initiated independently (see text).

chosen to indicate trials in which the right-hand response was initiated first. All of the control participants exhibited a consistent tendency to respond with one hand before the other. A t -test for each participant indicated that the mean asynchrony was always significantly different from zero (all P values < 0.003). For three of the control participants, the bias was for the right-hand response to be initiated first; the other three showed a bias for the left-hand response to be initiated first. On average, the first hand preceded the second by 20 ms.

In contrast, the mean onset asynchrony was not significantly different from zero for two of the three acallosal participants, for JW (-8 ms; $P = 0.06$) and RU (1 ms; $P = 0.65$). Only VP showed a significant right-hand lead of 8 ms ($P = 0.03$).

Although mean onset asynchrony indicates if there is a tendency for one hand to lead over the other, a more appropriate measure of temporal coupling is the SD of the onset asynchronies (Fig. 7). Overall, the acallosal group showed a significantly elevated onset asynchrony SD [$F(1,7) = 11.55$, $P = 0.011$]. Furthermore, the onset asynchrony SD for the control participants was substantially greater when the forces were different (39 ms) than when they were the same (24 ms) [$t(5) = 4.82$, $P = 0.005$]. In contrast, the acallosal group exhibited no difference between same- and different-force trials (56 and 57 ms), resulting in a significant Group \times Condition interaction [$F(1,7) = 6.21$, $P = 0.041$]. Thus the control group again exhibited a decrement in temporal coupling when the target forces were different, whereas the acallosal participants were unaffected by this variable.

The increased onset asynchrony SDs for the acallosal participants indicate that temporal coupling was weaker in these participants than for the controls. This conclusion, at least for the two split-brain patients JW and VP, is further supported by the error data. Note that trials in which the responses were not initiated within 150 ms of each other were scored as errors, a criterion adopted to preclude participants from staggering their responses. The frequency of these synchronization errors was 4.1% for the age-matched controls, 7.4% for VP, 14.4% for JW, and 0% for RU.

The high variability in onset asynchrony and the high synchronization error rates raise the question of whether the responses of the split-brain patients were, in fact, temporally coupled. A bootstrap procedure was employed to assess

whether the responses were initiated independently (i.e., temporally uncoupled). We generated a new sample of onset asynchronies by drawing randomly from the empirical RT distributions for the left and right hands on bimanual trials. These new RTs were then randomly paired. From this sample, we calculated the error rate based on the 150-ms onset asynchrony criterion and the SD of the onset asynchronies after exclusion of the error trials. We repeated this process 30 times to obtain an estimate of the mean and SE of these statistics for our given sample size. These measures were used to evaluate the hypothesis that the responses were initiated independently. Overall, this procedure indicated that the acallosal participants exhibited some degree of temporal coupling. The observed error rate and onset asynchrony SD for VP and RU differed significantly from the predicted value (as for the controls, all $P < 0.0001$). However, the results for JW did not differ significantly from the predictions derived by assuming independent response initiation for the two hands. His error rate was 14%, compared with a predicted value of 18% (SE: 3.6%), and his onset asynchrony SD was 70 ms compared with a predicted value of 74 ms (SE: 4.4 ms). In sum, these results indicate that, on this task, temporal coupling is substantially weakened (and perhaps abolished in the case of JW) in the two split-brain patients.

Temporal coupling of force pulses

Temporal coupling can also be evaluated by comparing the temporal feature of the two produced force pulses after the onset. In particular, a positive correlation is found between the two hands in terms of the time to peak force, calculated on a trial-by-trial basis (Rinkenauer et al. 2001; Steglich et al. 1999). This correlation was evident in our control group (0.63 for same-force trials, 0.52 for different-force trials) and reduced, but still present for the acallosal group (0.40 for same-force trials, 0.28 for different-force trials). An ANOVA on the Fisher-Z-transformed correlation coefficients did not reveal a significant difference between groups [$F(1,7) = 2.47, P = 0.159$] or between conditions [$F(1,7) = 3.93, P = 0.088$]. Furthermore, all of the correlations were significant when tested for each patient individually. The significant correlation of time to peak force for patient JW is surprising given the lack of temporal coupling in his performance at movement onset.

As a second measure of temporal coupling, we computed the cross-correlation function between the two force pulses for every trial. This approach has the advantage of being based on the shape of the entire pulse rather than on a single time point. We used the first derivative of force with respect to time because the linear correlation of the derivatives shows higher sensitivity to topological similarities and differences between the two force profiles. The correlation was calculated for different lags between the time series and the maximum cross-correlation and the lag at which this occurred were used in subsequent analyses. On average, the maximum correlation for the controls was 0.98, obtained at a lag comparable to the mean onset asynchronies. In comparison, the correlation for the acallosal group was 0.91, a significant reduction compared with the controls [$F(1,7) = 29.52, P = 0.001$]. Again, the mean and SD of the lag at which the maximal correlation was obtained were comparable to the onset asynchronies.

As with the onset asynchrony data, we used a bootstrapping

procedure to determine the correlation values that would be obtained if the two pulses were independently generated. Even under an independence assumption, one would expect to obtain positive correlations given that the force pulses produced by each hand consistently approximate a bell-shaped curve. Indeed, the average expected correlations were 0.94 and 0.86 for the controls and patients, respectively. The higher predicted value for the controls reflects the fact that they produced more consistent pulses across trials. These predicted values can be compared with the observed values, given that the bootstrap method provides an estimate of the SE. We tested the null hypothesis that the two pulses were independent for every participant separately. The independence assumption was rejected in 5 out of 6 comparisons for the controls and 2 out of 3 comparisons for the acallosal participants. Again, the performance of patient JW did not differ significantly from what would have been expected if he produced the force pulses in independent fashion.

In sum, the shape of the force pulses for the left and right hands were less similar for the patients than for the control participants, leading to significantly lower correlations. However, the bootstrap procedure revealed significant temporal coupling for two of the three acallosal participants. Temporal coupling is preserved in these individuals, albeit in weakened form compared with the controls.

Relationship between temporal and force coupling

The preceding analyses demonstrate some degree of temporal uncoupling in the acallosal participants, especially in the split-brain patients. This raises the question of whether the uncoupling in peak force was related to the extent of temporal uncoupling. In the controls, the correlation between the peak forces was lower and the SD of the onset asynchronies was greater in the different- than in the same-target condition, suggesting that the two measures might covary. If true, the low correlations in peak force for the acallosal participants might be accounted for solely by the high SD of onset asynchronies shown by this group. This would argue that the decrease in the force coupling is not an independent phenomenon from the impairment in temporal coordination.

To assess this possibility we divided the bimanual data of each participant along the median of the absolute onset asynchronies. This was done separately for each of 9 bimanual target–force combinations, yielding 18 subsets of data for each participant, including subset of trials in which temporal synchronization for the acallosal group was comparable to that observed in the controls. Within each subset we computed the correlation of the peak forces and average absolute onset asynchrony. The results averaged for the same- and different-force conditions for each half can be seen in Fig. 8. For the controls the amount of force coupling was related to the degree of temporal asynchrony: force coupling was greatest when the two responses were initiated in close proximity and declined as the asynchrony increased. However, this relationship did not hold for the acallosal participants. The correlation between peak forces was essentially invariant with respect to onset asynchronies, and consistently lower than that observed for the controls. Even after removing the common linear trend between the average absolute onset asynchrony and the Fisher-Z-transformed correlation coefficients, the residuals differed be-

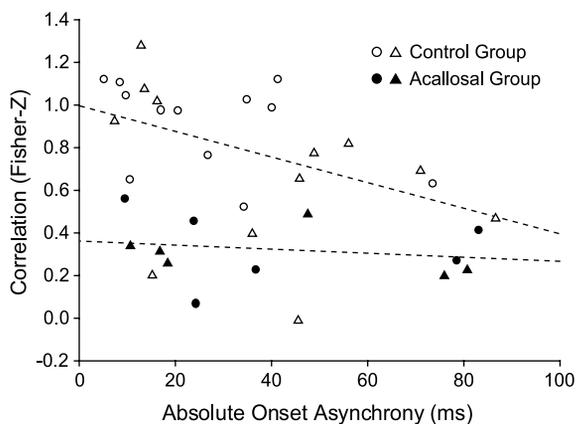


FIG. 8. Relationship between temporal asynchrony of responses and correlation of peak forces (Fisher-Z transformed). For each participant data were split along median of average onset asynchrony (see text), separately in each of 9 bimanual force-level combinations. Four data points are plotted for each participant, trials above and below median for same-target condition (circles) and trials above and below median for different-target condition (triangles). Regression lines are shown separately for each group.

tween groups [$t(7) = 3.28, P = 0.013$]. This analysis provides evidence that, although force and temporal coupling are related in normal participants, the force uncoupling in the acallosal group cannot be attributed to reduced temporal coupling.

DISCUSSION

The present experiment investigated the contribution of the corpus callosum in a bimanual force control task involving isometric responses. The results clearly indicate that coupling between the two responses primarily results from interhemispheric communication across the corpus callosum. Consistent with previous results (Rinkenauer et al. 2001; Steglich et al. 1999), we found substantial assimilation effects and correlations between the forces produced by the two hands in control participants. In contrast, participants without a corpus callosum, attributed either to the split-brain procedure or to callosal agenesis, showed minimal assimilation effects and dramatically reduced correlations between the peak forces produced by the two hands.

Is the coupling of forces completely abolished in the acallosal participants? Coupling effects in normal individuals have been hypothesized to arise at multiple levels of the motor hierarchy, including interactions that may occur between motor commands at a spinal level. For example, force coupling in people with congenital mirror movements has been attributed to interactions between crossed and uncrossed corticospinal fibers (Cohen et al. 1991) and similar mechanisms have been hypothesized to underlie the static, execution-related coupling between the hands in normal individuals (e.g., Cardoso de Oliveira 2002; Cattaert et al. 1999; Heuer et al. 2001; Weigelt and Cardoso De Oliveira 2003). Assuming ipsilateral projections in split-brain patients and controls are comparable, one would expect some degree of force coupling to persist.

Whereas the trial-by-trial peak force correlations were significantly lower in the acallosal group, the values were significantly greater than zero for all three acallosal participants. However, it may be premature to attribute these significant correlations to rudimentary preserved force coupling. Trial-by-trial correlations would be enhanced by various processes such

as arousal or fatigue. Assuming that such generic factors affect both hemispheres in a similar manner, positive correlations would be expected even if there were no interactions between the neural mechanisms underlying the generation of the responses. We believe the most conservative conclusion to be drawn from the current results is that force coupling for bimanual finger movements arises to a large degree from interactions involving the corpus callosum.

One exception to the general pattern of results for the acallosal group involves the assimilation effect observed for the right hand in patient VP. This result remains a puzzle. Unlike the other two acallosal participants, VP does have some spared callosal fibers in the rostral part of the corpus callosum. Thus her asymmetry may result from an inability of the left hemisphere to perform the task. At the start of the experiment, VP showed substantial deficits in her ability to produce the required forces with the right hand even in the unimanual condition. With extended practice, she was able to match the target forces, although not as well as with the left hand. It is possible that the ipsilateral, right hemisphere played a significant role in the specification and execution of the right force pulse. It should be noted, however, that on many other measures VP's performance was much more similar to the other acallosal participants than to the controls. For example, she showed little difference in RT or variability of peak forces between same-target and different-target trials, an effect that should be observed if the actions of both hands were controlled by a single hemisphere.

In terms of force production, the participant with callosal agenesis performed similarly to the two split-brain patients. Although the small sample size prohibits any generalization, the similarity does suggest that the effects observed here are not related to premorbid conditions of the two split-brain patients, given their epileptic status or a consequence of long-term use of antiepileptic agents. It is, of course, possible that the behavior of patients shortly after callosal resection would differ from that of our patients. Although reorganization is likely to have occurred and may account for the coordinated bimanual actions of these patients in their everyday life, one would have expected that such reorganization would favor the reemergence of coupling effects. Instead, the results show a dramatic attenuation of force coupling even in patients 20 yr postsurgery and in an individual born without a corpus callosum.

Interference of response selection and planning

Steglich and colleagues have proposed that coupling effects during bimanual force production are attributed to transient interactions that arise during the selection and/or planning of the responses (Steglich et al. 1999). Support for this view comes from the fact that the assimilation effects and correlations are substantially reduced when normal individuals are given a long preparation interval. The comparisons between the same- and different-target conditions for the control participants in the current experiment are congruent with this hypothesis.

First, control subjects initiated their responses more slowly in the different force condition, a cost that we attribute to increased demands on response selection (Diedrichsen et al. 2003) and planning (Steglich et al. 1999) when the two hands

are required to produce responses of different force. Second, the degree of coupling between the force traces was greater when the target forces were the same. This was evident in both the tighter temporal synchrony at movement onset and in the increased correlation between the peak forces. Third, the SD of peak forces was lower in the same-target condition, and in fact, comparable to that observed in the unimanual conditions.

One explanation for this finding is that the neurologically healthy participants subsume the two actions under a common generalized motor program (Schmidt et al. 1998) when the target forces are the same. In this manner, only one set of parameters would have to be specified, simplifying the planning process. In contrast, when the target forces are different, separate actions must be selected and prepared. The cost associated with this dual preparation is reflected in the reaction time measure and likely spills over into the execution phase, resulting in increased variability. Control participants may adopt a strategy of temporally desynchronizing their responses as one way to reduce interference on different force trials.

The acallosal participants dramatically differed from the controls in the comparisons between the same- and different-target conditions. On a range of measures including reaction time, peak force variability, and peak force correlation, the acallosal participants' performance was similar on trials requiring identical or different forces. These results strongly support the hypothesis that response selection and planning can occur independently for each hand in acallosal participants. Such independence has been demonstrated on bimanual drawing tasks (Franz et al. 1996) and in a variety of more cognitive tasks, such as when conflicting stimulus-response mappings (Ivry et al. 1998) or task sets must be maintained (Ivry and Hazeltine 2000).

Temporal coupling of isometric force pulses

Although the emphasis of this study was on force coupling, we also examined the temporal properties of the responses. We had expected to find relatively intact response synchronization given previous research involving tasks with relatively discrete responses (Ivry and Hazeltine 1999; Tuller and Kelso 1989; but see Eliassen et al. 2000; Kennerley et al. 2002). To our surprise the temporal coordination between the two hands was markedly reduced in the split-brain patients. Indeed, for patient JW we could not reject the null hypothesis that the responses were initiated independently. This temporal uncoupling is even more surprising given that the instructions and performance criteria favored response synchronization. Interestingly, onset asynchrony was one measure in which the agenesis patient's performance clearly deviated from that of the split-brain patients. Adaptation of CNS (e.g., transmission of information through anterior and posterior commissures) may help to restore the temporal coordination of movements in these individuals. Further research involving larger samples and manipulation of synchronization instructions are required to explore this issue. On other measures of temporal coupling, the acallosal group was more comparable to the controls. All three acallosal participants exhibited significant correlations between the rise times of the force pulses, and two of the patients exhibited significant cross-correlations between the force pulses on a measure that looks at coupling over the entire response.

Temporal coordination after callosotomy has been explored

in a number of studies. In general, this work has emphasized that such coupling is relatively preserved, although there may be an increase in variability (Eliassen et al. 2000). The most compelling evidence comes from studies involving finger tapping (Ivry and Hazeltine 1999; Tuller and Kelso 1989); coincident movement onsets have also been reported in a bimanual drawing task (Franz et al. 1996). We recently showed that such coupling is absent in repetitive movements when these movements are made continuously as in circle drawing (Kennerley et al. 2002). Based on this, we had proposed that movements involving discrete onsets or offsets remained coupled, consistent with the notion of a subcortical gating process of such events (Ivry and Richardson 2002).

However, the present results are at odds with this hypothesis given the discrete nature of the force pulses. One possible reason for the higher degree of temporal uncoupling in this situation is the isometric nature of the responses. Alternatively, the relative high task complexity compared with simple tapping movements could be the decisive factor. Further research involving the manipulation of movement requirements and instructions is required to explore this issue.

In our control group, a higher asynchrony of the responses was associated with a lower correlation of the peak forces (see also Rinkenauer et al. 2001). However, the reduced temporal synchrony observed for the participants without corpus callosum cannot fully account for the lack of force coupling. Even if we removed the influence of the synchrony at pulse onset or pulse peak, a significant and substantial difference remained between the groups. Thus it appears that the decrements in temporal coupling and force coupling reflect partially independent phenomena (compare Hore et al. 2002), although they may share a common underlying cause.

In summary, our findings indicate that interhemispheric connections through the corpus callosum are responsible for the coupling observed when people produce bimanual isometric responses. Acallosal participants showed little evidence of coupling between the two responses on a range of measures. Rather, response selection and planning, and implementation of the responses can occur independently in acallosal individuals. These results suggest that interactions at lower levels of the motor pathway, either subcortical or spinal, appear to play a negligible role given that these pathways are intact in the acallosal individuals.

This independence of the bimanual actions in this context seems to be at odds with the fact that split-brain patients do not report drastic deficits in the execution of bimanual actions after an appropriate time of recovery. A critical difference here might be that everyday bimanual skills are generally well practiced and require the hands to work one single task, rather than requiring independent responses. Which neural structures are essential for coordination in these situations remains to be explored.

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