Postural Context Alters the Stability of Bimanual Coordination by Modulating the Crossed Excitability of Corticospinal Pathways

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Carson RG, Smethurst CJ, Oytam Y, de Rugy A. Postural context alters the stability of bimanual coordination by modulating the crossed excitability of corticospinal pathways. J Neurophysiol 97: 2016–2023, 2007. First published January 10, 2007; doi:10.1152/jn.00868.2006. The tendency for movements of the upper limbs to be drawn systematically toward one another and to follow similar spatiotemporal trajectories is well known. Although suppression of this tendency is integral to tasks of daily living, its exploitation may prove to be critical in the rehabilitation of acquired hemiplegias. In general, however, the task-related factors that determine the degree of coupling between the upper limbs and the mechanisms that mediate bilateral interactions between neural pathways projecting to the muscles of the arm and hand are not yet well understood. We present evidence that the postural context in which human participants perform upper limb movements determines the relative stability of patterns of bimanual coordination. Manipulation of the axes of rotation of forearm movements reverses the relative stability of simultaneous and alternating patterns of bimanual coordination. Transcranial magnetic stimulation of motor cortex revealed that these manipulations of postural context altered the crossed modulation of excitability in corticospinal pathways that arises from movement of the opposite limb. Furthermore, modulation of responses to electrical stimulation of the cervicomedullary junction indicated that crossed modulation was also expressed at the level of the spinal motoneurons. Our data support the view that crossed modulation of excitability in corticospinal pathways mediates the stability of bimanual coordination. Furthermore, task-related factors that are sufficient to give rise to changes in the stability of bimanual coordination are accompanied by crossed modulation of excitability at multiple levels of the neuraxis, indicative of a failure of inhibitory control.

INTRODUCTION

Through the course of daily living we routinely engage in tasks in which quite different actions are executed by the two hands. The customary ease with which we thread a needle or unscrew the cap from a bottle belies the fact that there is a strong tendency for simultaneous movements of the upper limbs to be drawn toward one another. The origins of the constraints that govern these mutual interactions remain a topic of intense debate (Mechsner et al. 2001). Yet it is now evident that, in the absence of additional mediating factors (Swinnen 2002), patterns of bimanual coordination in which homologous muscles are simultaneously active are more stable than those in which homologous muscles are engaged in an alternating fashion (Riek et al. 1992). For example, in tasks in which participants are required to perform rhythmic flexion and extension movements of the wrists, patterns of coordination in which the wrists flex simultaneously and extend simultaneously are produced in a more stable and consistent fashion than alternating patterns in which flexion of one wrist is accompanied by extension of the other wrist (and vice versa). Indeed, when the frequency of movement is increased, spontaneous (unintentional) transitions from the alternating pattern to the simultaneous pattern are often observed and the latter pattern is typically the only one that can be sustained at maximal frequencies of movement (Cohen 1971; Kelso 1984).

Recent studies demonstrated that responses evoked in the musculature of the upper limb, by transcranial magnetic stimulation (TMS) of the motor cortex, are facilitated by tonic contraction of homologous muscles of the opposite limb (e.g., Hortobágyi et al. 2003). Pronounced modulation of the excitability of the corticospinal motor pathway also occurs during rhythmic movements of the opposite limb (Carson et al. 1999, 2004, 2005; Stinear and Byblow 2002). The largest motor-evoked potentials are obtained in those phases of the movement cycle in which the homologous muscle of the (opposite) dynamic limb is most active. Such crossed facilitation should favor patterns of bimanual coordination in which homologous muscles are engaged simultaneously and disrupt those in which these muscles are activated in an alternating fashion. It is thus tempting to infer that excitability in corticospinal motor pathways accounts for the relative stability of simultaneous and alternating patterns of bimanual coordination, although this conclusion would be more compelling if it could be demonstrated that the manipulation of task related factors has a direct and corresponding effect both on the modulation of corticospinal excitability brought about by movements of the opposite limb and on the stability of bimanual coordination. The objective of the present study was to determine whether changes in a specific task-related factor, in this case the postural context in which rhythmic pronation–supination movements of the forearm were performed, influenced the stability of bimanual coordination. By using TMS of the motor cortex it was also possible to determine whether the same changes in postural context had a corresponding effect on the crossed modulation of excitability in corticospinal motor pathways projecting to the homologous muscles of the opposite limb.

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METH O D S

Participants

Sixteen healthy right-handed adult volunteers (ages 20–31 yr) participated in the behavioral experiments and a separate group of 13 volunteers (ages 23–45 yr) participated in the electrophysiological experiments. All gave informed consent to the procedures, which were approved by the University of Queensland Medical Ethics Committee and conducted in accordance with the Declaration of Helsinki.

Manipulation of limb posture

Custom devices were used to manipulate the axes of rotation of the forearms (Fig. 1). The positions of horizontal shafts (instrumented to record angular displacement) could be adjusted to fix each axis of rotation adjacent to the radius, midway between the radius and ulna, adjacent to the ulna, or at two intermediate positions (Fig. 1A). When the seated participants grasped the device, their elbows always remained flexed at 90°. Their upper arms were secured to their sides. In the electrophysiological experiments only the two extreme positions were used.

Behavioral experiments

Participants were assigned at random to one of four groups (Fig. 1B). Each group performed Simultaneous and Alternating patterns of bimanual coordination (in separate trials) in five axis (symmetry) configurations ($\delta = 0, 0.25, 0.5, 0.75$, and 1). The Simultaneous pattern required synchronous pronation and synchronous supination of the forearms. In the Alternating pattern, the participants were required to synchronize maximum supination of one forearm with maximum pronation of the other forearm, and vice versa. A metronome that increased from 1.25 to 3.0 Hz (in eight steps each of 8-s duration) over the course of 64 s prescribed the frequency of movement. The participants were instructed to maintain the target pattern (Simultaneous or Alternating) as accurately as possible, but were also told that should the pattern change they were not to intervene. That is, they were not to actively resist pattern change but were to establish the most comfortable pattern compatible with the prevailing frequency (Kelso 1984).

Data analysis: behavioral experiments

The displacement data for each limb (sampled at 200 Hz) were low-pass filtered (8-Hz second-order Butterworth dual pass) and continuous (sample by sample) measures of movement phase determined using a Hilbert transform (Boashash 1992a,b). This yields the temporal variation of phase at a resolution equal to the original digital sampling frequency. The relative phase relationship between the displacement of the right limb and the displacement of the left limb was calculated from the instantaneous phase of the two signals. Instances of an abrupt change in the pattern of coordination were analyzed using a partially interactive procedure that allowed the experimenter to view relative phase profiles by a graphical interface. Cursors were positioned at either end of regions that were obviously pretransition or posttransition. Mean relative phase values were calculated for these regions. The relative phase value at the midpoint of the transition was also obtained. Previous research indicated that, to a close approximation, the change in relative phase is linear through the midpoint of the transition. A linear regression calculated on data about this point was used to derive the point in time of intersection with the pretransition mean. This point provided an index of the onset of the transition. On occasions on which the departure of relative phase from its target value was followed by phase wandering, the posttransition mean was assigned a value of $\pm 180^\circ$ the target value.

Electrophysiological experiments

Rhythmic pronation and supination movements of the left forearm were paced by metronome at a frequency of 2 Hz. The band-pass (30 Hz to 1 kHz) filtered electromyographic (EMG) activity of the flexor carpi radialis (FCR), and extensor carpi radialis longus (ECR) of the left arm was recorded (sampling rate of 2,000 Hz) using fine wire (75 micron) bipolar hook electrodes, inserted into the muscle by 27-gauge needles. EMG recordings of the left and right biceps brachii (BB) and right FCR and ECR were obtained using bipolar surface electrodes. For each participant, and for each muscle, root-mean-squared (RMS) values calculated on the basis of these recordings were expressed as a proportion of the maximum obtained for that muscle across all experimental trials and conditions.

Magnetic stimuli were delivered to the motor cortex of eight participants by a Magstim 200 stimulator (Magstim, Dyfed, UK), using a 55-mm figure-of-eight coil, located at the optimal position to evoke a short-latency response in the FCR muscle of the right arm (Fig. 2). The coil was placed so that the axis of intersection between the two loops was oriented at nearly 45° to the sagittal plane, to induce posterior to anterior current flow across the motor strip in the primary motor cortex. The optimal position for eliciting motor-evoked potentials (MEPs) in the contralateral FCR was established and marked directly on the scalp. The lowest stimulation intensity at which an

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**FIG. 1.** A: 5 axis-of-rotation positions were used to manipulate the postural context in which movements of the forearm were made: (1) axis of rotation adjacent to the radius; (5) axis of rotation adjacent to the ulna; (3) axis of rotation midway between positions 1 and 5; (2) axis of rotation 3 cm above position 3; (4) axis of rotation 3 cm below position 3. B: in the behavioral (bimanual) experiments 5 different combinations of the axis-of-rotation positions were used for each of the 4 groups of participants (4–D) to manipulate the symmetry of the postural context. Combinations used for the left (L) and right (R) limbs yielded for each group symmetry ($\delta$) values of 0, 0.25, 0.5, 0.75, and 1.0, respectively. In the electrophysiological (unimanual) experiments only the extreme axis of rotation positions (1 and 5) were used.
average potential with peak-to-peak amplitude of about 50 μV was evoked over eight trials was taken as the passive threshold. At the stimulation intensity corresponding to the passive threshold for FCR, MEPs were also observed in ECR. The level of stimulation used during each experimental trial was 115% of the FCR passive threshold. At these intensities, a corresponding potential was evoked in ECR and a smaller potential evoked in BB. Care was taken to ensure that the coil was held at the correct position on the scalp before each trial, by verifying that stimulation at the passive threshold evoked a small (~50 μV) response in FCR.

Stimulation of the cervicomedullary junction was carried out in eight participants (three of whom had participated in the previous experiment) by passing an electrical pulse (50-μs square wave, D180A stimulator, Digitimer, Herts, UK) between conductive gel–filled Ag–AgCl surface electrodes that were fixed over the mastoid processes (Fig. 2). The stimulus intensity was varied between 30 and 50% of stimulator output (450–700 V), to produce compound motor action potentials of ~100 μV in the right FCR. At these intensities, a potential of corresponding size was evoked in ECR and a larger potential evoked in BB.

The period between successive beats of the pacing metronome was divided into eight subintervals of 62.5-ms duration. An otherwise random stimulus sequence was constrained such that during the course of each trial, a single stimulus was delivered during each subinterval (mean interstimulus interval ~ 8 s; range 4–12 s). After completion of the experiment, each evoked response was classified in terms of the corresponding phase of the movement cycle in which the stimulus was delivered (Fig. 2). In the TMS experiments a separate block of 12 experimental trials was performed for each of the two axis-of-rotation positions. In experiments involving stimulation of the cervicomedullary junction, seven trials were performed in each block. Control trials, in which stimuli were delivered with the left forearm in a static neutral position, were conducted before and after each block of experimental trials. In every trial the right forearm was supported in a static neutral position. Auditory feedback of the EMG activity (amplified at high gain) of the ECR muscle of the static right arm was provided to the participants. The experimenters also monitored the EMG activity in the right FCR, ECR, and BB to ensure that the muscles were silent.

**Data analysis: electrophysiological experiments**

To take account of any transient variations in the postsynaptic state of the spinal motoneurons, the peak-to-peak amplitude of each evoked response was expressed relative to the (RMS) amplitude of the EMG recorded from the muscle in the period 22 to 2 ms immediately before delivery of the eliciting stimulus. The thus adjusted magnitudes of the responses elicited during each phase of movement of the opposite limb were then normalized with respect to the mean adjusted magnitude of the responses obtained during the control trials. The (RMS) amplitude of the EMG recorded in the muscles of the moving left arm was also calculated for the period 22 to 2 ms before the delivery of each stimulus.

**Statistical analyses**

Planned comparisons (based on ANOVA) were used to assess differences between postural conditions. The outcomes obtained for the behavioral experiments are reported in the text, whereas for the electrophysiological experiments, instances of statistically significant pairwise comparisons are indicated on the corresponding figures (Figs. 4 and 5). To further assist in the interpretation of the tests of significance, measures of effect size were calculated. The effect size index for ANOVA (f) is a dimensionless index that describes the degree of departure from no effect—in other words, the degree to which the phenomenon is manifested. A small effect size is consid-
ered by convention to be indicated by an f value of 0.1, a medium effect size by an f value of 0.25, and a large effect size by an f value of 0.4 (Cohen 1969).

RESULTS AND DISCUSSION

Influence of postural context on the stability of bimanual coordination

The postural context in which the bimanual movements of the left and right arms were performed had a profound impact on the relative stability of the Simultaneous and Alternating modes of coordination. When the position of the axis of rotation was equivalent for the left and the right limbs ($\delta = 1$), the Simultaneous pattern of coordination (Fig. 3A) could be maintained more accurately and reliably than the Alternating pattern (Fig. 3F). As the frequency of movement was increased, loss of stability occurred more rapidly when the participants were asked to perform the Alternating pattern ($t = 38$ s), than when required to execute the Simultaneous pattern ($t = 52$ s) ($P < 0.01, f = 0.62$). In marked contrast, when the positions of the axes of rotation for the left and right limbs were contradistinct ($\delta = 0$), the Alternating pattern of coordination (Fig. 3E) could be maintained more accurately and reliably than the Simultaneous pattern (Fig. 3J). In this configuration, loss of stability occurred at lower frequencies of movement when the participants were asked to perform the Simultaneous pattern ($t = 32.8$ s) than when required to generate the Alternating pattern of coordination ($t = 44.7$ s) ($P < 0.01, f = 0.57$). Thus when bimanual movements are performed in specific postural contexts, alternating patterns of coordination may be rendered more stable than simultaneous patterns (Carson et al. 2000). The intermediate axis configurations revealed that the relative stability of the two patterns of coordination varied consistently as the symmetry of the postural context was altered in stepwise fashion (Fig. 3).

We were careful to ensure that the manipulation of postural context did not alter the relative motion of the limb, defined either in egocentric (relative to the cardinal axes of the body) or allocentric (relative to external space, such as the gravitational field) coordinates. By altering the position of the external

FIG. 3. Distributions (mean of 16 participants) of the continuous relative phase relation between pronation and supination movements of the left and right arms, shown as a function of the 8 metronome pacing frequencies (plateaus), in the 5 axis (symmetry) configurations ($\delta = 0, 0.25, 0.5, 0.75$, and 1). A–E: trials that commenced in the Simultaneous (target relative phase $= 0^\circ/360^\circ$) pattern of coordination. F–J: trials that commenced in the Alternating (target relative phase $= 180^\circ$) pattern of coordination. Frequency of the metronome pacing increases (plateaus 1 to 8) from the front face to the rear of each figure. Accuracy of the behavior is indicated by the extent to which the peak of the distribution is aligned with the target relative phase. Variability of the behavior is indicated by the dispersion of the relative phase values.
axis of rotation of the forearm, we simply changed the patterns of muscle activation (and the associated afferent feedback) that were necessary to bring about the desired motion of the limb (see following text). When the postural context of the two limbs was identical, the Simultaneous pattern of coordination, in which the two forearms were pronated together and supinated together, was more stable than the Alternating pattern in which the pronation of one forearm was synchronized with supination of the other forearm and vice versa. In marked contrast, when the postural context of the two limbs was contradistinct (the axis of rotation of one forearm was adjacent to the radius and that of the other was adjacent to the ulna), the relative stability of the two patterns was reversed. That is, the Alternating pattern of coordination was more stable than the Simultaneous pattern. Clearly therefore it was not the relative directions of motion of the moving limbs that were critical in determining the stability of bimanual coordination (Carson et al. 2000), but rather the patterns of muscle engagement that generated that motion.

Influence of postural context on muscle activation patterns

The present findings corroborate previous reports (Carson and Riek 2000; Carson et al. 2000) that, when the axis of rotation is adjacent to the ulna, the activity of flexor carpi radialis (FCR) is appreciably modulated during the movement cycle and is at a maximum as the forearm moves from a supine to a prone position. In contrast, when the axis of rotation is adjacent to the radius, the moment arm of FCR is such that its capacity to contribute to pronation of the forearm is significantly diminished (Ettema et al. 1998). It was thus engaged to a lesser degree (Figs. 4A and 5A).

The pattern of recruitment of extensor carpi radialis (ECR) changed in a quite distinct fashion with alterations in the postural context. When the axis of rotation was adjacent to the radius, the activation of ECR was half a cycle out of phase with BB, whereas when the axis of rotation was adjacent to the ulna, the modulation of ECR activity was in phase with BB, and half a cycle out of phase with FCR (Figs. 4B and 5B). ECR and FCR are distinguished by an organization of recurrent and reciprocal inhibition that is distinct from that which characterizes other antagonist muscle pairs and points to the facility for task-specific alterations in their corecruitment required by movements of the wrist and forearm (Bawa et al. 2000).

The overall shape of the activation profile for biceps brachii was similar in the two postural conditions, although they were distinguished by a shift in phase. When the axis of rotation was adjacent to the radius, the greatest activation of this muscle occurred in phase 2 of the movement cycle, after maximum
pronation of the forearm. In the condition in which the axis of rotation was adjacent to the ulna, the highest levels of activation were observed in phase 8, slightly in advance of maximum pronation of the forearm (Figs. 4C and 5C). Although biceps brachii contributes to supination of the forearm in each case, the shift in the phasing of the activation profile relative to the movement cycle points to subtle variations in the mechanical role accorded to the muscle as a function of the position of the axis of rotation.

**Influence of postural context on MEPs elicited from the opposite limb**

Our working hypothesis was that task-related factors that alter the stability of bimanual coordination will do so by changing the pattern of crossed modulation in corticospinal motor pathways, resulting from activation of the muscles that drive the motion of the other limb. It was readily apparent that the pattern of modulation of MEPs elicited from right FCR was distinctly different for the two postural contexts in which the rhythmic movement of the opposite limb were performed (Fig. 4D). When the axis of rotation of the left arm was adjacent to the ulna, the pattern of modulation of the MEPs closely matched that of the EMG activity recorded from the homologous muscle of the opposite limb. The largest MEPs were recorded in right FCR during the phases in which the left limb moved from supination to pronation and the left FCR was most strongly engaged. When the axis of rotation of the left arm was adjacent to the radius, however, the pattern of modulation of the MEPs evoked in the right FCR was reversed. The smallest evoked potentials were obtained during the phases of movement in which the left limb moved from supination to pronation.

It was also the case that the pattern of modulation of MEPs evoked in right ECR when the axis of rotation of the left arm was adjacent to the ulna was the reverse of that obtained when the axis of rotation was adjacent to the radius (Fig. 4E). When the axis of rotation was adjacent to the ulna, the largest responses were evoked in right ECR during phases 1 and 8, when the arm was pronated. In marked contrast, when the axis of rotation of the left arm was adjacent to the radius, the smallest MEPs were obtained in these phases.

With respect to the potentials evoked in right BB during movements of the left arm, the differences between the two postural contexts were no less marked. In phases 1–5 of the movement cycle, as the left forearm was moved from pronation...
into supination, the MEPs recorded from the right BB when the axis of rotation of the left arm was adjacent to the ulna were appreciably larger than those elicited when the axis of rotation was adjacent to the radius (Fig. 4F).

It is clear that superimposing two unimanual movements does not simply generate integrated bimanual movements. There are mechanisms underlying bimanual coordination that cannot be inferred from the observation of single limb movements alone. Yet it is useful to establish those aspects of the behavior that can be accounted for on the basis of bilateral interactions arising from unimanual movements, before invoking mechanisms that are specific to bimanual coordination.

In the present study, it was clearly the case that the manipulations of postural context that had such a profound influence on the bimanual coordination—reversing the stability of the simultaneous and alternating patterns—had an equally dramatic effect on the crossed modulation of excitability in corticospinal pathways. Because the patterns of crossed facilitation observed in FCR and ECR when the axis of rotation was adjacent to the ulna were the opposite of those recorded when the axis was adjacent to the radius, an account is thus provided of the impact of postural context on the stability of bimanual coordination. When the postural context was the same for the left and right limbs, the pattern of crossed facilitation in these muscles would have favored the simultaneous pattern of coordination, whereas when the axis of rotation for one limb was adjacent to the radius, and for the other limb adjacent to the ulna, the crossed modulation of excitability in corticospinal pathways would have favored an alternating pattern of coordination.

Influence of postural context on cervicomedullary motor-evoked potentials (CMEPs) elicited from the opposite limb

By definition, any factors relating to the movement of a single limb that have an impact on the accuracy or stability of bimanual coordination depend for the means of their expression on alterations in the motor output of the opposite limb. However, when measurements are obtained during simple tonic (Hortobagyi et al. 2003) or phasic (Carson et al. 2004) contractions of muscles of the upper limb, crossed modulation of responses to cortical stimulation generally occurs in the absence of corresponding changes in the excitability of spinal motoneurons. The effective suppression of crossed excitatory inputs to the motoneurons is thought to arise from the activation of inhibitory circuits local to the motor cortex that are engaged in response to control signals from other brain areas (Rokni et al. 2003). In the present study we sought to determine whether changes in the stability of bimanual coordination that are contingent on manipulations of postural context that generate significant alterations in muscle activation patterns are mediated by concomitant variations in the excitability of the spinal motoneurons that innervate the muscles of the opposite limb. Such context-specific variations may arise from the failure of inhibitory control mechanisms that normally prevent crossed facilitation at the level of the cortical motor centers from being expressed as activation of the muscles of the opposite limb (e.g., Carson 2005).

Our results indicated that responses evoked in right FCR by stimulation of the cervicomedullary junction (Taylor and Gandevia 2004) varied with postural context in a similar fashion to those evoked by magnetic stimulation (Fig. 5D). Specifically, during phases 4, 5, and 6 the CMEPs evoked when the axis of rotation was adjacent to the ulna were larger than those obtained when the axis of rotation was adjacent to the radius. Furthermore, as with the responses to TMS, the overall pattern of modulation across the cycle was reversed by alteration of the postural context in which the movements of the left limb were performed.

A corresponding pattern of outcomes was obtained for the right BB muscle, in so much as the CMEPs recorded during phases 4, 5, and 6 were larger when the axis of rotation of the left forearm was adjacent to the ulna than when it was adjacent to the radius. There was likewise a tendency for the overall pattern of modulation obtained in one postural context to be the reverse of that obtained in the other context (Fig. 5F). Although the pattern of responses evoked in right ECR by stimulation of the cervicomedullary junction appeared superficially similar to that obtained for BB, no reliable patterns of variation across the movement cycle or differences between postural conditions were obtained (Fig. 5E).

Responses evoked by stimulation of the corticospinal tract at the level of the cervicomedullary junction are mediated by many of the same axons activated by magnetic stimulation of the motor cortex (Taylor and Gandevia 2004; Ugawa et al. 1991). Because cervicomedullary-evoked responses have a large monosynaptic component, their task-related variation is considered indicative of the responsiveness of spinal motoneurons at the time of stimulation. The CMEPs recorded in muscles of the right arm in the present study varied in size as a function of the postural context in which movements of the left arm were performed. These findings suggest that task-related factors that have a direct impact on the stability of bimanual coordination exert their influence by a failure of inhibitory mechanisms that normally prevent crossed modulation of motor output in the corticospinal pathways of the opposite limb.

In conclusion, our key finding was that the manipulation of a task-specific factor—the postural context in which upper limb movements were performed—brought about changes in muscle activation that had directly corresponding effects on the excitability of the corticospinal motor pathways of the opposite limb and the stability of bimanual coordination. The modulation of corticospinal excitability that arises from the recruitment of muscles on the opposite side of the body thus appears to be the neural mechanism that mediates bilateral interactions between the upper limbs. These findings also have clinical relevance. The systematic nature of the interactions suggests that increases in the excitability of motor pathways originating in the damaged cortex and functional improvements in the control of a paretic limb may be promoted when movements are performed in a bimanual context.

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