

Reduced Timing Variability in Patients with Unilateral Cerebellar Lesions during Bimanual Movements

E. A. Franz, R. B. Ivry, and L. L. Helmuth

University of California, Berkeley

Abstract

■ Timing variability on a repetitive tapping task was studied in subjects with unilateral cerebellar lesions. During unimanual tapping, within-hand variability was larger when tapping with the ipsilesional hand in comparison to tapping with the contralesional hand. However, variability in the impaired hand was greatly reduced when subjects tapped with two hands together. The improvement in within-hand variability during bimanual tapping was associated with a reduction in central

variability rather than response implementation variability according to the two-process model of Wing and Kristofferson (1973). It is proposed that (1) each half of the cerebellum independently regulates the temporal aspects of movements on the ipsilateral side and (2) temporal coupling constraints require these separate signals to be integrated prior to response implementation for bimanual movements. ■

INTRODUCTION

Damage to the cerebellum disrupts the temporal characteristics of movement. Evidence for this can be found in both the clinical and experimental literature. For example, patients with cerebellar lesions tend to make hypermetric movements on pointing tasks, primarily due to a delayed onset of the braking action provided by the antagonist muscle (Dichgans & Diener, 1984; Hallett, Shahani, & Young, 1975; Vilis & Hore, 1980). It has been proposed that the cerebellum plays a critical role in acquiring the temporal properties of a motor response during sensorimotor learning (Ivry, 1993; Perrett, Ruiz, & Mauk, 1993). Lesions of the cerebellar cortex disrupt the timing of conditioned responses following classical conditioning of the nictitating membrane response in the rabbit (Perrett et al., 1993; McCormick & Thompson, 1984). A prominent feature of recent computational models of the cerebellum is that they uniformly postulate explicit mechanisms to represent temporal information (Buonomano & Mauk, 1994; Desmond & Moore, 1988; Grossberg & Schmajuk, 1989; Pellionisz & Llinas, 1982).

To directly assess the role of the cerebellum in movement timing, Ivry and associates (Ivry & Keele, 1989; Ivry, Keele, & Diener, 1988) tested patients with cerebellar lesions on a repetitive tapping task (Wing & Kristofferson, 1973). In this task, a trial is initiated by the presentation of a series of evenly spaced tones to establish a target response frequency (e.g., 2.5 Hz). The subject then begins to tap in synchrony with the tones. After a series

of paced responses, the tones are terminated and the subject's task is to produce a set of unpaced intervals. The primary dependent variables are the mean and standard deviation of the unpaced intervals. Patients with cerebellar lesions were able to match the target pace, but their interresponse intervals were more variable. This effect was observed when tapping with either hand in patients with bilateral lesions (Ivry & Keele, 1989). For patients with unilateral lesions, variability was considerably larger when tapping with the ipsilesional hand in comparison to tapping with the contralesional hand (Ivry et al., 1988).

To analyze the source of this increased variability, Ivry et al. (1988) employed a formal model developed by Wing and Kristofferson (1973). This model is designed to partition the total variability into two sources. One source is associated with response implementation and might correspond to increased noise in the transmission of central commands to motor effectors. The other source is associated with response planning. While Wing and Kristofferson have labeled this component "clock variability," it actually includes all sources of variance not associated with response implementation (Ivry & Corcos, 1993; Ivry & Hazeltine, 1995). As such, we will refer to the two sources of variability as the "central" and "peripheral" components.

By restricting the analysis to patients with unilateral lesions, each subject could serve as his or her own control, allowing a comparison between performance of the impaired and unimpaired hands. A double dissociation was found in this analysis. For patients with medial

cerebellar lesions, the increased variability of the impaired hand was limited to the peripheral component. In contrast, the increased variability was associated with the central component in patients with lesions encompassing either the lateral hemispheric regions of the cerebellar cortex or the dentate nucleus. Ivry et al. (1988) argued that whereas the medial cerebellum is primarily involved in response implementation, the lateral cerebellum is concerned with response planning. In particular, the lateral cerebellum was hypothesized to play a critical role in establishing the temporal aspects of a movement (Ivry & Keele, 1989). For the repetitive tapping task, this function includes determining when each response should be initiated. The hypothesis that a healthy cerebellum is necessary to preserve precise internal timing is further supported by the finding that these patients are impaired on perceptual tasks that require processing of temporal information (Ivry & Keele, 1989; Ivry & Diener, 1991) as well as the temporal interpretation of the cerebellar role in sensorimotor learning (reviewed in Ivry, 1993).

These data provide strong support for the hypothesis that the cerebellum supplies an internal timing function. Yet, it must be kept in mind that the methodology was essentially a within-subject design. Since subjects served as their own controls, the purported timing problem in the lateral patients was evident when comparing performance of the impaired to the unimpaired hand. The results indicate that separate timing mechanisms are required for movements of the right and left hands. Thus, while the cerebellum may play a general role in the representation of temporal information, it need not be conceptualized as a unitary internal timing mechanism. The exact cerebellar tissue involved in a particular behavior may vary depending on the task requirements. For example, the timing of each hand appears to be regulated by different regions within the cerebellum.

The question of whether the temporal coordination of movements performed by different limbs depends on a single timing mechanism can also be approached by considering multilimb actions. A well-established phenomenon across many species is that the movements of different effectors are tightly constrained in the time domain. In both bipedal and quadrupedal locomotion, strong temporal coupling of the limbs can be seen across a range of gaits (Delcomyn, 1980; Grillner, 1975). Similar temporal coupling is found across a wide range of tasks with humans (Chang & Hammond, 1987; Klapp, 1979, 1981; Schoner & Kelso, 1988; Yamanishi, Kawato, & Suzuki, 1980). Kelso, Southard, and Goodman (1979) found that when people move their two hands different distances to reach separate targets, they tend to start and stop the movements of the limbs nearly simultaneously.

In continuous motor tasks performed bimanually, this phenomenon is even more compelling. Stable performance requires that both limbs move at the same fre-

quency and is possible with only a limited set of phase relations (e.g., in-phase and antiphase). These constraints can be overcome only with extensive practice, and, even then, there is a bias to revert to more stable conditions (Haken, Kelso, & Bunz, 1985; Zanone & Kelso, 1992). Skilled musicians find it difficult to play polyrhythms in which the two rhythms are not simple integer multiples of each other (Jagacinsky, Marshburn, Klapp, & Jones, 1981; Shaffer, 1981).

Results such as these indicate that processes involved in the temporal regulation of individual limb movements must interact during the production of bimanual movements. One form of interaction would occur if a single timing signal were invoked in the bimanual condition. Alternatively, each limb might be associated with an independent timing signal, but there might be some form of interaction between these two timing mechanisms. We will return to these issues in the General Discussion.

To explore the effects of temporal coupling in cerebellar patients, we employed a bimanual version of the repetitive tapping task. Patients with unilateral cerebellar lesions were asked to tap with a finger of each hand at the same time, first with a pacing signal and then without a pacing signal. As in the previous studies, our focus was on how well they could produce the intervals during the unpaced phase. Performance on this task was compared to performance on the basic unimanual version of the repetitive tapping task. Our primary interest was in comparing within-hand variability between the unimanual and bimanual conditions.

At least three different outcomes seemed possible. First, variability within each hand might stay unchanged. Coupling might occur in that the two hands would tap in synchrony. But, this synchronization may not affect within-hand consistency since the control of each hand may depend on the ipsilateral cerebellum. Such a result would suggest that the cerebellar timing processes affect the motor system downstream from coupling processes that constrain the limbs to move interdependently.

Second, performance might be limited by the impaired hand. By this hypothesis, variability within the unimpaired hand may become worse because of the coupling of this hand to the impaired hand.

Third, the consistency of movements made with the impaired hand might become better. This might occur for one of two reasons. It may be that the intact timing mechanism dominates performance when both ipsilesional and contralesional mechanisms are activated. Alternatively, an improvement in the impaired hand may emerge due to an interaction arising through the coupling of independent timing mechanisms. This last possibility is most provocative. It suggests that the movement problems associated with unilateral cerebellar lesions might be reduced if the patients simultaneously make similar movements with the unimpaired

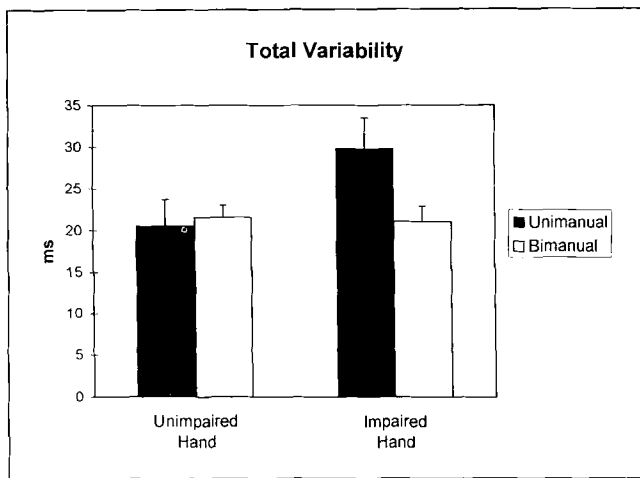


Figure 1. Total variability for all subjects. The bars indicate the standard errors of the means.

effector. While there may not be a direct clinical benefit to such a finding, we are not aware of any previous reports of experimental manipulations that ameliorated cerebellar dysfunction.

RESULTS

Overall, 15.8% of the trials were repeated with the majority of these being when the subjects tapped using the ipsilesional hand. For the most part, this was necessary when one of the intervals within the trial was excessively long (>600 msec), usually due to the fact that the subject failed to generate sufficient force to activate the microswitch. This problem was most marked for DOM, who accounted for 58% of the repeated trials. Nonetheless, in most conditions, the target number of 36 error-free trials was obtained with the lowest value being 28 trials. Thus, the data set is relatively large for making the component estimates.

The subjects were able to match the target frequency (2.5 Hz) with little difficulty. Across all blocks, the mean interresponse interval was 392 msec. There was no difference between these values when tapping with the impaired hand (392 msec) in comparison to the unimpaired hand (391 msec). In addition, tapping rate was similar for unimanual (390 msec) and bimanual (393 msec) conditions.

Figure 1 depicts the total variability of the interresponse intervals, averaged across all of the blocks and subjects. The most striking feature of the results is that performance using the ipsilesional hand is improved when the patients make homologous movements with the contralesional hand. To assess the reliability of this effect, a repeated measures three-way ANOVA was performed using as factors Hand (ipsilesional or contralesional), Tapping Mode (unimanual or bimanual), and Sessions treated as a repeated measure. As expected, subjects were significantly less variable when tapping with the contralesional, unimpaired hand, $F(1,3) = 42.60, p < 0.01$. This effect can be seen for both the unimanual and bimanual conditions and there was no effect of tapping mode, $F(1,3) = 1.83, p > 0.25$. However, the difference between the performance of the impaired and unimpaired hands is reduced during bimanual tapping. This effect is verified by the Hand $\times$ Mode interaction, $F(1,3) = 18.37, p < 0.05$. The reduction in tapping variability during bimanual tapping was only evident for the ipsilesional hand. The results were stable across all six blocks and there were no consistent changes in performance across the blocks, $F(5,15) p < 1.0$.

While the effects on total variability are quite compelling, the Wing-Kristofferson model was applied to ascertain the contribution of central and peripheral sources of variability to these effects. To verify that the model would be appropriate for these data, two basic predictions were assessed. First and most important, as predicted, the Lag 1 covariance was negative on 95.8% of the blocks (92 out of 96). This percentage is comparable to that observed with both healthy subjects (Helmuth & Ivry, in press; Ivry & Hazeltine, in press) and patients with cerebellar lesions (Ivry et al., 1988). Moreover, there was no consistent pattern in the covariance function for lags greater than 1 and this result was similar for unimanual and bimanual conditions. Helmuth and Ivry (1996) have found that the basic assumptions of the model hold during bimanual tapping with normal subjects.

Given these confirmations, the total variability was decomposed into estimates of central and peripheral components. Figure 2 presents the results averaged across the four subjects. The top panel shows the estimates for the central component for the four conditions. The corresponding estimates of the peripheral component are given in the bottom panel. As can be seen, only the estimate of the central component of variability was reduced during bimanual tapping, $F(1,3) = 14.54, p < 0.05$. During unimanual tapping, the estimates of central variability were 13.7 and 21.5 msec for the contralesional and ipsilesional hands, respectively. During bimanual tapping, the estimate for the unimpaired hand was reduced to 11.2 msec. A much larger reduction was observed for the impaired hand. Here, the estimate dropped to 14.4 msec. The bimanual reduction was 33% for the impaired hand. The Hand $\times$ Mode interaction, however, was not significant, $F(1,3) = 5.18, p = 0.11$.

In contrast to the effect of the tapping mode on the central variability estimates, the estimate of peripheral variability did not decrease during bimanual tapping. The estimate of the peripheral variability component was greater for the impaired hand (11.6 msec) in comparison to the unimpaired hand (9.5 msec), but this difference

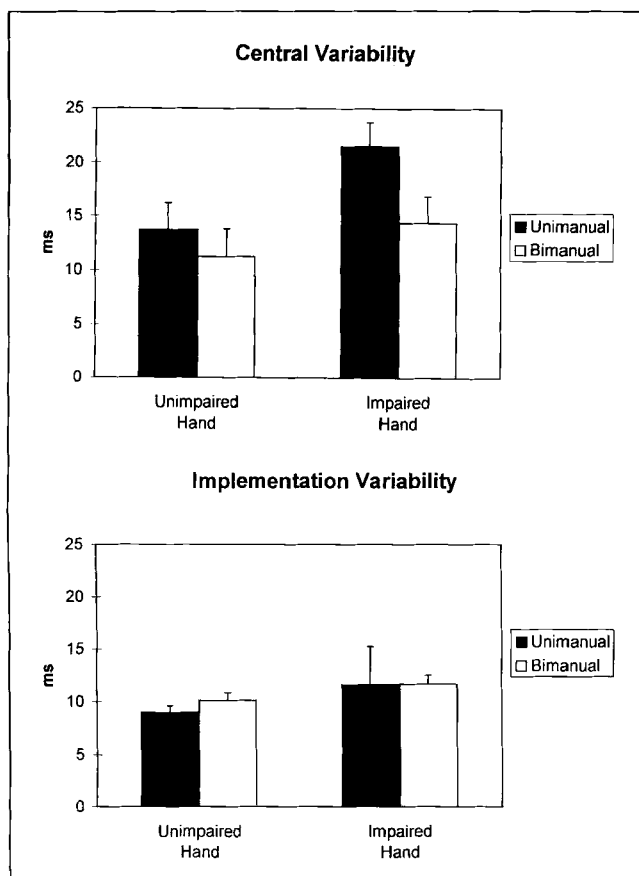


Figure 2. Central and implementation components of variability for all subjects. The bars indicate the standard errors of the means.

was not significant, $F(1,3) = 1.74, p > 0.25$. This difference was comparable during both unimanual and bimanual tapping.

To summarize, the group analyses reveal two novel findings. First, ipsilesional movements of patients with unilateral cerebellar lesions become temporally more consistent when concurrent movements are made with the contralesional hand. Second, the improvement is associated with reduced variability in processes linked to response planning rather than response implementation.

The four panels in Figure 3 present the estimates of the central component for each of the subjects individually. The effects of bimanual tapping on the central variability estimate are quite consistent. For PRI, DOM, and COT, there is a substantial reduction in this estimate for the ipsilesional hand during bimanual tapping. The effect is not as marked for KID. However, the central variability estimate for this subject when tapping with his impaired hand is lower on five of the six blocks during bimanual tapping in comparison to unimanual tapping.

In the experiment reported above, only the intervals

between successive responses were recorded by the computer. Thus, we could not assess any phase differences in the bimanual conditions. It seemed of interest to determine if there was a consistent phase difference between the two hands. For example, perhaps the unimpaired hand taps prior to the impaired hand and thus can "lead" the impaired hand.

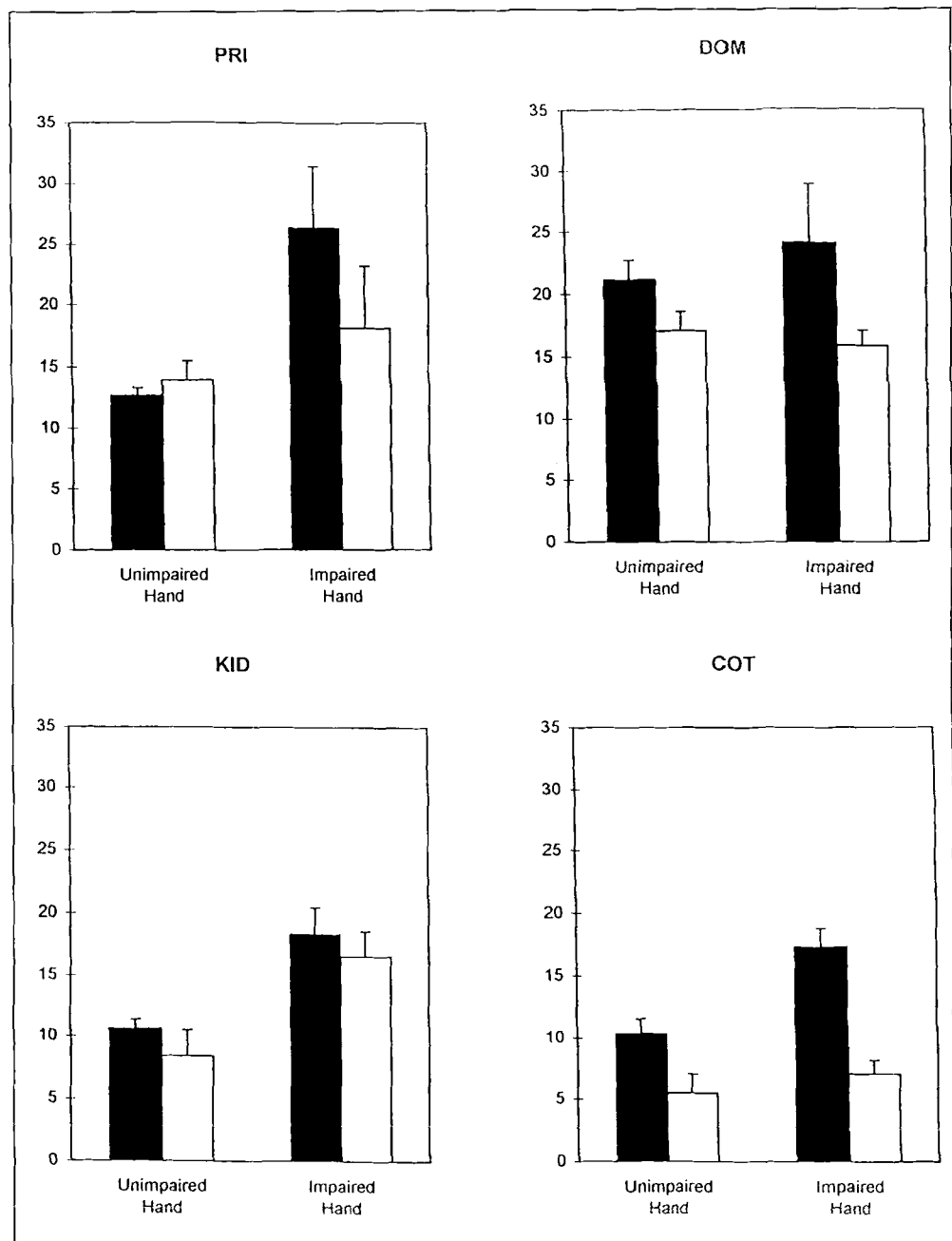
As a follow-up experiment, two of the subjects were tested on an additional session in which the actual times of each response were recorded. KID completed two more bimanual blocks and COT completed three additional blocks. In addition to the measures of within-hand variability, we also computed the between-hand phase difference for each bimanual response. The mean phase difference was calculated over the 30 unpaced intervals for each trial. The overall variability component estimates were similar to those reported above for these subjects. More importantly, the phase analysis did not indicate that one hand consistently led the other. For KID, the contralesional right hand led the left hand by an average of 11.4 msec (SD = 15.0 msec). For COT, the mean phase difference was 0.0 msec (SD = 5.8 msec). Neither of these values was significantly different from zero (sign test, $p > 0.05$). Thus, the bimanual reduction does not appear to be due to the unimpaired hand "leading" the impaired hand. For both subjects, the two responses appeared to be produced simultaneously.

A second follow-up experiment focused on the possible role of auditory feedback in producing the bimanual improvement. While the evidence suggests that feedback is minimal in this task (see Wing, 1980; Ivry & Keele, 1989), depression of the response keys does produce a sound. We wondered whether the impaired hand benefited because the subject could hear the more evenly spaced intervals produced by the unimpaired hand during bimanual tapping. To test the effect of auditory feedback, three of the subjects were tested on one or two additional sessions in which the pacing signal persisted through the entire trial. As in the basic experiment, subjects produced 45 intervals on each trial and the analysis was limited to the final 30 intervals. However, the computer tones continued to be played every 400 msec throughout the trial.

If enhanced auditory feedback were important, we would expect two results to emerge in this follow-up experiment. First, unimanual tapping with the impaired hand should be better with the pacing signal than without the signal. Second, the reduction in variability during bimanual tapping might disappear since the subject is provided with a perfect model of the target interval in both unimanual and bimanual conditions.

Neither prediction was supported. Including the pacing signal produced essentially no change in the overall variability scores. For these three subjects, the overall standard deviation of the interresponse intervals for the impaired hand during unimanual tapping was 25.9 msec

Figure 3. Central component of variability for individual subjects. Unimanual performance is shown in black and bimanual performance is shown in white. The bars indicate the standard error of the means.



in the basic experiment. This value actually increased slightly to 27.2 msec when tapping with a continuous pacing signal. Moreover, the reduction in variability for this hand during bimanual tapping was comparable for unpaced (3.5 msec) and paced (4.9 msec) tapping.

GENERAL DISCUSSION

It has been hypothesized that the cerebellum plays a critical role in regulating the temporal aspects of movement (Ivry & Keele, 1989; Ivry, 1993; Perrett et al., 1993).

One source of evidence for the timing hypothesis is that unilateral lesions lead to increased temporal variability when repetitive movements are produced by the ipsilesional hand. For patients with lesions of the lateral cerebellum or dentate nucleus, this increase is not linked to greater variability associated with response implementation (Ivry et al., 1988). A corollary of this interpretation is that there are separate timing mechanisms associated with those portions of the cerebellum contributing to ipsilesional and contralesional movements. That is, this structure does not operate as a single, unified timing

mechanism. Rather, different effectors (or tasks) rely on different regions within the cerebellum, even if these regions perform a similar computation related to timing.

In the current study, we focused on temporal interactions that might emerge when patients with unilateral lesions were required to make bimanual movements. The primary finding was that within-hand variability was reduced for movements produced by the impaired hand. Concurrent movements with the unimpaired hand led to improved performance on the affected side. The improvement does not appear to be the result of the unimpaired hand "leading" the impaired hand, nor is it the result of enhanced auditory feedback.

A possible account of the present results is that the patients were somehow able to rely on the intact cerebellar hemisphere during bimanual tapping. In other words, the bimanual condition allowed them to bypass an impaired timing mechanism in the lesioned hemisphere. While the current results are in accord with this hypothesis, there are two reasons to question this account. First, although the effect was not significant, three of the patients showed a trend suggesting that temporal variability in the unimpaired hand also was reduced during bimanual tapping. If the limiting factor in performance was the accuracy of an unimpaired timer, then there is no reason to expect bimanual performance to be better than unimanual performance.

Second, we have conducted similar experiments with healthy, college-aged subjects (Helmuth & Ivry, 1996). With these subjects, the comparison is between performance with the dominant and nondominant hands under either unimanual or bimanual conditions. For unimanual tapping, there is only a slight advantage for the dominant hand, and this difference is entirely attributed to the response implementation component (see also Sargent, Hellige, & Cherry, 1993). More importantly, both hands demonstrate a reliable reduction in overall variability under bimanual conditions (Helmuth & Ivry, 1996). As with the current findings with cerebellar patients, the reduction in temporal variability was attributed to reduced central variability. If a single timer took control in bimanual tapping, then this reduction should not be observed. Rather, at best, bimanual performance would be equal to the level of performance found with the more consistent of the two limbs. Given that a bimanual advantage is found for normal subjects and tends to occur for both the impaired and unimpaired hand in the patients, it seems unlikely that the improved performance for the patients is due to greater reliance on the nonlesioned half of the cerebellum.

An alternative hypothesis is that the reduced timing variability is an emergent property of constraints underlying temporal coupling in bimanual movements. From a variety of tasks, it is well established that the two hands are strongly coupled during bimanual movements (e.g., Franz, Zelaznik, & McCabe, 1991; Kelso & Scholz, 1985;

Kelso et al., 1979; Klapp, 1979). Temporal coupling in multilimb movements has been well described from a dynamic systems perspective (Kelso, 1984; Schoner & Kelso, 1988). In this form of modeling, each limb is conceptualized as an oscillatory system. For bimanual movements, these oscillators become coupled.

The focus of this literature has been on describing how the coupling produces certain between-hand interactions. For example, coupled oscillators are expected to be stable in a limited range of phase relations, a prediction that is well supported by experimental observations (Kelso, 1984; Schoner & Kelso, 1988). Less studied have been the effects of coupling on within-limb variability. Perhaps coupling two oscillators has the effect of making the unified output more stable than that of either oscillator in isolation. The coupled system may be less sensitive to perturbations, thus reducing deviations from its stable, limit cycle. Applied to the current situation, each limb could be viewed as an independent oscillator. The lesion would add instability to the oscillator and thus increase variability. Indeed, the movements of cerebellar patients have often been described as resembling those of an underdamped oscillatory system (e.g., Vilas & Hore, 1980). Coupling the oscillators as in bimanual movements might mitigate the effects of this underdamping.

While the preceding hypothesis seems to offer a useful description of how coupling might produce changes in variability, it remains unclear how this coupling is achieved. In developing a process model to account for the reduced temporal variability during bimanual movements, Helmuth and Ivry (1996) proposed that response commands to the periphery are constrained by a central bottleneck. This model assumes that there are separate control processes (including timing mechanisms) associated with different limbs, but the outputs from these processes are constrained by a common output gate. We postulate that there are separate timing signals associated with the movements of each hand, but the implementation of these commands is constrained to occur simultaneously. There are at least two possible advantages for having a common output gate. First, it could reduce the computational demands by making communication between central processes and movement more discrete. Second, it might be a means for ensuring that different limbs perform actions that are coordinated, or at least not incompatible.

How would a gating operation lead to reduced within-hand variability during bimanual movements? Suppose that on each trial, the appropriate time for the next movement is determined independently for each limb. However, due to the gating operation, these separate timing signals must be combined so that the commands to each limb are issued synchronously. As a simplest case, consider what happens if the two timing signals were averaged. This form of signal integration would lead to a

reduction in variability. For example, extreme values generated by one of the individual timers would be brought closer to the mean by the value generated by the other timer.¹ An averaging model of this sort is formally described by the statistics of a distribution formed by averaging independent samples taken from two distributions. If the distributions have identical means and variances, then the standard deviation of the new distribution will be reduced by the square root of two. Indeed, the bimanual advantage for healthy subjects closely approximates this predicted value (Helmuth & Ivry, 1996).

In the case of patients with unilateral cerebellar lesions, the two distributions are unequal. In this situation, the predicted change in variability for each distribution is dependent on the magnitude of the difference between the two distributions. If the difference is relatively small, then the simple averaging model would predict that both hands would show a reduction in variability during bimanual tapping. If the difference is relatively large, then the model would predict that performance with the more variable hand would improve during bimanual tapping, while performance with the less variable hand would become worse. This pattern of results is evident in the current data set. PRI, who had the largest difference on the unimanual blocks, was the only patient for whom performance with the unimpaired hand became more variable during bimanual tapping. For the other three patients, movements with both the impaired and unimpaired hand were more consistent when tapping with both hands.

The hypothesis of a common output gate provides an account of the observed reduction of within-hand variability during bimanual movements in both normal subjects and patients with unilateral cerebellar lesions. The validity of this hypothesis remains to be tested. Nonetheless, an important point to be emphasized is that the current results suggest a dissociation of processes involved in temporal regulation and those involved in temporal coupling. Unilateral cerebellar lesions produce an increase in temporal variability for ipsilateral movements. Despite this increase, bimanual movements in these patients are temporally coupled. The intact coupling has the effect of reducing the problems associated with the loss of temporal control.

METHOD

Subjects

Four patients were tested. Each of the patients had a focal, unilateral lesion of the cerebellum. The foci of the lesions were verified by either CT or MRI scans. Figure 4 contains photographs of the images from each patient in which the damage is most extensive. The extent of the lesions are sketched in Figure 5 on a set of templates

derived from postmortem sections through an intact cerebellum.

In addition, the patients received a neurological examination to assess the extent of cerebellar symptoms. None of the patients showed evidence of a loss of strength or muscular atrophy. Moreover, the patients showed minimal symptoms indicating cerebellar damage when using their contralesional limbs.

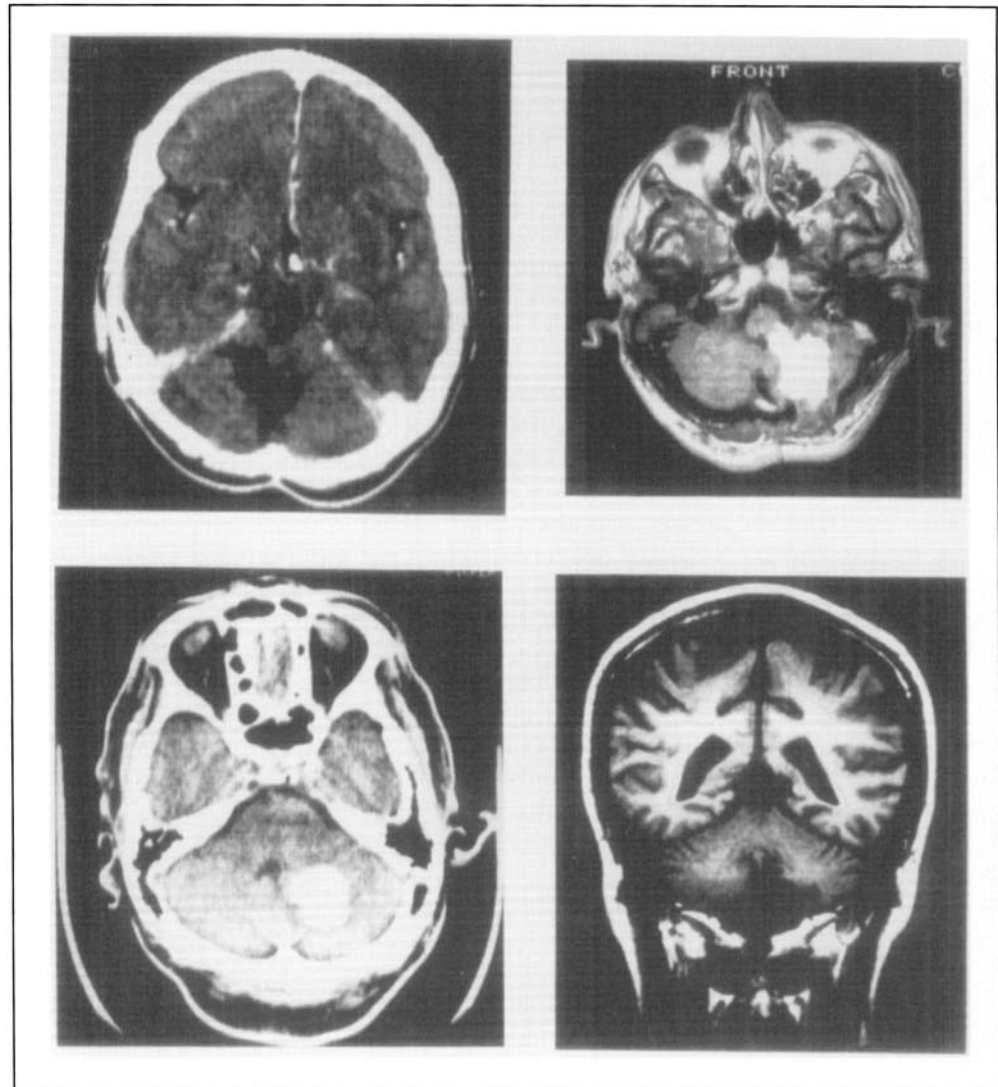
There were two main criteria for inclusion in this study. First, neuroimaging results had to provide evidence of focal, unilateral damage restricted to the cerebellum. Second, the patients were pretested to verify that their tapping variability was consistently larger in the ipsilesional hand in comparison to the contralesional hand. Ivry and Keele (1989; also Ivry et al., 1988) had found increased variability in tapping by the ipsilesional hand even in patients who appeared to be asymptomatic in a clinical examination. This observation was confirmed for one of the patients in the present study (Case 4).

The subjects were all right-handed. Healthy subjects show a small difference between the performance of their dominant and nondominant hands (Helmuth & Ivry, 1996; Sergent et al., 1993). However, we do not expect that handedness is of great relevance in the present study. First, handedness differences on the repetitive tapping task are associated with reduced response implementation variability and not with differences in timing variability (Helmuth & Ivry, 1996; Sergent et al., 1993). Second, the lesion was on the right side for one of the patients, yet her affected right hand was much more variable than her nondominant left hand.

Case 1, PRI, is a right-handed 51-year-old female who suffered a hemorrhage in the right cerebellum in 1984. The postoperative CT shows a large lesion extending into the posterior cerebellar hemisphere. Given that the lesion is evident in the image showing the fourth ventricle, it is likely that portions of the dentate nucleus are damaged (Angevine, Mancall, & Yakovlev, 1961). Although PRI has shown excellent recovery from the stroke, she continues to show persistent motor dysfunction in her ipsilesional hand and arm. Behavioral symptoms include hypermetria in pointing and dysdiadochokinesia during rapid wrist movements. A mild intentional tremor is also present.

Case 2, DOM, is a right-handed 52-year-old male who had a cerebellar tumor resected in 1990. The MRI scan shows a large mass of blood from postsurgical hemorrhage. This pool is primarily inferior, extending throughout the left cerebellum and midline regions, including the region around the dentate nucleus. Shortly after the surgery, DOM experienced severe balance problems and was unable to walk unassisted. These problems had subsided by the onset of testing, although he continues to adopt a moderately wide stance when walking. No evi-

Figure 4. Scans showing region of greatest extent of lesion for each subject. Top left: PRI; top right: DOM; bottom left: KID; bottom right: COT. Left and right sides are reversed so that the right hemisphere is shown on the left side, and vice versa.



dence of dysmetria or intentional tremor can be seen at present, although there is a nystagmus during smooth pursuit eye movements to the left. DOM has a history of alcoholism, although there is no evidence of alcohol-related cerebellar atrophy. Cortical scans reveal a small left hemisphere lesion in the white matter in the posterior frontal lobe. This lesion appears to be in the vicinity of the motor strip corresponding to the lower extremities. However, such lesions are typically asymptomatic and all of the symptoms presented by DOM are consistent with the cerebellar lesion.

Case 3, KID, is a right-handed 73-year-old male who suffered a stroke affecting the left cerebellar hemisphere in 1991. The noncontrast CT scan shows an extensive hemorrhage. The lesion appears to encompass the dentate nucleus, with relative sparing of the cerebellar cortex. At the time we began testing KID, he continued to show mild hypermetria, intentional tremor, and dysdiado-

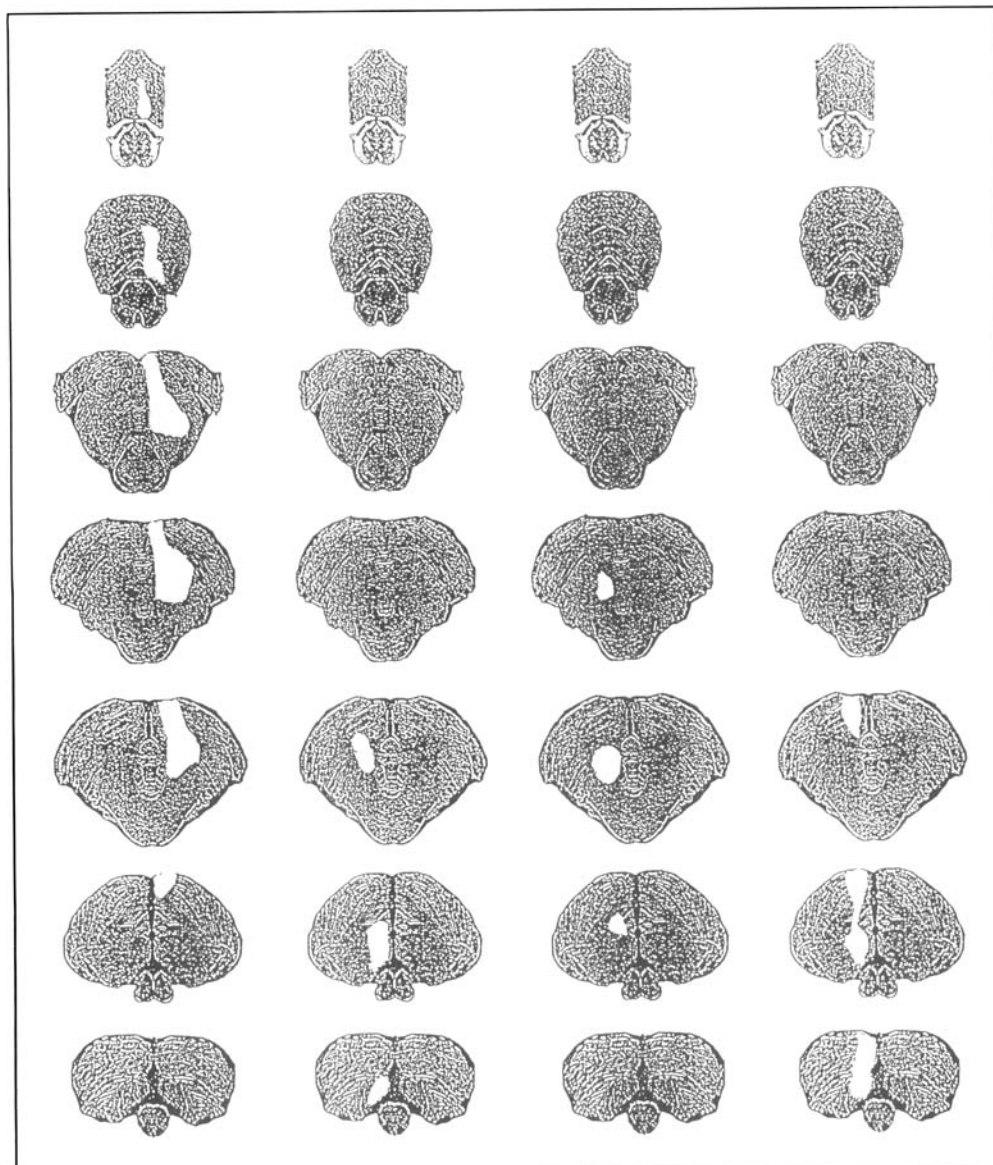
chokinesia when moving the ipsilesional hand. KID is also noticeably slow in making movements involving touching each finger to the thumb in succession.

Case 4, COT, is a right-handed 73-year-old male who suffered a stroke in the left cerebellum in October 1991. The MRI scans indicate that the lesion was the result of an infarction of the posterior inferior cerebellar artery and produced damage restricted to the inferior left cerebellum. The damage appears to be below the level of the dentate nucleus. In accord with this, COT presented minimal signs of cerebellar dysfunction when examined at the beginning of his first test session.

Procedure

All responses were made with flexion-extensions of the index fingers. The subjects were seated with their arms resting on a table, palms down. The response keys ($2 \times$

Figure 5. Lesion size and extent depicted for each subject on a standardized set of templates. From left to right: PRI, DOM, KID, and COT. A horizontal series of seven slices of the cerebellum is shown with an outline of the lesion in white. The side of the template matches the side of the actual lesion. From top to bottom, the templates run from most superior to most inferior and approximate the slices presented in Angevine et al., (1961), on pp. 81, 83, 87, 91, 95, 103, and 105, respectively. The dentate nucleus is most prominent in the fourth and fifth slices from the top.



10 cm) were mounted flush on the surface of a response board (20 × 30 cm). A distance of 6 cm separated the two keys used in the bimanual conditions. Approximately 25 g of force was required to activate a microswitch, located underneath each key. Changes in the state of the microswitch were detected by a desktop computer.

Each trial began with a series of 50 msec tones, presented at regular intervals of 400 msec. The subject was instructed to tap in rhythm with these tones and then to continue to tap at the same rate after the tones were discontinued. After the subject had produced 13 paced intervals, the tones terminated and the subject tapped for an additional 32 responses. A tone signaled the end of the trial. On unimanual trials, the subject tapped with either the right or left index finger alone. On bimanual

trials, both fingers were used. For these trials, the subjects were instructed to tap with both fingers at the same time.

At the end of each trial, feedback was displayed on the monitor indicating the mean and standard deviation of the interresponse intervals during the paced and unpaced phases. The last 10 paced intervals and 30 unpaced intervals were used in these calculations. On bimanual trials, feedback was given for both hands separately.

Design

The subjects completed a total of 18 blocks, six with the left hand, six with the right hand, and six bimanually. A

block of trials was composed of six error-free trials. Trials were excluded (i.e., counted as an error) when one of the 30 unpaced intervals was less than 200 msec or greater than 600 msec. Intervals less than 200 msec usually indicate tremorous responses or bounces on the response key. Intervals longer than 600 msec generally occur when the subject fails to generate sufficient force to activate the response key or stops tapping in the middle of the trial. Excluded trials were repeated. However, a block was terminated if six rejected trials were recorded. In these blocks, the number of error-free trials was less than six.

The blocks of trials were run over multiple sessions. Across sessions, the order of conditions (left, right, bimanual) was approximately counterbalanced. For some sessions, subjects completed a single block in the left hand, right hand, and bimanual conditions. In other sessions, each condition was tested twice. In these sessions, a different order was used for each triplet. Each block lasted approximately 7 mins. The data were collected over a 2-year period.

Data Analysis

Only the tapping data for the intervals performed without the tones (unpaced portion) were included in the analyses. The mean of the interresponse intervals indicates how well the subjects were able to maintain the target pace.

The primary focus in this study was a comparison of within-hand consistency in the unimanual and bimanual conditions. To obtain the standard deviation of the interresponse intervals, the raw data were fitted by linear regression to a trend line and the deviation from this trend line was calculated. This transformation eliminates variability due to constant drift in the timing process (Keele, Pokorny, Corcos, & Ivry, 1985; Ivry et al., 1988; Wing & Kristofferson, 1973). The standard deviation and component estimates are minimally affected by this transformation.

The overall standard deviation scores were decomposed into estimates of central and peripheral variability by the Wing-Kristofferson (1973) model. The basic model assumes that there are two processes involved in repetitive timed behavior: central timekeeping processes, which determine when the movement should occur, and a peripheral implementation system, which executes the response. Each component is represented as a random variable with normal variance. Because the model assumes independence of these processes, total variability of the interresponse intervals (IRI) is the summed variability of these two processes. Thus, the duration of each IRI is represented as the sum of the central timekeeper interval plus the difference between the delays due to motor implementation associated with the initiation and termination of each interval, j . Formally,

$$I_j = C_j + MD_j - MD_j - 1 \quad (1)$$

where I , C , and MD represent duration of the total IRI, timekeeper interval, and motor implementation delays, respectively. By the independence assumption, the total variance can be described as

$$\text{var } I = \text{var } C + 2 (\text{var } MD) \quad (2)$$

The total variance ($\text{var } I$) can be directly calculated from the data. To obtain estimates of the relative contributions of the two components, an estimate must be made of one of the components. The other can then be obtained by subtraction. Wing and Kristofferson (1973) propose that an estimate of the motor delay variance ($\text{var } MD$) can be made given two assumptions. The first is that successive responses are generated in an open-loop mode of control. That is, subjects do not use feedback from each response to influence the timing of the next response. Second, successive clock times and implementation delays are assumed to be independent samples from their respective distributions. From these assumptions, it can be shown that an estimate of the motor delay variance ($\text{var } MD$) is given by the covariance function between successive intervals, or Lag 1 [$\text{Cov}(n, n-1)$]. An estimate of the central component is then made by inserting the observed and estimated terms in Eq. (1) and performing the simple algebraic manipulations. A detailed description of the underlying logic is given in Ivry et al. (1988).

The various assumptions of the model have received experimental support in a variety of studies with healthy (Ivry & Hazeltine, 1996; Wing & Kristofferson, 1973; Wing, 1980) and neurologically impaired subjects (Ivry & Keele, 1989). For example, the covariance function is almost always negative at lag 1 and not significantly different from zero at higher lags (but see Wing, 1977). Furthermore, the slope of the function describing variance of the timekeeper process changed with the duration of the base interval, whereas variance associated with the motor implementation delay remained constant (Ivry & Hazeltine, 1996; Wing, 1980).

In the present study, the covariance function was calculated for each trial and averaged over the six trials that constituted a block. The total variance for that block was then obtained from the Lag 0 (auto)covariance function. Estimates of the contributions associated with response implementation and central control processes were then obtained for that block according to the procedure described above.

Acknowledgments

We are grateful to Robert Knight and Robert Rafal for their assistance in evaluating the patients and neuroimaging data. Support for this research was provided by NIH Grant NS30256 to the second author. The first author was supported by NIH postdoctoral fellowship NS09318.

Note

1. To provide a concrete example, consider a case where the target interval is 400 msec and the two clocks generate signals indicating responses should occur at 340 and 410 msec, respectively. If the output of the gate occurred at the average of these two signals, then the response would occur at 375 msec. For this particular example, the error from the less accurate timer would be mitigated while the error from the more accurate timer would be increased. Over a series of intervals, the variability associated with each mechanism would be reduced. It may seem paradoxical to propose that a temporal average could be computed prior to the occurrence of the latter signal. However, Helmuth and Ivry (1996) propose a resolution to this paradox by treating the timing signals as continuous variables rather than discrete events.

REFERENCES

- Angevine, J. B., Mancall, E. L., & Yakovlev, P. I. (1961). *The human cerebellum: An atlas of gross topography in serial sections*. Boston: Little, Brown.
- Buonomano, D. V., & Mauk, M. D. (1994). Neural network model of the cerebellum: Temporal discrimination and the timing of motor responses. *Neural Computation*, 6, 38-55.
- Chang, P., & Hammond, G. R. (1987). Mutual interactions between speech and finger movements. *Journal of Motor Behavior*, 19, 165-174.
- Delcomyn, F. (1980). Neuronal basis of rhythmic behavior in animals. *Science*, 210, 492-498.
- Desmond, J. E., & Moore, J. W. (1988). Adaptive timing in neural networks: The conditioned response. *Biological Cybernetics*, 58, 405-415.
- Dichgans, J., & Diener, H. (1984). Clinical evidence for functional compartmentalization of the cerebellum. In J. Bloedel, J. Dichgans, & W. Precht (Eds.), *Cerebellar functions*. Berlin: Springer-Verlag.
- Franz, E. A., Zelaznik, H. N., & McCabe, G. (1991). Spatial topological constraints in a bimanual task. *Acta Psychologica*, 77, 137-151.
- Griffner, S. (1975). Locomotion in vertebrates: Central mechanisms and reflex interaction. *Physiological Review*, 55, 247-304.
- Grossberg, S., & Schmajuk, N. (1989). Neural dynamics of adaptive timing and temporal discrimination during associative learning. *Neural Networks*, 2, 79-102.
- Haken, H., Kelso, J. A. S., & Bunz, H. (1985). A theoretical model of phase transitions in human hand movements. *Biological Cybernetics*, 51, 347-356.
- Hallett, M., Shahani, B., & Young, R. (1975). EMG analysis of patients with cerebellar deficits. *Journal of Neurology, Neurosurgery, and Psychiatry*, 38, 1163-1169.
- Helmuth, L. L., & Ivry, R. B. (1996). When two hands are better than one: Reduced timing variability during bimanual movements. *Journal of Experimental Psychology: Human Perception and Performance* (in press).
- Ivry, R. B. (1993). Cerebellar involvement in the explicit representation of temporal information. In P. Tallal (Ed.), *Temporal information processing in the nervous system*. Annals of New York Academy of Sciences, 682, 214-230.
- Ivry, R., & Corcos, D. (1993). Slicing the variability pie: Component analysis of coordination and motor dysfunction. In K. Newell & D. Corcos (Eds.), *Variability and Motor Control* (pp. 415-447).
- Ivry, R. B., & Diener, H. C. (1991). Impaired velocity perception in patients with lesions of the cerebellum. *Journal of Cognitive Neuroscience*, 3(4), 355-366.
- Ivry, R. B., & Hazeltine, R. E. (1995). The perception and production of temporal intervals across a range of durations: Evidence for a common timing mechanism. *Journal of Experimental Psychology: Human Perception and Performance* 21, pp. 1-12.
- Ivry, R., & Keele, S. (1989). Timing functions of the cerebellum. *Journal of Cognitive Neuroscience*, 1, 136-152.
- Ivry, R., Keele, S., & Diener, H. C. (1988). Dissociation of the lateral and medial cerebellum in movement timing and movement execution. *Experimental Brain Research*, 73, 157-180.
- Jagacinsky, R. J., Marshburn, E. A., Klapp, S. T., & Jones, M. R. (1988). Tests of parallel versus integrated structures in polyrhythmic tapping. *Journal of Motor Behavior*, 20, 46-442.
- Keele, S., Pokorny, R., Corcos, D., & Ivry, R. (1985). Do perception and motor production share common timing mechanisms: A correlational analysis. *Acta Psychologica*, 60, 173-191.
- Kelso, J. A. S. (1984). Phase transitions in and critical behavior in human bimanual coordination. *American Journal of Physiology*, 15, 1000-1004.
- Kelso, J. A. S., & Scholz, J. P. (1985). Cooperative phenomena in biological motion. In H. Haken (Ed.), *Complex Systems: Operational approaches in neurobiology, physics and computers* (pp. 124-149). Berlin: Springer.
- Kelso, J. A. S., Southard, D. L., & Goodman, D. (1979). On the coordination of two-handed movements. *Journal of Experimental Psychology: Human Perception and Performance*, 5, 229-238.
- Klapp, S. T. (1979). Doing two things at once: The role of temporal compatibility. *Memory and Cognition*, 7, 375-381.
- Klapp, S. T. (1981). Temporal compatibility in dual motor tasks II: Simultaneous articulation and hand movements. *Memory and Cognition*, 9, 398-401.
- McCormick, D. A., & Thompson, R. F. (1984). Neuronal responses of the rabbit cerebellum during acquisition and performance of a classically conditioned nictitating membrane-eyelid response. *The Journal of Neuroscience*, 4(11), 2811-2822.
- Pellionisz, A., & Llinas, R. (1982). Space-time representation in the brain. The cerebellum as a predictive space-time metric tensor. *Neuroscience*, 7, 2949-2970.
- Perrett, S. P., Ruiz, B. P., & Mauk, M. D. (1993). Cerebellar cortex lesions disrupt learning-dependent timing of conditioned eyelid responses. *The Journal of Neuroscience*, 13(4), 1708-1713.
- Schoner, G., & Kelso, J. A. S. (1988). Dynamic pattern generation in behavioral and neural systems. *Science*, 239, 1513-1520.
- Sergent, V., Hellige, J. B., & Cherry, B. (1993). Effects of responding hand and concurrent verbal processing on time-keeping and motor-implementation processes. *Brain and Cognition*, 23, 243-262.
- Shaffer, L. H. (1981). Analyzing piano performance. A study of concert pianists. In G. E. Stelmach & J. Requin (Eds.), *Tutorials in motor behavior* (pp. 443-454). Amsterdam: North-Holland.
- Vilis, T., & Hore, J. (1980). Central neural mechanisms contributing to cerebellar tremor produced by limb perturbations. *Journal of Neurophysiology*, 43, 279-291.
- Wing, A. M. (1977). Effects of type of movement on the tem-

- poral precision of response sequences. *British Journal of Mathematics and Statistics in Psychology*, 30, 60-72.
- Wing, A. M. (1980). The long and short of timing in response sequences. In G. E. Stelmach & J. Requin (Eds.), *Tutorials in Motor Behavior*. Amsterdam: North-Holland.
- Wing, A. M., & Kristofferson, A. B. (1973). Response delays and the timing of discrete motor responses. *Perception and Psychophysics*, 14, 5-12.
- Yamanishi, J., Kawato, M., & Suzuki, R. (1980). Two coupled oscillators as a model for the coordinated finger tapping by both hands. *Biological Cybernetics*, 37, 219-225.
- Zanone, P. G., & Kelso, J. A. S. (1992). The evolution of behavioral attractors with learning: Nonequilibrium phase transitions. *Journal of Experimental Psychology: Human Perception and Performance*, 18, 403-421.