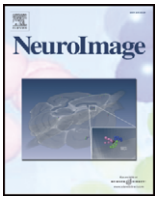
NeuroImage 42 (2008) 1295–1304

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg



Asymmetric control mechanisms of bimanual coordination: An application of directed connectivity analysis to kinematic and functional MRI data

Yohko Maki [a,b], Kin Foon Kevin Wong [c,d], Motoaki Sugiura [a,b], Tohru Ozaki [c,d], Norihiro Sadato [a,b,d,*]

[a] *Department of Physiological Sciences, The Graduate University for Advanced Studies (Sokendai), Kanagawa, Japan*
[b] *National Institute for Physiological Sciences, Okazaki, Japan*
[c] *Institute of Statistical Mathematics, Tokyo, Japan*
[d] *Japan Science and Technology Corporation (JST)/Research Institute of Science and Technology for Society (RISTEX), Kawaguchi, Japan*

ARTICLE INFO

Article history:
Received 17 February 2008
Revised 23 June 2008
Accepted 29 June 2008
Available online 16 July 2008

ABSTRACT

Mirror-symmetrical bimanual movement is more stable than parallel bimanual movement. This is well established at the kinematic level. We used functional MRI (fMRI) to evaluate the neural substrates of the stability of mirror-symmetrical bimanual movement. Right-handed participants (n=17) rotated disks with their index fingers bimanually, both in mirror-symmetrical and asymmetrical parallel modes. We applied the Akaike causality model to both kinematic and fMRI time-series data. We hypothesized that kinematic stability is represented by the extent of neural "cross-talk": as the fraction of signals that are common to controlling both hands increases, the stability also increases. The standard deviation of the phase difference for the mirror mode was significantly smaller than that for the parallel mode, confirming that the former was more stable. We used the noise-contribution ratio (NCR), which was computed using a multivariate autoregressive model with latent variables, as a direct measure of the cross-talk between both the two hands and the bilateral primary motor cortices (M1s). The mode-by-direction interaction of the NCR was significant in both the kinematic and fMRI data. Furthermore, in both sets of data, the NCR from the right hand (left M1) to the left (right M1) was more prominent than vice versa during the mirror-symmetrical mode, whereas no difference was observed during parallel movement or rest. The asymmetric interhemispheric interaction from the left M1 to the right M1 during symmetric bimanual movement might represent cortical-level cross-talk, which contributes to the stability of symmetric bimanual movements.

Introduction

Bimanual coordination in the mirror-symmetrical mode, in which homologous muscles are active simultaneously, is more stable than in the parallel mode, in which homologous muscles are engaged in an alternating fashion (Swinnen et al., 1997). When a subject performs a cyclical movement in the parallel mode, increasing the movement frequency ultimately results in a phase transition towards the mirror-symmetrical mode, but the opposite transition does not occur (Kelso, 1984). This phenomenon was first formalized theoretically by dynamic-systems theory at the behavioral level (Haken et al., 1985; Schöner and Kelso, 1988). Furthermore, the reversal in direction at the phase transition was mainly associated with the non-dominant hand (Walter and Swinnen, 1992; Byblow et al., 1994, 1998, 2000; Sherwood, 1994; Semjen et al., 1995; Treffner and Turvey, 1995; Rogers et al., 1998; Garry and Franks, 2000). These kinematic data suggest that the left hemisphere is dominant for bimanual movement.

To associate the process of bimanual coordination with the neural structures that control hand movements (de Oliveira, 2002), the concepts of inter-manual and neural cross-talk (Marteniuk and MacKenzie, 1980) have been introduced. Interactions between the movements of the two hands (inter-manual cross-talk) are assumed to result from neural cross-talk at multiple levels between the signals controlling the two limbs. The lowest level of cross-talk supposedly occurs downstream from the specification of movement parameters, possibly through the ipsilateral corticospinal tract (Cattaert et al., 1999), as each effector receives signals from both contralateral and ipsilateral descending pathways. The mirror-symmetrical condition requires the activation of homologous muscles, and so the signals of both pathways are always congruent. By contrast, the parallel condition requires non-homologous muscles to be activated, and so conflict between crossed and uncrossed cortical pathways might arise (cross-talk). This is supported by the findings of Kagerer et al. (2003), who reported that participants in whom transcranial magnetic stimulation (TMS) elicited distal ipsilateral motor-evoked potentials exhibited higher variability during a bimanual parallel circling task than participants whose ipsilateral pathways could not be activated transcranially. This suggests that the common signal sent to both effectors through the contralateral and ipsilateral pathways enhanced

---

[*] Corresponding author. Section of Cerebral Integration, Department of Cerebral Research, National Institute for Physiological Sciences, Myodaiji, Okazaki, Aichi, 444-8585 Japan. Fax: +81 564 52 7786.
E-mail address: sadato@nips.ac.jp (N. Sadato).

1053-8119/$ – see front matter
doi:10.1016/j.neuroimage.2008.06.045

the stability of mirror-symmetrical movement as compared to parallel movement, resulting in the increased variability during parallel movement (Cattaert et al., 1999).

Cross-talk might also occur at a higher level through interhemispheric interaction (Kennerley et al., 2002). Kennerley et al. (2002) reported that callosotomy patients exhibited a lack of temporal coupling during continuous circle drawing, with the two hands oscillating at non-identical frequencies. They concluded that synchronization between the hands depends on interhemispheric transmission across the corpus callosum.

Several neuroimaging studies support the concept that interhemispheric interaction exists during the phase transition. Meyer-Lindenberg et al. (2002) demonstrated neuronal dynamics conforming to the predictions made by the non-linear system theory. Using positron-emission tomography (PET), they depicted the cortical regions related to the extent of behavioral instability, assuming that neuronal activity in these “unstable” areas increases as the frequency of the movement increases. Within these areas, they found that minor disruption by double-pulse TMS to the right dorsal premotor cortex (PMd) evoked large-scale phase transitions in participants' performance. Meyer-Lindenberg et al. (2002) concluded that an increase in behavioral instability corresponds to increasing neural instability represented in the right PMd.

Using event-related functional MRI (fMRI), Aramaki et al. (2006a) depicted the transition-related activity in multiple right-lateralized parieto-premotor regions. These areas were different from the regions activated by bimanual movement execution. Aramaki et al. (2006a) concluded that at the phase transition, the cortical neural cross-talk occurs in distributed networks upstream of the primary motor cortex through asymmetric interhemispheric interaction.

These studies imply that there is some “default” setting by which the two hands are linked together to produce identical motor output, and that an additional mechanism is required to uncouple the hands in order to generate different movements (Evans and Baker, 2003). However, the neural substrates of the default linking that makes bimanual mirror-symmetrical movement so stable have remained unknown, particularly at the cortical level.

The purpose of the present study was to delineate the cortical cross-talk that stabilizes mirror-symmetrical movement. Using fMRI, we compared the kinematic relationship between both hands and the neural relationship between the primary motor cortices of both hemispheres during mirror-symmetrical and parallel bimanual cyclical movements. We focused on cross-talk at the level of the bilateral primary motor cortices (M1s), where movement parameters are specified and transmitted to the effectors.

We used a continuous circle-drawing task instead of a discrete movement task, such as tapping, for mainly technical reasons: continuous kinematic data are more easily handled by the multivariate autoregressive (MAR) model of time-series analysis. Previously, it was supposed that the neural substrates for continuous bimanual coordination might differ from those for discrete movements (Kennerley et al., 2002; Spencer et al., 2003). In split-brain patients, bimanual coordination during discrete tasks was well preserved (Preilowski, 1972; Franz et al., 1996; Ivry and Hazeltine, 1999), whereas coordination was impaired during a continuous bimanual task (Kennerley et al., 2002). However, this does not necessarily restrict the transcallosal neural cross-talk to the continuous cyclical movements (Bonzano et al., 2008).

Previous kinematic studies (Stucchi and Viviani, 1993; Semjen et al., 1995; Treffner and Turvey, 1995, 1996; Swinnen et al., 1996; Byblow et al., 2000; Kennerley et al., 2002) have indicated right-hand dominance. Previous clinical and imaging studies have shown that the left hemisphere is dominant for the representation of motor skills (Sirigu et al., 1996; Haaland et al., 2000), including bimanual coordination (Serrien et al., 2003). Accordingly, we predicted that asymmetric cross-talk from the left M1 to the right M1 is more prominent than vice versa.

We further hypothesized that this asymmetric cortical cross-talk is more prominent during mirror-symmetrical movement than during asymmetric parallel movement. During the mirror-symmetrical mode, the movement command from the dominant left hemisphere would facilitate, or at least not negatively influence, symmetric movements. In this sense, the cross-talk at the cortical level during mirror movement can be understood as a gating of the signal from one hemisphere to its homonymous counterpart, in order to ensure shared neural control of the movements of both limbs in which homologous muscles are to be activated. During the asymmetric parallel mode, by contrast, there would be ongoing interference due to conflicting information. Parallel asymmetric movement usually requires a greater workload than mirror-symmetrical movement, which is represented as more prominent activation in the supplementary motor area (SMA) and the right PMd (Sadato et al., 1997). Double-pulse TMS of the right PMd caused a phase shift from the parallel mode to the mirror mode (Meyer-Lindenberg et al., 2002). Thus, this additional workload was interpreted as the conversion of the motor program or the suppression of conflicting information issued in the left hemisphere to its right counterpart, and hence no gating occurred during the parallel mode.

As signal gating might not be depicted by the increment of the neural activity, we adopted statistical time-series modeling. The MAR model represents a general statistical time-series model that propagates information from the past to the future. The Akaike noise-contribution ratio (NCR; Akaike, 1968) quantifies the portion of the power-spectral density of an observed variable from the independent noise of the MAR, which becomes a measure of causality among variables. It allows interpretation of the causality from one hand to the other, or from the motor cortex of one hemisphere to the other. Thus, the extent of cross-talk can be quantified by the causality that is represented by the NCR. Unlike the mathematical formulation of the dynamic-systems model that is usually employed to deal with the relative phase via a differential equation in order to evaluate the stability of the system (Haken et al., 1985; Schöner and Kelso, 1988; Meyer-Lindenberg et al., 2002; Kennerley et al., 2002), which cannot be directly applied to neuroimaging datasets, the MAR can be applied to both kinematic data and neural activities. According to our *a-priori* hypothesis, the gating might be represented as the asymmetric NCR from the left M1 to the right M1, which, in turn, brings the asymmetric NCR from the right hand to the left hand during mirror-symmetrical movement more prominently than during parallel movement.

Materials and methods

Participants

In total, 19 subjects participated in the fMRI study. None of the subjects had a history of psychiatric or neurological illness. The protocol was approved by the Ethical Committee of the National Institute of Physiological Sciences, Japan. All subjects gave their written informed consent for participation in the study. During the experiment, we stopped the testing of one subject due to stomach pain, and one subject fell asleep; the data from these two subjects were excluded from the analysis. The 17 participants included in the analysis comprised eight men and nine women, aged between 20 and 32 years, all of whom were strongly right-handed according to the Edinburgh Handedness Inventory (mean score ± standard deviation [SD] = 0.956 ± 0.072; Oldfield, 1971).

Subject setup

The subjects lay supine in a 3.0 T MR scanner (Allegra; Siemens, Erlangen, Germany). Their elbows and wrists were slightly flexed and relaxed so that each hand could be placed on the non-ferromagnetic frames set over the participant's body. On the frame, two discs were placed on both sides of the subject (Fig. 1). Each disc was attached to the