General Discussion

A review of the papers

The four papers presented provide a solid introduction to the existence of and the implications of the “bimanual related” effect. They demonstrate that many neurons in both primary motor cortex (MI) and the supplementary motor area (SMA) show a strong “bimanual related” effect, and that this effect can exist even when the movements are very similar, that it is not correlated with a “bimanual related” effect in the movements, and that it is not generally related to the trial-by-trial variations in the movements. Further, they show that the activity in bimanual movements is not a linear combination of activity in unimanual movements.

The analysis of the LFP extends the discussion of the “bimanual related” effect to another neural signal providing information about neural processing complementary to the information in the single unit activity. Activity in the LFP during bimanual movements is almost always greater than activity in the LFP during unimanual movements, which suggests that there is indeed a difference in cortical processing of bimanual movements going beyond differences in kinematics or dynamics of the movements. One explanation for the increased LFP activation is that LFP reflects a summation of activity from both hemispheres and that this sum is greater during bimanual movements because of reduced ipsilateral activation during unimanual movements. The fact that this increase appears equally in MI and in SMA suggests that MI is involved in processing information from both hemispheres just as much as SMA.

However, analysis of the LFP, and particularly of the relationship between single-unit activity and LFP, reveals clear-cut differences between MI and SMA that are not seen in the single unit activity. First of all, a contralateral preference during unimanual movements can be seen in the LFP in MI that is clearly stronger than the contralateral preference in SMA. In the single units the contralateral preference of the two areas is similar. Another difference between the two areas is in the correlation of the strength of single unit activity recorded by an electrode and the strength of LFP activation recorded by that same electrode. It seems that the LFP in SMA (particularly the late peaks) is more directly related to the single unit activity than the LFP in MI. This may reflect a greater influence of recurrent collateral activation in SMA than in MI, but this is mere speculation without some anatomical or physiological support. In any case, most studies comparing the physiology of SMA and MI find that the two areas are very similar, so there is significance to any difference which can be found in their activity.

The review paper provides a discussion of the significance of the "bimanual related" effect to our understanding of bimanual control. The review particularly questions the cortical basis of interlimb coupling, suggesting that there may be two different kinds of "bimanual coordination" – spatial and temporal – which are mediated by different mechanisms. In this sense, the existence of the "bimanual related" effect is seen to argue for the involvement of cortex in mechanisms of bimanual coordination. The review also discusses some of the directions which our research has developed since the discovery of the "bimanual related" effect. One direction is the extension of population vectors to bimanual movements. This analysis shows that it is indeed possible to extend the notion of a population vectors to situations where the hands move in different directions, a fact which was surprising to me. Indeed, the population vector analysis goes one step further by suggesting the possibility that we may be able to quantify the extent of coupling and decoupling of cortical activity in producing bimanual movements by analyzing the coupling and decoupling of the population vectors.

Finally, the review paper discusses the issue that (as mentioned in the General Introduction) originally brought me to the study of cortical involvement in bimanual movements. This is the issue of the functional role of neuronal interactions. The review mentions preliminary results in which we have found that SMA lesion leads to increased interhemispheric correlations. Four months after the lesion, correlation levels returned to their normal levels. As discussed in the review, this could result from pathological lack of interhemispheric inhibition or compensatory increase in interhemispheric collaboration. Thus the result cannot speak directly to the question of the nature of interhemispheric interaction discussed in the General Introduction without further research. However, it does suggest that the correlations do play some role in interhemispheric interaction.

Addressing the larger issues

The "bimanual related" effect is at the heart of all the results presented in this doctoral thesis. However, I have yet to relate the existence of the "bimanual related" effect to the larger issues raised in the General Introduction. In the introduction, I motivated the study of the cortical physiology of bimanual movements primarily by relating it to two larger questions: the first was the question of the functional relevance of neuronal interactions in binding together complex behaviors and the second was the question of whether motor control was best studied by studying the whole movement or by trying to study component pieces of the movement. The very existence of the "bimanual related" effect makes a fairly clear statement regarding the second question. That is, it seems that both in the psychophysics – as shown in the review paper – and in the physiology of the motor cortex – as shown by the "bimanual related" effect – there are aspects of bimanual movements which transcend the combination of two unimanual movements. Indeed, the literature leaves one with the impression that a bimanual movement is a single movement, controlled as a whole in many respects.

But where does this single bimanual movement come from? One of the most interesting directions of future research is into the parallel between the development of the "bimanual related" effect and the motor learning associated with the monkeys' ability to perform the bimanual task. One reasonable prediction is that until the monkey effectively learns to generate a coordinated bimanual movement, the motor cortical activity (either in MI or in both MI and SMA) will simply be the same during the bimanual trials as it is during unimanual trials. Thus, the research presented here leads us ultimately to the understanding that activity of neurons in our motor system must reflect the totality of movements we are capable of performing, and that this totality varies greatly from one individual to another and is plastic as we learn new skills and practice old ones. This speculation is supported by results showing widespread plasticity of motor cortex during motor learning (Classen et al., 1998;Karni et al., 1995;Liepert et al., 1999;Pascual et al., 1994;Rioult et al., 1998). If, indeed, the "coding" of movements in motor cortex varies greatly between individuals and is heavily influenced by the history of motor learning of each individual, this could partially explain the fact that different laboratories seem to find the motor cortex coding different aspects of the movement. It is possible that the training which monkeys undergo in learning the different tasks has allowed their motor cortex to specialize its coding for those specific aspects measured by each task. Of course, this raises questions regarding how this specialization might be accomplished and how it would be reflected in the activity of single cells. This is an area of research in which, to my knowledge, no work has been done.

The connection between the research presented here and the functional significance of neuronal interactions is less direct. While the finding of changes in interhemispheric correlations in MI following SMA lesion is promising, it is only the beginning of research to characterize interhemispheric correlations in bimanual movements. The analysis of the LFP is also encouraging in suggesting strongly that the hemispheres are influencing each other in producing the "bimanual related" effect. This needs to be tested more rigorously using techniques such as callosotomy or reversible inactivation which can show more directly how the activity of one hemisphere is affecting the activity of the other. In a sense, this doctoral thesis has only accomplished the preliminary work necessary to address the question I originally intended to answer. Of course, it is possible that in trying to take the next step towards addressing the question, there will be another finding which is so compelling that it will be impossible to proceed without first pursuing it more fully. This is not necessarily a failure of the research program, but rather a serendipitous success. While this research failed to address its original goal, it succeeded in shedding light on a number of issues, some of which are of fundamental importance to our understanding of how we move and to our understanding of how the cortex works.

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