

7. Top-down control over the motor cortex

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Goal-directed behavior requires the selection of task-relevant information and the suppression of task-irrelevant noise. A prominent element of most current models of cognitive control is that this is mediated by higher-level control signals that bias the state of lower-level neural processing^{14-15,31}. The prefrontal cortex is commonly seen as the origin of these control signals^{31,43}. In the context of action selection, top-down control is particularly needed during situations of response conflict, where a predominant response needs to be inhibited in favour of an alternative response or no response at all. In this chapter, we discuss recent advances in the study of top-down control over motor cortex during action selection under conflict and action inhibition. We discuss the network of brain areas commonly indicated as having a role in the top-down control over the motor cortex and discuss the potential roles of some of these brain areas within the larger network.

Tasks evoking response conflict or response inhibition tend to consistently activate a large cortical and subcortical network. In one of the first imaging studies looking at action inhibition, Garavan and colleagues²¹ reported that inhibition recruits a mostly right lateralized network of regions in addition to the normal action selection network. This network (Fig. 7.1) involves mostly frontal areas, including the pre-supplementary motor area (pre-SMA) and right inferior frontal gyrus (rIFG), but also subcortical structures, of which the subthalamic nucleus (STN) has recently received particular attention. In addition to this well-described network, parietal regions, particularly the right inferior parietal lobule, are also often found to be important in these tasks^{21,42}. This network or parts of it is active in situations of response conflict⁴⁵, action inhibition², action reprogramming²⁹, and task switching⁴¹. In the course of this

chapter, we will focus specifically on two nodes of this network that have been implicated in top-down control over the motor cortex, the pre-SMA and the right IFG.

[Figure 7.1 about here]

This chapter is structured as follows. First, we will discuss some evidence that there is indeed such a thing as top-down control over the motor cortex and that the pre-SMA and rIFG have some causal role in mediating this control. Then, we will discuss how this control is exerted by looking at interactions between the frontal lobes and the motor cortex. We will focus specifically on insights gained using recent advances in transcranial magnetic stimulation (TMS). Thirdly, we look at the wider interactions within the frontal lobe and discuss how they influence top-down control. Finally, we discuss some caveats of the current approaches and open issues that remain to be investigated in the near future.

Evidence for top-down control

In this section we review some of the evidence that there is indeed such a thing as top-down control from (pre)frontal cortex over the motor cortex. In order to establish whether this is the case, we must first look at modulation of activity in the motor cortex to establish whether its activity shows patterns related to predominant responses during conflict tasks, indicating that there is activity that needs to be controlled in the motor cortex at all rather than that all control

is dealt with earlier in the processing stream, and whether the modulation of this activity during the course of a trial indicates that this predominant action representation is modulated. Second, it has to be shown that this modulation is indeed the result of (pre)frontal activity.

Control in the motor cortex

The notion that multiple response alternatives can be simultaneously active in the motor cortex has already been suggested in the 1980s¹³ and this notion is present in most current models of action selection^{5,10}. Gratton and colleagues²² provided early evidence that the presence of multiple, conflicting response alternatives influences activity all the way into the motor cortex. They used an event-related potential known as the lateralized readiness potential (LRP). The LRP is a measure reflecting the differential activation of the motor cortex in the two hemispheres. Participants were required to perform the Eriksen flanker task, in which participants have to respond with one of either hands in response to a stimulus array¹⁸. The array can contain both the target stimulus to which the participant needs to respond and distracters which are designed to lure the participants into preparing the incorrect response (Fig. 7.2a). These 'conflict trials' are generally associated with longer reaction times and more errors than trials without distracter information. Using the LRP, Gratton and colleagues were able to show that the motor cortex associated with the incorrect, distractor response was originally active as reflected by the 'incorrect-dip' in the LRP (Fig. 7.2b). Later in the response period, presumably following increased processing of the stimulus, the preferential activity of the incorrect motor cortex was replaced by preferential activity of the correct motor cortex.

These results provided early evidence that information associated with incorrect responses can be present in the motor cortex even when the trial ends in a correct response. Thus, under these conditions there is the need for top-down control over the motor cortex.

[Figure 7.2 about here]

A problem with the LRP is that it is by definition a difference measure. Therefore, the disappearance of the 'incorrect-dip' can be attributable to the inhibition of the incorrect response, the facilitation of the correct responses, or a mixture of both. This problem can be addressed by probing the excitability of the motor cortices with transcranial magnetic stimulation (TMS). A supra-threshold single pulse of TMS elicited over the representation in the motor cortex of the effector will elicit a motor-evoked potential (MEP) in the EMG recorded from the effector muscle. The amplitude of the MEP is a measure of the excitability of the motor cortex and is modulated during the preparation and execution of a response⁴⁶. A nice example of this approach is provided by a recent study of Verleger and colleagues⁴⁹, who probed MEP amplitude during the time of the 'incorrect-dip' in the LRP in the flanker task. They showed that on incongruent trials, the MEP associated with the incorrect response effector first increased and then decreased during the first 90 ms of the response period. Simultaneously with the decrease in the prematurely activated effector was an increase in MEP recorded from the correct response effector. These results thus detail the effects underlying the 'incorrect-dip' in the LRP. There is indeed an incorrect activation of the effector associated with the incorrect

response that is later inhibited, while the correct response effector is activated. Similar results have been obtained by Michelet and colleagues³⁰.

Evidence for a role of the frontal cortex

The most direct evidence for a necessary role of the frontal cortex in action inhibition comes from lesion studies. Early work by Aron and colleagues established the necessary role of the rIFG in the inhibition of actions, but also in the inhibition of task sets and during memory retrieval³. Lesion mapping showed that this was a unique contribution of rIFG along the regions along the lateral frontal cortex. Similarly, applying repetitive transcranial magnetic stimulation (rTMS) over rIFG to create a so-called 'virtual lesion' also impairs response inhibition, but not normal response execution⁸.

The involvement of pre-SMA in top-down control may be illustrated by a study by Isoda and Hikosaka in which they recorded activity from single neurons in the pre-SMA of monkeys during an action reprogramming task²⁴. They report neurons that are active just before the initiation of successful reprogramming, at a time early enough to cause the behavioral change. When the monkey fails to reprogram its action, however, the neurons are not active before the action, but the neurons show a delayed increase in activity. These results show that pre-SMA seems a likely candidate for a role in top-down control over the motor cortex. As with rIFG, lesions in the pre-SMA show some evidence for a causal role. Although lesions in pre-SMA are rare, a recent study showed difficulty in action inhibition in a patient with just such a lesion³⁴,

dove-tailing with results showing increased activation of pre-SMA during inhibition in healthy participants using the same task³³.

Although lesion methods are quite informative and an improvement over correlative methods such as imaging and electrophysiology, they are not free of interpretational limitations. Lesions do not respect anatomical boundaries and it is thus often difficult to establish which part of damaged tissue is responsible for the behavioral changes observed. Furthermore, the lesions act as a 'global' influence that is always present, making it difficult to delineate the precise contribution of the neural structure in the number of processes involved in any task. Finally, the brain is remarkably adaptive and lesions in one brain area might lead to compensatory, or at least modulated, activity in other parts of the brain. Although the studies reviewed above were generally conducted quite carefully, often employing quite sophisticated lesion mapping techniques and carefully controlling for confounding effects of the lesions on behaviour, more direct experimental evidence of the type of influence these regions exert in the normal brain would be quite beneficial.

More direct evidence for a top-down role of the pre-SMA was obtained by two studies using stimulation techniques to investigate brain function. First, Taylor and colleagues⁴⁴ combined rTMS with the LRP approach described above. Using the Eriksen flanker paradigm, the researchers studied the 'incorrect-dip' in the LRP. On some trials, rTMS was applied over the pre-SMA just before and during the presentation of the stimulus. Interfering with pre-SMA activity in the manner resulted in an increased 'incorrect-dip' in the LRP, indicating that the top-down control influencing this resolution of this conflict is diminished. A second example is the study of Isoda and Hikosaka described above²⁴. In a follow-up to the earlier experiments,

instead of recording from the pre-SMA, the researchers artificially stimulated the same region on trial requiring action reprogramming. On 65% of the sessions, this stimulation increased the number of correct action reprogramming trials, at least for one response. Note that, although these studies show apparently opposite results, this comparison is not valid. rTMS globally affects an expanse of cortex, interfering with its normal function, while the microstimulations target very specific neuronal targets. The overall point of both studies, however, is that pre-SMA seems to have a causal influence on activity in the motor cortex and behavior.

How control is exerted: Examples from action reprogramming

Paired-pulse TMS studies of action reprogramming

In the previous section we showed that there is evidence that there is indeed such a phenomenon as top-down control over the motor cortex. In this section we will discuss some novel insights into the precise nature of the top-down control of both pre-SMA and rIFG on the primary motor cortex during action selection under conflict. We will focus on the specific case of action reprogramming, i.e. the inhibition of a prepared response in favour of an alternative in response to a change in the environment²⁹. In a series of recent studies, we have explored top-down control of the pre-SMA and the rIFG over the motor cortex by means of the technique of paired-pulse transcranial magnetic stimulation (ppTMS). During ppTMS, two TMS coils are placed over an experimental subject's head. A 'test' coil is placed over the primary motor

cortex, over the representation of the response effector, in most cases the hand. As discussed above, a single supra-threshold TMS pulse will elicit a motor-evoked potential (MEP) in the EMG recorded from the effector. A second, 'conditioning' coil is placed over the region that is hypothesized to influence the motor cortex. PpTMS relies on the fact that the MEP elicited by the test coil can be modulated by a pulse through the conditioning coil a few milliseconds earlier (Fig. 11.2). The ratio of the MEP elicited by the test pulse preceded by a pulse through the conditioning coil and the MEP elicited by a test coil pulse only provide an indication of the influence of the area underneath the conditioning coil over the motor cortex. It is important to emphasize that ppTMS is thus a 'probing' technique; the pulses are not applied continuously to achieve the 'virtual lesion' as in rTMS. Paired-pulse TMS was first used within the motor cortex²⁷ and between the motor cortices of the different hemispheres¹⁹, before being applied outside the motor cortex, most notably in the dorsal premotor cortex^{26,32,40}.

We applied this technique during an action reprogramming paradigm, modelled on the task developed by Isoda and Hikosaka²⁴. In this task, participants are looking at a computer screen on which two colored boxes ('flankers') are presented, one to each side of fixation. After a short delay, a central fixation cue takes the color of one of the two flankers, instructing the participant to press a button using the index finger of the hand on the congruent side. The critical manipulation of the task was that the central fixation took the same color for 3-7 consecutive trials, allowing participants to build up an expectation of the response that was required on each trial. Previous studies have shown that participants exploit these types of regularities in the trial sequence and prepare likely actions⁵. Following a number such trials that build up and confirm expectations ('stay trials'), the central fixation would take the opposite

color ('switch trials'). On these switch trials, participants had to reprogram their response, by inhibiting the prepared response and selecting and executing the alternative. Behavioral data confirm the effectiveness of this experimental manipulation, with participants responding slower and making more errors on switch as compared to stay trials. We then probed the influence of pre-SMA and rIFG during switch and stay trials just after the central fixation color change, signalling the participant to reprogram their action or simply execute the prepared action, respectively.

[Figure 7.2 about here]

We first probed the pre-SMA/M1 interactions by applying pulses solely over M1 or over M1 preceded by a pre-SMA pulse 6 ms earlier²⁸. Pulses were applied either 75, 125, or 175 ms after the central fixation color change. These time points were chosen based on the earlier monkey results²⁴ and the timing of conflict-related signals originating from the medial frontal cortex, such as the N2⁴⁷. Pre-SMA had a strong facilitatory influence over the motor cortex only on switch trials and only 125 ms following the reprogramming instruction. The effect of pre-SMA manifested itself by a facilitation of the MEP elicited by M1 stimulation. This effect was most prominent when participants were switching towards the stimulation M1. The effect was specific to reprogramming/switch trials. On stay trials, there was no significant effect of pre-SMA on M1. If anything, there was a trend towards an inhibitory effect. The effect of pre-SMA on M1 was thus specific to the action reprogramming condition and temporally specific in time.

To test whether this effect was also anatomically specific, we then repeated the experiment, but with the conditioning coil not placed over the pre-SMA, but over the rIFG³⁸. Again, we probed the influence over the left M1, but presenting either single pulses over M1 or pulses over M1 preceded by a pulse over rIFG 8 ms earlier. The effects were remarkably different from those of pre-SMA. Whereas pre-SMA had a facilitatory effect on M1, rIFG stimulation resulted in an inhibition of the MEP elicited by M1 during stimulation on reprogramming trials. This influence was later than the pre-SMA influence, at 175 instead of 125 ms. Moreover, although the pre-SMA facilitation was most pronounced when participants switched toward the stimulated M1, the inhibitory effect of rIFG was more global, independent of whether participant were switching towards or away from the stimulation M1. Thus, although pre-SMA and rIFG tend to often co-activate in fMRI studies of action inhibition or action reprogramming^{2,16}, ppTMS shows that the effects are actually qualitatively and temporally distinct from one another.

White matter pathways mediating top-down control

Given that there is this top-down control over the motor cortex the question then is how the signal travels from the (pre)frontal cortex to the motor cortex. In the ppTMS studies described above, we are stimulating a precisely defined region and we have a direct measurement of motor cortex activation, but we have no information over the route this signal is taking. In the action inhibition literature, there is a particular emphasis on a subcortical, hyperdirect pathway

from the (pre)frontal cortex, via the subthalamic nucleus, globus pallidus, and thalamus, to the motor cortex^{20,35}.

One way to investigate which routes might be involved in transporting the information from the stimulated frontal region to M1, is to look at diffusion-weighted magnetic resonance imaging (DW-MRI)²⁵. DW-MRI allows one to obtain an estimate of the diffusion of water in the brain. In the brain's white matter the water diffusion is directionally dependent. In a fiber bundle, the water diffusion is less constrained along the axis of the bundle, and hence more diffusion will be measured along the axis of the bundle. In contrast, water diffusion is more isotropic outside the white matter. This technique thus allows the quantification of white matter integrity on a voxel-by-voxel basis. One can then correlate individual differences in white matter in a given area with individual differences in the functional interactions measured by ppTMS. The rationale is that voxels in which individual differences in the structural white matter measure correlated with the functional ppTMS measure mediate the interaction between the area underneath the conditioning coil and M1. This technique was first used by Boorman et al. to study the pathways mediating premotor/M1 interactions during conditional action selection⁶.

We applied this technique to the data from the pre-SMA/M1 ppTMS study described above²⁸. We found evidence for the involvement of direct cortical pathways between pre-SMA and M1, such as the white matter underlying the medial frontal cortex, the lateral premotor cortex, and M1. The same analysis was performed on the data obtained from a study investigating rIFG/M1 interactions during action reprogramming in a grasping task⁷. Again, there was evidence only for the involvement of direct cortical pathways between rIFG and M1.

At first glance, these results seem at odds with the results of imaging studies, which emphasize the importance of a subcortical route, the so-called 'hyperdirect route' via the STN, in mediating action reprogramming². However, it should be noted that the interval between the conditioning and test pulses in these experiments was 6 for the pre-SMA study and 8 ms for the rIFG. Although these inter-pulse intervals (IPIs) are normal in the ppTMS literature, any signal travelling through the hyperdirect pathway would be expected to take more than this time³⁶. Therefore, the standard ppTMS setup would not be able to pick up signals travelling through this pathway.

To address this issue, we repeated the pre-SMA/M1 and rIFG/M1 interactions experiments using the Isoda and Hikosaka action reprogramming paradigm. Instead of using a constant short IPI, the IPI was varied between 3 and 18 ms³⁸. The results are displayed in figure 7.3. During action reprogramming, we found a facilitatory effect of pre-SMA at an IPI of 6 ms, replicating our previous results²⁸, but also at 9 and 12 ms. For the rIFG, we replicated the inhibitory effect at a short IPI, and also found an inhibitory effect at a longer latency of 12 ms. Correlating the individual differences in effect sizes at different IPIs showed that although short-IPI effect sizes are correlated with one another and long-IPI effect sizes are correlated with one another, there is a much lower correlation between the effect sizes at short and long IPIs. This provides some preliminary indication that different systems might mediate the short and long-IPI effects.

We then again correlated the effect sizes at short IPIs (6 ms) and long IPIs (12 ms) with white matter to investigate which pathways mediate these effects. At the short IPI, we found evidence only for the involvement of direct cortical pathways, replicating our previous

results^{7,28}. At the long IPI, however, we find additional white matter clusters in the vicinity of the STN correlating with effect size³⁸. We then used the cluster found in the correlation analysis as the basis for probabilistic fiber tracking⁴ to show which white matter pathways these clusters are part of. While at the short IPI there was only evidence for cortical pathways, at the long IPI there was evidence for additional subcortical pathways (Fig. 7.3). We then formally quantified this by counting the number of identified tracts passing through a region of interest around the STN. Both the in the pre-SMA and rIFG experiments there was strong evidence for involvement pathways around the STN at the long IPI, but not at the short IPI. These results show strong evidence in favor of a view that separate pathways are mediating the influence of pre-SMA and rIFG over M1 during action reprogramming: a direct cortical pathway and an indirect, subcortical pathway, likely involving the STN. This second pathway is only probed in ppTMS experiments at longer IPIs.

Interactions within the frontal lobes

Interactions between pre-SMA and rIFG

In the previous sections, we have focused on the interactions between nodes within the frontal lobes and the motor cortex. However, it seems plausible that the frontal nodes interact with one another as well. Indeed it has been shown that the regions involved in top-down control over the motor cortex have direct white matter connections with one another² (Fig. 7.1b).

Duann and colleagues¹⁶ used fMRI to study the interactions between the nodes of the action reprogramming network described in this chapter during action inhibition. They asked participants to perform a standard stop-signal task. They showed that during successful inhibition trials rIFG activity correlated more with pre-SMA activity than during unsuccessful inhibition trials. Note that the functional connectivity measure used was purely correlative and as such cannot provide any information on whether rIFG was influencing pre-SMA, vice versa, or both.

Breaking the network

An open question then is whether the interaction between pre-SMA and rIFG has some relevance with regard to the top-down influence of either of these regions. This question can be investigated by probing the top-down control from one of these regions over the motor cortex while the influence of the other region is disrupted, either via lesions or using repetitive TMS. We have done exactly that in a recent follow-up to our action reprogramming work described above.

Considering the timing of pre-SMA and rIFG effects found by Swann and colleagues and Neubert and colleagues, we chose to probe rIFG/M1 interactions following temporary interference with pre-SMA. Participants were asked to perform the same action reprogramming task as described above while ppTMS was applied to rIFG and M1. Following an experimental session participants received 15 mins of 1 Hz rTMS over the pre-SMA. Directly after this, they again performed the action reprogramming task. 15 mins of 1 Hz rTMS is a standard method to

decrease the activity in a brain region, producing effects usually lasting up until 20 mins. In the pre-TMS session, we replicated the earlier effect of an inhibitory influence of rIFG on M1 during action reprogramming. Following the rTMS over pre-SMA, however, this effect disappeared³⁸.

Conclusions and outlook

In this chapter, we have reviewed the evidence that a network of frontal regions, primarily pre-SMA and rIFG, exerts top-down control over the motor cortex during action selection under conflict. We have shown that there are signals in the motor cortex that are modulated in a fashion consistent with the influence of top-down control. Furthermore, we have shown that when activity in frontal regions is disrupted these M1 signals change in a different matter. We have then looked at studies using paired-pulse TMS to study the nature of this top-down control in the situation of action reprogramming. Finally, we have looked at some of the interactions within the frontal network itself and its role in shaping the top-down control signals. In this concluding section, we discuss some of the interpretational limitations of the reviewed results and present some questions that need to be addressed in the near future.

The nature of control

An important question is what the nature of the top-down control is. Although a number of studies focus on the role of rIFG on inhibition of irrelevant actions³, one prominent theory

suggests that the prefrontal cortex exerts control through the amplification of task-relevant information, rather than via inhibition¹¹. Support for this position was obtained by Egner and Hirsch, who investigated the nature of top-down control outside the motor cortex¹⁷. They asked participants to perform a variant of the Stroop task, in which the face and the name of a famous person were presented on top of each other and the participants had to choose whether the relevant stimulus dimension belonged to an 'actor' or 'politician' category. As an example, when a participant had to classify the face stimulus and was presented with the face of Robert de Niro and the name Mao Ze Dong, top-down control could either result in inhibition of activity in the visual word form area or amplify activity in the fusiform face area³⁹. The results were consistent with the amplification model.

However, some of the TMS results reviewed above could be interpreted to argue the opposite. First, the MEP results obtained by Verleger and colleagues⁴⁹ showed that there was actual inhibition of the incorrect response tendency. However, one could argue that this is due not to top-down inhibition of the incorrect response tendency, but to lateral inhibition, which in turn is the result of amplification of activity related to the correct response. Second, the ppTMS results obtained by Neubert and Buch show a clear inhibitory effect of rIFG on the MEP elicited by M1 stimulation during action reprogramming, consistent with the proposed role of this region in inhibition. However, although these results are certainly highly consistent with models assigning an inhibitory role of rIFG, it remains to be established whether the physiological inhibition measured with ppTMS is actually a reflected of cognitive inhibition¹.

Apart from this uncertainty about the nature of inhibition, some recent studies have challenged the notion that rIFG is purely involved in inhibition, arguing instead for a more

general role in either allocating attention to the stimulus or updating of the action representation. For instance, Hampshire and colleagues²³ found that rIFG was more active whenever important stimuli were detected, independent of whether that detection was followed by the inhibition of a motor response. One potential explanation for the divergence of results in the literature is that there is an increasing appreciation that the region commonly referred to as the rIFG consists of subregions, each with different, albeit related, functions. For instance, Verbruggen and colleagues assign a role in updating the current action plan to the posterior ventral rIFG and a role in visual detection of changes in the environment to the more dorsal inferior frontal junction area⁴⁸. A similar distinction has been suggested by Chikazoe and colleagues⁹.

Towards a neurocomputational framework

One drawback of most of the studies reviewed in this chapter is that they mostly distinguish only two conditions, those with and those without top-down control over M1. However, it is highly unlikely that the brain is organized along such a binary distinction. In a recent study, Vossel and colleagues⁵⁰ analyzed activity in the rIFG during attentional reorienting in a location cueing paradigm as a function of the number of preceding trials. They showed that activity in the rIFG increased on reorienting trials as a function of the number of preceding correct trials. Their results are interpreted in the context of Bayesian statistical theory, which—roughly—states that the brain continuously tries to predict the current state of the environment. Brain activity such as that described in rIFG in the study by Vossel and colleagues can then be described as a

prediction error, implementing the need for adjustments and updating the brain's model of the environment. In this context, top-down control over the motor cortex is the implementation of control following a failure of the brain's predictive systems in adequately performing the task at hand. The advantages of such a model are that they provide a general framework for a large body of neural phenomena and that they can be captured in formal computational models. The parameters of these computational models can be related to brain activity in parametric fashion, rather than the binary distinctions described above, and can be used to dissociate some of the different processes described in the studies by Hampton, Chikazoe, and Verbruggen^{9,23,48}, such as detection of the prediction violation, the implementing of the behavioral adjustments, and the updating of the brain's internal models³⁷ (see also Chapter 23, this volume). In future, these formal computational models will hopefully be linked to these data on top-down control over the motor cortex described in this chapter.

Outstanding questions

- What are the different contributions of subregions of the frontal lobes to top-down control and what are the functional properties of different routes mediating frontal/M1 interactions?
- What is the relationship between physiology inhibition and cognitive inhibition in top-down control?
- What is the relationship between top-down control over the motor cortex and other forms of top-down control?
- Can format computation models be used to describe top-down control in a single framework?

Further reading

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A comprehensive review that postulates a role for the prefrontal cortex in cognitive control via the biasing of information processing in posterior brain areas.

Aron AR (2007) The neural basis of inhibition in cognitive control. Neuroscientist 13:214-228

This review provides a wide-range discussion of the concept of inhibition, looking at inhibition in different domains and from a variety of perspectives.

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Figure captions

Figure 7.1 Areas commonly activated in conditions that require the top-down control over the motor cortex. *(a)* Brain activity during action selection based on learned visual instructions and under conflict (action reprogramming²⁹). Some areas in this network are activated exclusively during conflict trials, such as the right inferior parietal lobule (IPL) and the rIFG, while some areas are present both during action selection with and without conflict, such as left posterior parietal cortex (PPC) and left dorsal premotor cortex (PMd). During conflict, the regions active during normal action selection tend to be more active as well, as noticed most often for the pre-SMA. Based on data from Mars et al.²⁹ *(b)* Diffusion-weighted imaging show that areas activated during response inhibition, such as pre-SMA, rIFG, and STN, are all connected with one another via direct white matter fibres. Adapted from Aron et al.² with permission.

Figure 7.2 *(a)* Stimulus arrays typically employed in an arrow version of the Eriksen flanker task¹⁸. Participants are required to respond as quickly as possible with the response hand on the side indicated by the center arrow. *(b)* Schematic LRPs as expected during incompatible trials in this task show a preferential activation of the incorrect response hand due to the presence of the incompatible flankers in the stimulus array ('incorrect-dip') before preferential activation of the correct response hand. After Coles¹² and Gratton et al.²².

Figure 7.3 White matter pathways mediating rIFG/M1 and pre-SMA/M1 functional interactions. Middle panel shows the influence of a single pulse of TMS over pre-SMA (black) and rIFG (grey) on the motor-evoked potential elicited by a single TMS pulse over M1. X-axis indicates the interval between the pre-SMA or rIFG pulse and the M1 pulse. The effect sizes at 6 ms inter-pulse intervals correlate only with direct cortical pathways between the pre-SMA (*a*) and rIFG (*b*) and M1, while at 12 ms intervals there was also evidence for subcortical pathways (*c,d*). Adapted from Neubert et al.³⁸ with permission.

Figure 1

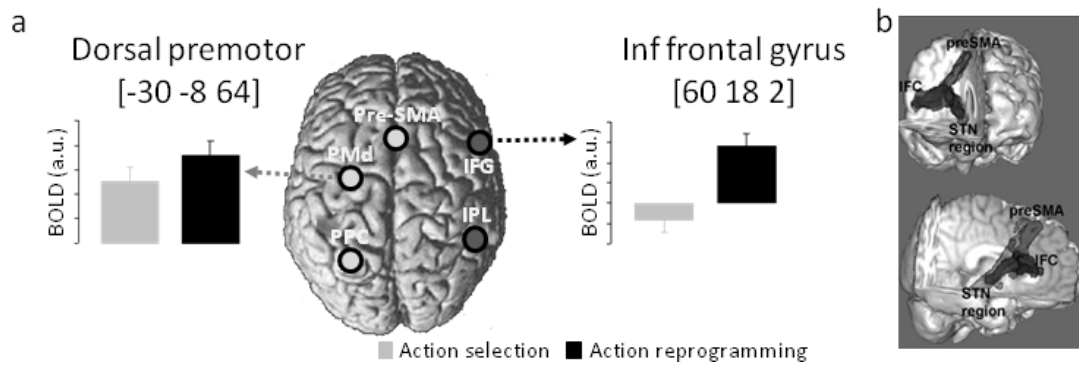


Figure 2

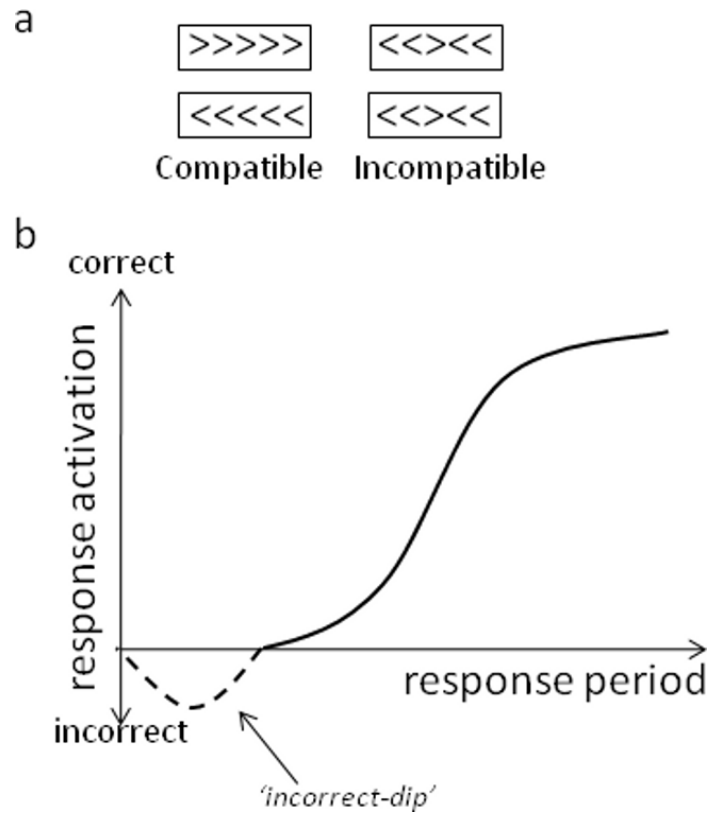


Figure 3

