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Interactions Between Cognitive and Sensorimotor Functions in the Motor Cortex: Evidence from the Preparatory Motor Sets Anticipating a Perturbation

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SYNOPSIS

The many signs of cognitive processes in the activation pattern of the primary motor cortex or in corticospinal (CS) excitability gave rise to the idea that the motor cortex is a crucial node in the processing of cognitive information related to sensorimotor functions. Moreover, it became clear that the preparatory motor sets offer a privileged window to investigate the interaction between cognitive and sensorimotor function in the motor cortex. In the present review, we examine how the study of the preparatory motor sets anticipating a mechanical movement perturbation contributes to enlightening this question. Following the initial observation made by Hammond that some components of the stretch reflex can be modulated by a prior intention either to resist or to relax in response to a subsequent perturbation, first evidence of the phenomenon was obtained in behaving monkeys [29]. Moreover, this study [29] related this peripheral fact to the observed anticipatory activity of motor cortex neurons after a prior instruction telling the animal how to respond to the subsequent perturbation, which triggered the instructed movement. Indeed, this anticipatory activity was found to be different according to the instruction. In the 1980s, this work inspired a lot of studies in human beings

that brought support to the idea of a cognitive tuning of the long latency stretch response (LLSR). Specifically, the M2 component of the response was shown to be modulated by a prior intent to resist versus to let go when faced with the perturbation. Recently, new approaches have been developed to obtain evidence of a cognitive tuning of CS excitability, thanks to transcranial magnetic stimulation (TMS). TMS has been used both as a reliable tool for quantifying the CS excitability via the motor evoked potentials (MEPs), and to centrally perturb the organization of movement. Such central perturbations offer the unique opportunity to activate the descending motor tracts while shunting, for a short time period, the ascending tracts assisting the movement. Thus, CS excitability was measured before the movement was perturbed. These studies demonstrated the readiness of the CS tract to be involved in anticipatory compensatory responses to central movement perturbations induced by TMS in relation to the subject's cognitive attitudes. The question of the cerebral regions upstream of the motor cortex that could be responsible for this modulation in CS excitability remains largely open.

KEY WORDS

motor cortex, corticospinal excitability, preparatory motor sets, long-latency stretch response, mechanical perturbation

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1. INTRODUCTION

Over the two last decades, there has been a growing amount of neurophysiological evidence, from both monkeys and humans, that cognitive and motor functions are so intimately linked that cognitive factors set neural activity in motor related cortical areas, even at the level of the primary motor cortex /30,38,70,71/. Indeed, using single cell recording in behaving monkeys and the movement-precueing method, it has been shown many times that a prior instruction provided to the animal about what he has to do modifies the activity of neurons in the motor cortex (without any change in muscle activation patterns). The modified neuronal activity in the motor cortex occurs while the animal is waiting for the trigger signal, a fact that has often been referred to as set-related neuronal activity /3,21,28,29,31,39,72/. Moreover, using partial prior information about an upcoming movement task, it was found that the shape of preactivation patterns depends on the range of precued movement directions /5/.

Strong evidence of cognitive influences over the primary motor cortex has also been found in humans. Indeed, several brain imaging studies (using fMRI, PET or EEG) conducted on movement simulation have shown that the primary motor cortex can be activated in the absence of any movement if the subject simply mentally simulates a movement /43,68/, though the activation is, of course, much less than during the overt movement itself. It has also been shown that the primary sensorimotor cortex is activated during movement preparation /4,24/, with a tendency to be more active when some precueing information was present than when it was absent /24/. Finally, transcranial magnetic stimulation (TMS) has been used to demonstrate the intermingling of cognitive and motor processes in the tuning of corticospinal (CS) excitability. Indeed, this technique offers a unique opportunity to enter the cognitive-motor loop and test CS excitability at different stages, from the initial intention to the realization of a motor action. CS excitability has been found to change selectively depending on the subject's intentions during motor preparation using Go/No-go protocols /45/, during mental movement

simulation /33,48,73/, and even during movement observation /34/.

These many signatures of cognitive processes in the activation pattern of the primary motor cortex or in CS excitability gave rise to the idea that the motor cortex is a crucial node in the processing of cognitive information related to sensorimotor functions. Moreover, it became clear that the preparatory motor sets offer a privileged window to investigate the interaction between cognitive and sensorimotor function in the brain.

2. NO UNIVOCAL LINK BETWEEN BRAIN ACTIVATION PATTERNS AND MOTOR FUNCTIONS

Before considering further the interaction between cognitive and sensorimotor function in the motor cortex, we would like to shed some light on the context in which this question needs to be addressed. In particular, we would like to emphasize that there can be no *a priori* univocal relationship between motor-related brain activation patterns and a motor behaviour, due to two fundamental losses in the chain: (i) the loss of the descending motor pathways (the pyramidal tract among others), and of the spinal cord, known to be fundamental integrative levels between the brain and motor behaviour, and (ii) the loss of the external environment, especially the external forces that are known to collaborate to movement production /49,50/. Concerning this latter point, we argue that there is an urgent need to clearly separate between brain involvement in *movement production* and brain involvement in *movement control* /10/.

The importance of the integrity of the corticospinal tract for the realization of motor behaviour is nicely illustrated by a longitudinal study of stroke patients with an affected upper limb /36/. Indeed, during upper limb motor tasks, it was reported that, following an initial period of recruitment of additional ipsilateral and contralateral areas, two main patterns of cortical activation could be observed. One pattern, referred to as focusing, was characterised by a gradual evolution towards cortical activation restricted to the contralateral sensorimotor cortex (i.e. approximating the normal activation pattern); such a pattern was mainly

observed in patients with spared M1. The second pattern showed a persistent recruitment, in which the initial recruitment of ipsilateral activity was maintained; it was mainly observed in patients with M1 injury. The most interesting fact, however, was that these patterns had no relation to the degree of motor recovery. In particular, focusing did not imply recovery. However, there was a clear relation between the degree of recovery and the degree of Wallerian degeneration of the corticospinal tract, with the degree of recovery being inversely related to the degree of Wallerian degeneration.

The importance of the spinal cord as a fundamental integrative level for movement production is now largely accepted. However, new evidence concerning the interaction between the spinal cord and the brain in cognitive-motor functions has emerged from studies in patients with spinal cord injuries. For example, patients with complete spinal cord injury can imagine moving their disconnected feet. When comparing their cerebral activation patterns with those observed in healthy humans during this task, they showed stronger activity in primary and all non-primary motor cortical areas and subcortical regions than healthy humans. In fact, in paraplegic patients, the primary motor cortex was consistently activated, even to the same degree as during movement execution in the control subjects /2/.

Another important point to take into account when considering the interaction between cognitive and motor functions in the brain is that motor-related brain activation patterns are related to at least two different mechanisms: 1) generation of the motor command organizing the muscle forces required for movement production, and 2) controlling the movement outcome so that it corresponds with the desired movement. For example, we recently showed that gaining awareness of the muscle forces produced during movement execution, compared to gaining awareness of the kinematics of movement outcome, makes much higher demands on many brain structures, in particular, primary sensorimotor areas and associative somatosensory areas /23/. Thus, in our opinion, there is an urgent need to clearly separate, in motor-related brain activation patterns, the elements that relate to movement production (that

most of the time remains at the unconscious level of motor command organization) from the components related to the product control at the intentional level of the sensorimotor action /10/. This would better enable identification of the true role of the brain in movement organization, recognizing that if the brain is the only actor in movement control, it is only a collaborator in movement production. Indeed, as demonstrated in biomechanics and movement physiology, all biological movements are the result of the integration of two types of force: active muscular forces and external forces, such as gravitational and inertial forces /8/. Thus, when observing a movement outcome, one cannot infer the motor command without knowing the external forces; indeed, no univocal relationship exists between motor command and movement outcome. For example, a rhythmic forearm movement performed in the horizontal plane requires an out-of-phase brachial biceps/triceps activation pattern. A similar out-of-phase pattern is observed if the same movement is performed in any plane under microgravity, but as soon as gravity increases, several patterns can be observed for maintaining a rhythmical movement in the plane of gravity /9/. Under hypergravity, a biphasic activation of the biceps not only allows achievement of the forearm flexion but also slows down the extension. This is of importance for conceiving the relationships between motor and sensory functions. Indeed, sensory consequences are generated by the movement outcome, but this movement can originate from various motor commands organizing muscle force production in relation to the external forces present in the environment (in our previous example, out-of-phase biceps/triceps, biphasic biceps activation, etc.). The initial hypothesis of the efference copy /84/, proposing that the motor command is used to cancel the reafferences from that movement, has been hotly debated /63/. In 1981, McCloskey /62/ addressed the question once again and pointed out that the efference copy (which he judiciously named corollary discharge) could never be compared directly to the sensory afferences generated by the movement outcome due to differences in the nature of their informational content. Moreover, MacKay argued that "from an

information-engineering standpoint, the need is not for the changes due to voluntary movement to be eliminated from the sensory input, but for them to be appropriately evaluated by the central mechanism responsible for the organism's 'conditional readiness' to reckon with its environment" /54/.

Taking these points into account, the question of the interaction between cognitive and sensorimotor functions in the motor cortex can be addressed while keeping in mind that we will never see any overt movement in the brain, only movement-related activation that is fundamental for organizing the production and control of a motor behaviour. Therefore, it appears that when looking at the motor-related brain activation patterns, we have to be very careful concerning the hypothetical link of these patterns to the motor behaviour.

3. DIFFERENT KINDS OF PREPARATORY MOTOR SETS

An important point to note is that the literature regarding preparatory motor sets is not uniform. Indeed, at least two complementary approaches should be distinguished because, in our opinion, they do not give access to the same brain mechanisms. The first approach was top-down and consisted of studying how the preparation for a voluntary movement influences motor cortex activation /38,70,71/. In this approach, the top-down processes are devoted to organizing the motor command according to an *a priori* knowledge of the movement to come (that is more or less complete) and to trigger it (most of the time, as soon as possible) in response to an external trigger. In simple reaction time tasks, following the Go signal it takes at least 100 ms to observe a voluntary EMG activation in the prime movers of the upper limb. The second approach was bottom-up and consisted of studying how the anticipation of a movement perturbation influences motor cortex activation. The bottom-up approach was promoted by the work of Evarts and colleagues /28,29,79/ and, for the broad feature, brought support to Phillips's original 'transcortical servo' hypothesis /60,63,67/. In anticipation of a movement perturbation, the trigger is the external perturbation and not the subject himself, and it was

observed that the reafferent sensory flow is processed differently according to the subject's prior intention in the face of the perturbation. Interestingly, in such a case a difference in the EMG patterns (referred to as long latency stretch response [LLSR]) can be observed in about 50 ms, i.e. well under any voluntary reaction time but clearly above the short latency response due to spinal integration. Therefore, one might believe that all the top-down processes are devoted to gate the primary motor and sensory areas in a different way so that the appropriate motor output is automatically triggered in response to the perturbation. Originally different (the top-down approach being pushed by cognitive psychologists, while the bottom-up approach was promoted by neurophysiologists), these two approaches became mixed in the 1980s because studying the LLSR was the only non-invasive technique with which to get access, from the periphery, to central processing in healthy humans /12,13,55/. With the arrival of non-invasive functional brain exploration techniques (EEG, TMS, fMRI, etc.), the two approaches separated out again. Together, these top-down and bottom-up approaches have brought to the fore the idea that, during voluntary movement, the pyramidal tract neurons (PTNs) in the motor cortex are a summation point for top-down cognitive and bottom-up sensorimotor processes /37,58,60,63,86/.

Because the preparation of a voluntary movement (top-down approach) has attracted a lot of interest and has been the topic of several reviews on the interaction between cognitive and motor functions in the motor cortex /38,70,71/, we direct the reader to these reviews, and we now concentrate on the preparatory motor sets anticipating a mechanical movement perturbation to emphasize their main contribution to the study of the interaction between cognitive and sensorimotor functions in the motor cortex.

4. PREPARATORY MOTOR SETS ANTICIPATING AN EXTERNAL PERTUBATION

Hammond /44/ was the first to report that motor responses to somatosensory stimuli induced by mechanical perturbations are profoundly modified by the establishment of preparatory states of man to

initiate an intended movement. Moreover, he is credited with the suggestion that responses to muscle stretch might use pathways extending to the brain. But little was known on possible long loop cerebral responses to muscle stretch until the studies of Phillips in 1969 /16,58,60,63,67,86/.

4.1. First evidence from behaving monkeys

In monkeys, these preparatory motor sets anticipating an external perturbation have been investigated at both the central and peripheral levels by the pioneering work of Evarts and Tanji /29/. Indeed, they demonstrated for the first time an anticipatory activity of motor cortex neurons after a prior instruction telling the animal how to respond (either by pushing or by pulling) to a subsequent perturbation (delivered a few seconds later), which triggered the instructed movement. Recordings in the precentral motor cortex revealed differential instruction-induced changes of neuronal activity during the period between the instruction and the perturbation-triggered movement. In addition, the short latency motor cortex response (20 ms) evoked by the subsequent perturbing stimuli differed markedly depending upon the prior instruction. Further, they reported a correlation between the instruction's effect on neuronal discharge and the subsequent motor performance. They used the very rare instances in which mistakes did occur to show that if a cell shows the 'wrong' response to the prior instruction, the following perturbation elicits the 'wrong' movement. They concluded that the prior intent (preparatory motor set) gated the motor cortex reflexes /29,31/. This first evidence received much support from later studies that demonstrated that some of the PTNs in the motor cortex show a differential discharge according to whether the peripheral disturbance opposes the active movement (i.e. stretching the target muscles) or assists the active movement (i.e. shortening the target muscles) /17,19,32/.

4.2. Peripheral evidence from humans

In the 1980s, the work of Hammond /44/ and Evarts and Tanji /29/ inspired a lot of studies in human beings, in whom similar instructions to 'resist' versus 'let go' when faced with a rapid joint

angular displacement were found to modulate the LLSR /18,47,51,52,74/. Many investigations were conducted using torque pulses applied during maintenance of steady postures against a pre-load torque and several interesting results were observed concerning the influence of cognition on these LLSRs. Of particular interest was the fact that the LLSRs were decreased if the perturbation could be predicted by the subject /41,42,76/, the clearest case being during self-triggered perturbations /42/. Moreover, the LLSRs were found to be deeply modulated during movement preparation /12,13/ or during movement execution /41,55/. The origins of these long-latency EMG responses and their function in motor control have been extensively debated /16,57-60,86/, oscillating between two alternative hypotheses, one being that this delayed stretch response is due to a transcortical reflex pathway, following Philipps's original suggestion, and one other being that it might be due to a segmental reflex. This latter hypothesis is divided into several possible alternatives /60,86/. It was further proposed that this LLSR was not the result of a simple feedback mechanism controlling muscle length only, but, rather, reflected the co-ordinated activation of muscles which is necessary for an adequate behavioural response /40/. Indeed, these authors demonstrated the remarkable fact that the LLSR can be routed to an apparent antagonist if its contraction is mechanically advantageous. From this perspective, the advantage for routing the 'stretch reflex' via the cortex would be to make use of its machinery to establish complex and shifting patterns of connectivity. Finally, in 1991, based on a collection of new converging experiments, Matthews /60/ proposed that the transcortical hypothesis was the most likely. Since then, this conclusion has not been consistently contested, at least for the hand muscles, because the possibility that the LLSR is not invariably mediated over transcortical pathways is still under debate /83/. Concerning the question of the modulation of LLSR by a subject's intents, it is now widely accepted that the M2 response is enhanced when the subject prepares to resist the perturbation, in comparison to when he/she prepares to relax in response to the perturbation, although this has been contested /15/.

4.3. Central evidence from humans

Although fundamental for understanding how the nervous system ensures the adaptive capabilities of motor functions, the above-mentioned results in humans constitute only indirect evidence, inferred from the periphery, of the involvement of the motor cortex in the LLSR. The first central evidence in humans came from patients with neurological disorders /58,60/, with the most convincing evidence obtained from patients with Klippel-Feil syndrome who display characteristic mirror movements. These patients are thought to have abnormal pyramidal projections from the motor cortex, which branch and innervate the extremities bilaterally /61/. In these patients, stretch of muscles in one hand evokes short-latency responses in the ipsilateral hand but long-latency responses in both hands, a fact that fits nicely with the transcortical hypothesis. In healthy humans, thanks to the arrival of non-invasive techniques allowing exploration of brain function, several attempts have been made to approach the brain mechanisms underlying the intentional modulation of LLSR.

a. EEG studies

EEG studies were conducted to investigate whether the modulations of the LLSR according to the subject's intentions can be related to differences in cortical activity using event related potentials (ERPs). The first such study /1/ reported that when the subjects were asked to 'react' to the stretch, the secondary component (P1/P2-N2) of the cerebral response (from 32 to 76 ms) was reduced while, at the EMG level, the LLSR was enhanced. In contrast, a subsequent study on ERPs /20/ did not find any difference in the earliest cortical response (up to 70 ms) across the central sulcus in the 'react' versus 'let-go' conditions, and thus concluded that the intention to react does not seem to affect afferent transmission to the primary sensorimotor cortex. More recently, MacKinnon *et al.* /56/ addressed the question once again. They showed that motor cortical potentials precede LLSR but, again, they were unable to show any instruction-related differences in the early evoked potential (up to 75 ms), and therefore concluded that instruction-dependent modulation of the LLSR occurs down-

stream from inputs to the primary motor cortex. Taken together, these EEG studies do not bring a very clear picture of the way the primary motor cortex could be involved in the gating of reflexes anticipating a transitory mechanical perturbation.

b. TMS studies

Much clearer evidence in favour of a cortical mediation of the LLSR in healthy human subjects has come from transcranial magnetic stimulation studies. Indeed, for the first time in humans, this technique allowed investigation of the interaction between central and peripheral mechanisms in the motor cortex /75/. The method to demonstrate the presence of a cortical component of the LLSR consists of conditioning a stimulus delivered over the contralateral motor cortex, using transcranial electric (TES) or magnetic (TMS) stimulations, with an imposed stretch of the target muscle /22,25,65/. Studying the interaction of the stretch reflex with responses to transcranial or electrical stimulation of the motor cortex, it has been shown that the excitability of the motor cortex increases during the interval that would correspond to the passage of an afferent signal from the stretched muscle through the cortex /22/. This suggested that the stretch input could facilitate the cortex at the time expected for operation of a transcortical pathway /22,65/. Moreover, using high intensity stimulation of the ipsilateral motor cortex to induce interhemispheric inhibition /35/, Taylor *et al.* /82/ reported that an appropriate timed stimulation could inhibit the LLSR of the long flexor of the fingers with little effect on the early spinal component. It has to be noted that in all of these studies, TMS or TES have been used to make central and peripheral information simultaneously converge at the level of the cortical neurons in order to study how they interact in the tuning of cortical or CS excitability.

In recent TMS studies /11,14,78/, a new approach was designed to dissociate, in the tuning of CS excitability, the influence of cognitive processes from the above-mentioned interaction between central and afferent signals. In these studies, a TMS pulse was applied over the contralateral primary motor cortex with an intensity above motor threshold to induce central movement

perturbations. Compared to peripheral mechanical perturbations /29,76,77/, such central perturbations offer the unique opportunity to activate the descending motor tracts (CS tract among others) and to obtain a measurement of the CS excitability before the movement is perturbed, i.e. while shunting, for a short period of time, the ascending tracts assisting the movement. Thus, TMS was used both as a reliable tool for quantifying the CS excitability via motor evoked potentials (MEPs) and to centrally perturb the organization of movement.

We performed a series of experiments in order to investigate whether a prior intention allows an anticipatory modulation of the corticospinal excitability in humans. Subjects were engaged in the same motor task but with two opposing cognitive attitudes (active/passive) with respect to potential movement perturbations, as in the studies of Hammond /44/. However, in our case, the unpredictable selective perturbations were central, i.e. induced by applying a TMS pulse over the primary motor cortex evoking a movement that was superimposed onto the voluntary movement /85/. The occurrence of the evoked movement in the sequence could never be predicted, and according to the conditions, two opposite instructions were given to the subjects with respect to these evoked movements /11,14/. As in Hammond's studies /44/, one instruction was to prepare to let the evoked movement be performed, i.e. to 'let go' without voluntarily intervening to avoid it. Conversely, the other instruction was to prepare themselves, but only by thinking (and not by co-activating their muscles), so that no evoked movement was observed. This latter instruction always required further motivation of the subjects, all of them initially believing that nothing could be done to attenuate a TMS-evoked movement. In a first study /11/, the subjects were engaged in rhythmical flexion/extension movements of the wrist and the TMS-evoked movements, although unpredictable in time, were known by the subjects as always directed toward an increased flexion of the wrist. We studied the simultaneous evolution of both the motor performance and the MEPs in the wrist flexor and extensor, separately for the successful trials (on average 66% of the trials regardless of the

condition) and the unsuccessful trials. This allowed us to dissociate the intention-related and performance-related processes. To their great surprise, subjects were found to be able to cognitively prepare themselves to resist a TMS-induced central perturbation; they all reported an important cognitive effort on the evoked movement. When comparing successful trials performed under the two instructions, this capacity of intentional preparation to compensate was found to be underlaid by a change in the MEPs of the flexor muscle, while its ongoing EMG activity was similar under the two instructions. Moreover, when taking into account both successful and unsuccessful trials under the two instructions, the amplitude of the MEPs was found to be related, in a continuous way, to the actual movement whatever the prior intention. Thus, it appeared that a motor intention does indeed influence CS excitability, only if it is going to be realized. This suggests that the CS excitability relates to the intention realization (i.e. the binding of cognitive and motor processes), and not to the intention in itself. These findings provide direct evidence of the role of CS excitability in the binding between cognitive and motor processes in humans.

Interestingly, similar results were obtained by Sohn *et al.* /78/ who asked the subject either to imagine squeezing hands (positive imagery) after a Go cue or to imagine suppression of a TMS-induced twitching movement (negative imagery) after receiving a No-go cue. In this study, the subjects had their left arm supported and were asked to remain at rest without imagination (control) and during motor imagination sessions (positive and negative). Compared to the control state, the authors reported a suppression of MEPs in the first dorsal interosseus in negative motor imagery but no differences in MEPs during positive motor imagery. This demonstrates that the excitatory CS drive is suppressed during imagination of suppressing movement. Surprisingly, during such imagination of suppressing movement, the authors did not report any significant change in short and long intracortical inhibition, intracortical facilitation, or in F-wave responses.

In a recent experiment /14/, we investigated whether the cognitive tuning of CS excitability

adapts to the type of evoked movement (flexion vs extension), and the question was addressed during human gait for two main reasons. Firstly, although the existence of LLSR seems to be established for hand muscles and discussed more or less positively for the rest of the upper limb, it is much more controversial for lower limbs. Still, some evidence exists in favour of this hypothesis /64,66/. The second reason was that the degree of involvement of the CS tract during voluntary gait adaptation seems to vary according to the locomotor phases. Indeed, several studies have emphasized a greater role of the motor cortex in the control of the accuracy of locomotor movement during the swing phase /6a,7,27/ than in the control of the vigour of locomotor movement during the stance phase /6b/. In one condition, the TMS occurred at mid-stance, evoking additional hip extension, whereas in a second condition, the TMS occurred at the beginning of the swing phase, evoking additional hip flexion. Again, in both conditions, the subjects were asked to cognitively prepare either to not intervene or to compensate for these evoked movements. The results showed that, regardless of the type of evoked movement, preparing to compensate resulted in a selective increase in the CS excitability to those muscles which would be involved in counteracting the possible central perturbation, i.e. the hip extensor muscle (biceps femoris) to compensate for an evoked flexion during the swing phase or the hip flexor muscle (rectus femoris) to compensate for an evoked extension during the stance phase. In conclusion, the cognitive tuning of CS excitability was found to adapt to the gait phases. Moreover, the same selective preparation strategy (selective increase in CS excitability to those muscles which would be involved in counteracting the possible central perturbation) was observed whether the central perturbation occurred during the stance or the swing phase of the step cycle.

The CS tract is known to be involved in both the organization of voluntary movement /67/ and the intentional adaptation of sensorimotor automatisms /7,27/. In addition, the above-mentioned studies demonstrate the readiness of the CS tract to be involved in anticipatory compensatory responses to central movement perturbations mimicking such

movements (when involuntarily induced by TMS) in relation to the subject's cognitive attitudes. Moreover, three essential properties of these intention-related anticipatory modulations of the CS excitability were emphasized: 1) They were found to be selective, concerning only muscles involved in the compensation of the evoked movement. This selectivity is remarkable and has to be considered in relation to an observation of Matthews, questioning whether the LLSRs are homologous in monkeys and humans /60/. Indeed, monkeys usually respond to the mechanical disturbance by co-contracting agonists and antagonists, so that a given muscle gives the same LLSR irrespective of whether it has been stretched or released. 2) These intention-related anticipatory modulations of corticospinal excitability were efficient, giving the intended motor behaviour the chance to be realized /11/. 3) Finally, they were found to be flexible, adapting to the type of evoked movement /14/. Moreover, they were observable at both the level of the upper limb and the level of the lower limb.

4.4. Supplementary motor area and gating of the motor cortex reflexes

All the above-mentioned results, observed at both the central and peripheral levels in monkeys and humans, argue strongly in favour of a gating of motor cortex reflexes by a prior intent. However, the question as to which cerebral regions upstream of the motor cortex are responsible for this modulation in its input/output function remains largely unanswered. To this point, all efforts have concentrated on the SMA, which has been hypothesized to be part of the system involved in modulating responses of the motor cortex to sensory inputs /80,81/. Indeed, using the same protocol as Evarts and Tanji /29/, Tanji *et al.* /81/ showed an instruction-induced modulation in the discharge of neurons in the SMA during the period intervening between the instruction and the perturbation-triggered movement. Interestingly, of the 201 neurons exhibiting this change, 94 neurons showed a differential modulation for the two instructions. Therefore they concluded that the SMA plays an important role in the preparatory process leading to correct initiation or suppression of a movement in

response to forthcoming sensory signals. Interestingly, a study conducted with a patient after infarction in the right supplementary motor area arrived at the same conclusion /26/. The authors reported abnormalities in the LLSR in the arm contralateral to the lesion: in the absence of muscle weakness, his LLSR in wrist flexor was substantially prolonged in the arm contralateral to the SMA lesion, whereas the short latency responses were bilaterally symmetrical. Finally, Hummelsheim and colleagues /46/ reported that, in monkeys, microstimulation of the SMA could decrease the response of motor cortical cells to peripheral afferent input, suggesting that the SMA could indeed exert a modulatory influence on the size of the LLSR.

5. CONCLUSIONS

All the above-mentioned studies brought to the fore the idea that many signs of cognitive processes (task dependent, context dependent, intentional and attentional modulations) can be observed at the more executive cortical level, in the so-called motor cortex. This makes the distinction between motor and cognitive processes, which is still often used in the field of cognitive neuroscience, rather questionable. Moreover, it has to be clear that even if we concentrated on the interaction between cognitive and motor functions in the brain, the influence of cognitive processes in the presetting of motor executive structure is not limited to the brain but also extends to the spinal cord. During a Go/No-go task, it has been demonstrated that primate spinal interneurons show pre-movement instructed delay activity, whose timing and properties are similar to those observed in motor cortical areas /69/. All these results strongly argue in favour of a general presetting of the cognitive processes over all the sensory and executive motor nervous structures, whether at the brain level (primary motor and sensory cortex) or at the spinal level.

Elucidating the mechanisms of this general presetting requires adequate paradigms, and it is our position that studying the preparatory motor sets anticipating a movement perturbation (whether central or peripheral) is an optimal paradigm for investigating the interaction between cognitive and

sensorimotor function in the brain (rather than the influence of the former over the latter) because it takes into account the motor behaviour in its functional meaning, which is thus meaningful for the brain. Therefore, this approach allows an integration of top-down and bottom-up processes. Concerning the bottom-up processes, even if we concentrated on long-latency responses to stretch, there is strong reason to believe that these responses are part of a more general system of cortically mediated responses controlling limb movement /53/, and that this involves convergent input from different modalities (muscle, cutaneous and joint inputs) on the motor cortex PTNs. Convergence from different modalities and from different nerves is indeed a characteristic feature for the majority of motor cortex PTNs /37/. In addition, cognitive processes can have some influence over the processing of these convergent inputs via tuning or pre-setting processes.

Elucidating the mechanisms of the interaction between cognitive and sensorimotor function in the motor cortex also requires addressing the question at different levels of analysis (behaviour, brain activation patterns, etc.) and with different techniques of functional brain exploration (EEG, fMRI, TMS, etc.). This is now possible in healthy humans, and the limitations of each of these techniques (that can be at least attenuated by combining several of them) are largely compensated by the possibility to refine the instructions given to the subjects. Indeed, it could be questioned whether obtaining a behavioural response through conditioning involves the same brain mechanisms as those used by conscious humans to whom a verbal instruction to produce an intended behaviour can be given. To this end, Matthews's question /60/ as to whether the long-latency stretch responses are homologous in monkeys and humans (given the fact that monkeys responded to the disturbance by co-contracting agonists and antagonists whereas humans produce much more selective responses) is particularly illustrative.

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