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Research report

The role of inhibition in the hierarchical gating of executed and imagined movements

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Abstract

A theory is presented concerning the neuronal mechanisms which may underlie the organisation of imagined versus executed movements. A review is first presented of previous theoretical and experimental evidence suggesting that the brain can use the same mechanisms for the imagination and the execution of movement. In particular the fact that adaptation of the vestibulo-ocular reflex can be obtained by pure mental effort and not solely by conflicting visual and vestibular cues has been suggestive of the fact that the brain could internally simulate conflicts and use the same adaptive mechanisms used when actual sensory cues were in conflict. The saccadic system is taken as a good model for the study of this question because the mechanisms which underlie saccade generation are now partially understood at different levels from the brain stem to the cortex. The central idea of the theory is based upon the fact that, in parallel with the excitatory mechanisms underlying saccade generation, several inhibitory mechanisms in cascade allow the selective modulation and blockage of saccades. Synaptic inhibition is therefore supposed to play a major role in a hierarchical selective gating of saccade execution not at one but at several levels allowing a variety of different types of 'imagined movements' some involving only the higher levels some in which the execution is only blocked at the very immediate premotor level. But in all cases the theory proposes that imagination and execution have many mechanisms in common. PET data showing that indeed the same structures are activated in both types of movements support this idea although the final answer will have to be brought by neuronal data.

Keywords: Motor imagery; Saccade; Inhibition; Prism adaptation; Selective attention; Colliculus

1. Introduction

This paper will address the question of the neuronal mechanisms underlying the control of executed imagined or intended movements. It will also deal indirectly with the problem of selective attention. I believe that there is no fundamental difference between the internal mechanisms underlying motor decision and the neural mechanisms of selective attention or, at least the orientation of attention. Most theories of selective attention focus essentially on the sensory aspect of attention (in fact mostly within the restricted problem of vision) and suppose that attention shifts are accompanied by enhancements of the sensitivity of neurones to specific sensory inputs. In my view selective attention is never a purely sensory process it is always related to an internally simulated action. The views expressed in the present paper are very much in agreement with the 'pre-motor hypothesis of spatial attention' proposed in 1987 by Rizollatti and his coworkers [88,89] which suggests that shifting attention to a particular location corresponds to programming a saccade to this location. Covert orienting occurs, according to these authors, when the programme for the saccade has been completed but the movement is internally blocked.

We have, in the last ten years, also proposed experimental evidence and theoretical ideas which insist upon the importance of internally generated simulations of action. Most of our movements and our perceptions involve discrete decisions and internal simulation of the potential consequences of action which in turn require selection of both expected sensory stimuli and anticipated motor states. I will, in this paper, shortly review these ideas and results and propose a theory concerning the mechanism by which selective gating of executed action can be performed by cascade of inhibitory mechanisms in sensory-motor systems. We shall take as an example the oculomotor system but the same reasoning could be made with other elements of the motor repertoire.

We have proposed [6,24] that, during an action, sensory motor processes are operating through two parallel modes.

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One mode consists of sensory motor loops linking the sensors to the central nervous system and the effectors. These sensory-motor loops work as conservative processes like cybernetic loops. They are continuous, have properties similar to servomechanisms, deal with sensory signals which are transformed into motor commands through the estimation of motor errors and are regulated by feed-back or feed-forward mechanisms. They operate on a repertoire of motor synergies which generate a set of motor primitives. In this mode the brain operates as a *controller*. Most of the modern theories of motor control deal with this level of operation. Illustration of this conception of the organisation of sensory-motor systems is provided by models of the saccadic system [11,72,94,106] or models of the cerebellum [37,51,53,80,99].

But we have also proposed the idea that, in parallel with this controller, higher central loops, which have increasingly gained complexity during evolution, operate on another mode which we have called a PROJECTIVE process. In this mode, signals are processed in internal loops having no direct link with sensors, the operations are discontinuous (they can be triggered in an intermittent fashion), they occur on neural maps in which the important parameters are the topological relations between the neurones. This mode produces predictions of future states, it preselects strategies (which themselves are combinations of synergies and combinations of expected states of sensors). It also selects reference frames for the control of movement and posture [10]. In this mode the brain works as a modular *simulator*.

At the present time no definite proof has been obtained to demonstrate the validity of this model. However the emphasis recently placed on the importance of self sustained inner loops, like for example the possible functional role of basal ganglia-thalamo-cortical loops [1] and the importance of intrinsic neuronal properties to determine the oscillatory properties [62] which, in turn, may synchronise neurones in many structures thus creating a temporal binding.

We have also proposed [6] the idea that the brain is not a machine which responds to external stimuli but a machine which formulates hypothesis based upon internally generated simulations of movements and of the corresponding expected states of the sensory receptors. In other words, together with the planning of a movement the brain builds an internal expectation of the state of selected configurations of sensory receptors. The sensory systems involved will be the ones which are necessary for the accomplishment of each phase of the task. Many recent studies using brain imaging techniques have insisted upon this aspect of brain operation [17,20,21,26,54,93]. The decision to make a movement rather another one is therefore an essential part of the normal function of sensory-motor systems. It will also involve not only the prefrontal cortex but many different levels which will participate in decisions at multiple degrees of complexity with respect to the choice of the effectors, the choice of the motor repertoire, the relations with the context, the integration of memories of past episodes etc...

2. Mental training can induce sensory-motor adaptation

The importance of mental simulation of movement and the probable similarity between the structures involved in the mental imagination of a movement and its execution have been suggested by the experiments we have conducted with Melvill-Jones [4,65–67] concerning the adaptation of the vestibulo-ocular reflex. Melvill-Jones and Gonshor [38,64] had demonstrated that when a subject was asked to wear reversing prisms during several weeks one could observe an adaptive modification of the gain and the phase of the VOR tested in darkness. This plasticity which in a sense, is akin to the general problem of the compensation of vestibular function after peripheral lesions, has been a challenging problem ever since and the exact mechanisms underlying this plasticity is not yet understood. A local theory has been proposed by Ito [52] who hypothesised that the flocculus of the cerebellum was essential in this process which would involve long term depression at the level of the Purkinje cells induced by heterosynaptic interactions from the mossy and the climbing fibres. This theory has been challenged by Llinas [63] who supported the idea of a more distributed process occurring during compensation of vestibular lesions. This was confirmed by recent findings from Lisberger [69] who proposed models involving plastic elements in the brainstem which contribute to the cerebellar modifications.

We proposed the idea that, in fact, the plasticity of the VOR does not involve only low level mechanisms which require the presence of conflicting stimuli acting in sensory motor loops. We demonstrated that a clear adaptation of the gain of the VOR could be obtained by *mental effort*. This result was, to my knowledge, the first experimental demonstration of a direct effect of motor imagery on a neural process which had been attributed so far to direct sensory-motor interactions. However, the precise mechanisms which would underlie this effect were not investigated. I proposed subsequently a theory [5] which can be formulated in the following way: during prism adaptation, the brain recognises, by error detection, that the VOR, the basic reflex, is non functional. It then shuts off the reflex by cerebellar mechanisms as it is well known that there is a mechanism for visual suppression of the VOR which involves the flocculus of the cerebellum. The inhibitory nature of the cerebellar output is well suited for this parametric suppression of the VOR. Then, having suppressed the non-functional VOR, the brain replaces it by another type of eye movements and creates a PSEUDO-VOR produced by the pursuit or the saccadic system. The eye is then driven by an internal representation of the target which drives the pursuit or a succession of blended saccades which resembles a reversed VOR. This theory which I have called the 'saccadic substitution hypothesis' has been confirmed recently by the fact that in hemi-labyrinthectomised patients who show an apparently compensated 'VOR' at low frequency, the real VOR tested with rapid head shakes and the measurement of the gain within the first 30 milliseconds, is not compensated. The eye movements made by these patients during the low frequency VOR test could very well be a movement created by an internal representation of the target driving a pursuit of this target in darkness because we know that it is not necessary to have a physical stimulus in order to trigger a pursuit (as demonstrated by the work of Grüsser on sigma OKN) (see review in [43]). Therefore, as long as the brain could reconstruct internal target motion from the information of the remaining labyrinth a pseudo-VOR could very well be generated. These results support the idea of the existence of some mechanisms which can allow the internal simulation of movement without execution which in turn suggest that some gating mechanism will prevent execution.

3. The saccadic system: a model of hierarchical gating

One of the most important elements of the repertoire of motor behaviour is visual exploration. This fundamental behaviour is performed by a very simple movement: eye saccades. But this apparently simple movement is in fact an extremely interesting model for the study of motor selection and gating, in other words of decision making. If, as Yarbus [111] first did, we ask a subject to look at a lady's face and pay attention to whether this lady is rich or is sad, or if now we ask the subject to look at a landscape and analyse the scene to find if there are animals or trees, or if the sky is clear, the 'scan-path' of saccades will be different in these different cases. Complex cognitive decisions have to be made in order to scan a part of the face or the scene.

Eye saccades are fast shifts of eye position produced by the oculomotor system. They are obeying to several constraints which have been documented in the literature. These constraints relate their amplitude to peak velocity and duration, this is called the 'main sequence', and they are also constrained geometrically in the three dimensional space by Donders law which states that saccades are constrained to two degrees of freedom, or the more recent formulation as Listing's law which states that the axis of rotation of all saccades are located in the frontal plane. Each saccade is composed of a rapid movement sometimes followed by a slower adjustment of the eye displacement which can be followed by a corrective saccade.

Horizontal saccades which involve the lateral and medial recti muscles are subserved by a distinct neural mechanism. Without entering the details of the neural mechanisms which lead to the production of saccades we shall examine the various stages of saccade production in order to gain in overall view what we loose in the fine grain of our analysis. We shall examine this system starting from its output stage: the brainstem and moving up to the cortex. This bottom-up method of description will allow us to point out to the successive stages of inhibitory gating which can contribute to the hierarchical selection between mental imagination and motor execution.

3.1. Brainstem mechanisms

The saccade is produced by a pulse step discharge of extraocular motoneurons. This discharge is induced by a single premotor mechanism [7,16,27,45,56,73,74,100,102, 103,112] which is the discharge of 'excitatory burst neurones' (EBNs) and their inhibitory counterparts 'inhibitory burst neurones' (IBNs) [112], located in the pontine reticular formation for horizontal saccades and in the mesencephalic reticular formation for vertical saccade. The EBNs activate an integrator circuit whose exact nature is yet unknown but which involved certainly a structure called the nucleus prepositus hypoglossi whose function in eye movement control has been discovered by Baker and Berthoz [3]. It is the combination of the burst produced by the EBNs and the tonic component of the tonic (T) premotor neurones which produce the adequate motor discharge of the extraocular motoneurons during a saccade. It is important to note that the final common premotor interneuron for saccades are the EBNs. They receive descending activation from neurones (T long lead bursters: TLLBS) located in the intermediate layers of the superior colliculus [70,71], which may be either direct or through local so called long lead bursters.

A second group of neurones which controls ocular motoneurons during saccades is composed of so-called 'reticulo-spinal' neurones (RSNs) whose soma is located in the reticular formation surrounding the abducens nucleus. These neurones have been studied by morpho-functional techniques which allow the complete description of both their morphology and firing rate characteristics [8,40,41]. Some of them project to both the abducens nucleus, to several centers in the brain stem which are implied in eye movement control, and the spinal cord. Therefore they subserve the ipsilateral orienting synergy of the eye and the head during orienting movements. They are eye-head coupling neurones (ENRSNs).

Others only project to the neck and produce phasic eye head movements (NRSNs). They play for the neck the same role as the EBNs for the eye, that is they have a firing rate related with eye (or most probably gaze) velocity and can be therefore called 'neck bursters'. As most species have coupled eye and head movements during rapid orienting movements in the horizontal plane these neurons are a fundamental component of the orienting synergy.

The important point for the present set of ideas is that this immediate premotor machinery is under control of a locking neuronal device called the 'pause neurones' [18]. These neurones are located in the midline of the reticular formation rostrally to the abducens nucleus. They have been also called the 'omnipause' (OPN) neurons because they pause for all saccades in the horizontal direction. They discharge tonically and are inhibitory in nature. They inhibit the EBNs and possibly the RSNs. How is pause neuron activity suppressed therefore opening the gate for a saccade to be executed? Pause neurons have been shown to be involved in the eye fixation mechanism and they receive a direct excitation from the fixation zone of the superior colliculus [78]. This disinhibiton could be also triggered directly from the frontal eye field by the excitation of another inhibitory interneuron located in the brain stem [95]. Therefore saccade execution would also require the excitation by FEF neurones of an inhibitory interneuron which inhibits the inhibitory pause neuron thus releasing the EBNs, IBNs, and probably RSNs from their tonic inhibition.

The exact relation between the pause neurons and the two categories of RSNs has not yet been precisely determined but one can suppose that the inhibitory control exerted on ENS by OPNs must have some equivalent for RSNs, and that in fact some subtle inhibitory gating allows the brain to play on the 'triad' of neurons: EBNs (eye only movements), ENRSNs (coupled eye and neck) and NRSNs (neck only) which constitute at least a part of the final motor synergy for the control of gaze.

The first point I want to make here is therefore that supra brain stem neuronal centres involved in the production of saccades can be activated, but if the pause neurones continue to fire, eye or head saccades will not be executed because of the inhibitory gating by pause neurones at this immediate premotor level. We have here a mechanism which can allow the brain to internally simulate an orienting of gaze without execution. The decision to make a saccade can be implemented by the release from premotor inhibitory gating.

It should be also noted that the RSNs are under control from both the cortex and the cerebellum (whose output is itself inhibitory) and that a cascade of inhibitory gating mechanisms may therefore be also involved at this premotor level.

3.2. Spatial and temporal gating on retinotopic maps of the superior colliculus.

We shall now turn to the next level at which selection can be made. It is known that the intermediate layers of the superior colliculus contain efferent neurones, in the cat these neurons have been identified [42] and called tecto-reticulo-spinal neurones (TRSNs), they project to the brain stem and spinal cord and are premotor during saccadic eye movements. Several kinds of neurones have been described by Moshovakis et al. [70,71] and others [100,107–110] in this category, which differ by their somatic or axonal characteristics and also by their physiological properties. In the monkey there are mainly two types of efferent tectal cells called TLLBs and TRSNs: TLLBS are T cells, that is they are small, with sparse dendritic trees, thin axons, they deploy recurrent collaterals, a commissural collateral, and they project to five places in the brain stem (NRTP, NRPo, EBN area, IBN area, OPN area). In contrast TRSNs are X cells, that is they are big, with large complex dendritic trees, large axons no commissural collaterals, no recurrent collaterals an they project to most places in the brain stem.

The exact mechanisms of their contribution to the generation of saccades is still controversial but a consensus has been reached concerning the fact that, at least for part of these neurones, they project to the brain stem and constitute the input to the EBNs and RSNs involved in the production of the saccade. Each of them constitutes a motor vector [33] in the sense that the geometry of the saccade which will be triggered by any neurone is determined by the axonal connectivity of the TRSNs in the brain stem and/or mesencephalic saccade generators [39–42].

Geometry is therefore coded by axonal geometry. The remarkable property which I would like to stress is that these neurones are organised in a retinotopic map which is in register with the superficial layers of the superior colliculus. This motor map is under inhibitory control from the substantia nigra (SN). This inhibition has been discovered in the rat [22], and in the cat [46]. Its physiological properties have been extensively studied in the monkey by Hikosaka and Wurtz [50] who showed that their is a clear relation between the pause of the SN cells and the activity in the neurons of the superior colliculus which are involved in the generation of saccades. Deniau and Chevalier have, in addition, shown that the projection from the SN to the superior colliculus is very precisely organised and it can therefore be supposed that the SN exerts both a temporal and a spatial selection of the triggering and production of the saccade by SC neurones. The control of saccade execution at the level of the superior colliculus involves a second mechanism: a group of neurones located at the rostral pole of the superior colliculus fires during eye fixation [75,76]. This group of neurones probably projects to the brainstem neurones involved in the blockage of the saccade (pause neurones) but it could also inhibit the collicular map. The exact nature of the mechanism subserving gaze fixation is not elucidated at this moment but it is important to note that saccade execution is gated at the level of the SC by these two mechanisms: active inhibition from the substantia nigra and eye fixation by the fixation neurones probably also acting through inhibition.

At the level of the SC what we may call a spatio-temporal decision is therefore elaborated which allows 'selective attention' to be shifted to a given zone of space. This attentional mechanism is certainly quite motor in essence and it could be argued that this is not really attention but rather motor preparation. However, the selection by disinhibition on the colliculus intermediate layers and the enhancement of the response to visual stimuli noted long ago by several authors seems to belong to a basic mechanism orienting attention to a important source of interest in the world. This orienting reaction is by no mean a simple visual reflex, it involves a high degree of multisensory processing [68,108], and also probably high level mechanisms among which even the hippocampus may contribute for the detection of novelty and the suppression of the orienting reaction when habitual stimuli are presented. The idea of the similarity between the mechanisms of selective attention and the orientation of gaze shifts have also been proposed recently by Rizzolatti et al. [88,98,105] who have also insisted upon the role of the caudate-nigro-collicular inhibitory chain in the modulation of activity during attention shifts and have attributed a role to this mechanism in the observed deviation of saccades when attention is re-allocated to a spatial location different from an initial target.

3.3. Inhibitory control of the SN spatio-temporal selection by the striatum.

A third level of saccade selection is provided by an inhibitory action of caudate neurones. Hikosaka and colleagues have studied the physiological properties of the caudate long lead burster neurons which fire before saccades [47–49]. They have shown that a particular set of saccades (and in particular saccades from memory) can only be triggered if caudate neurones (themselves activated probably by frontal eye field neurones) inhibit SN neurones, which, in turn induce a disinhibition of SC neurones, which themselves excite EBNs if inhibitory pause neurones are inhibited. It has been shown that caudate neurones fire during memorised saccades and are probably involved in cognitive control of saccade initiation. We have therefore another fine cascade of inhibitory mechanisms which may play a role in the decision processes of saccade planning.

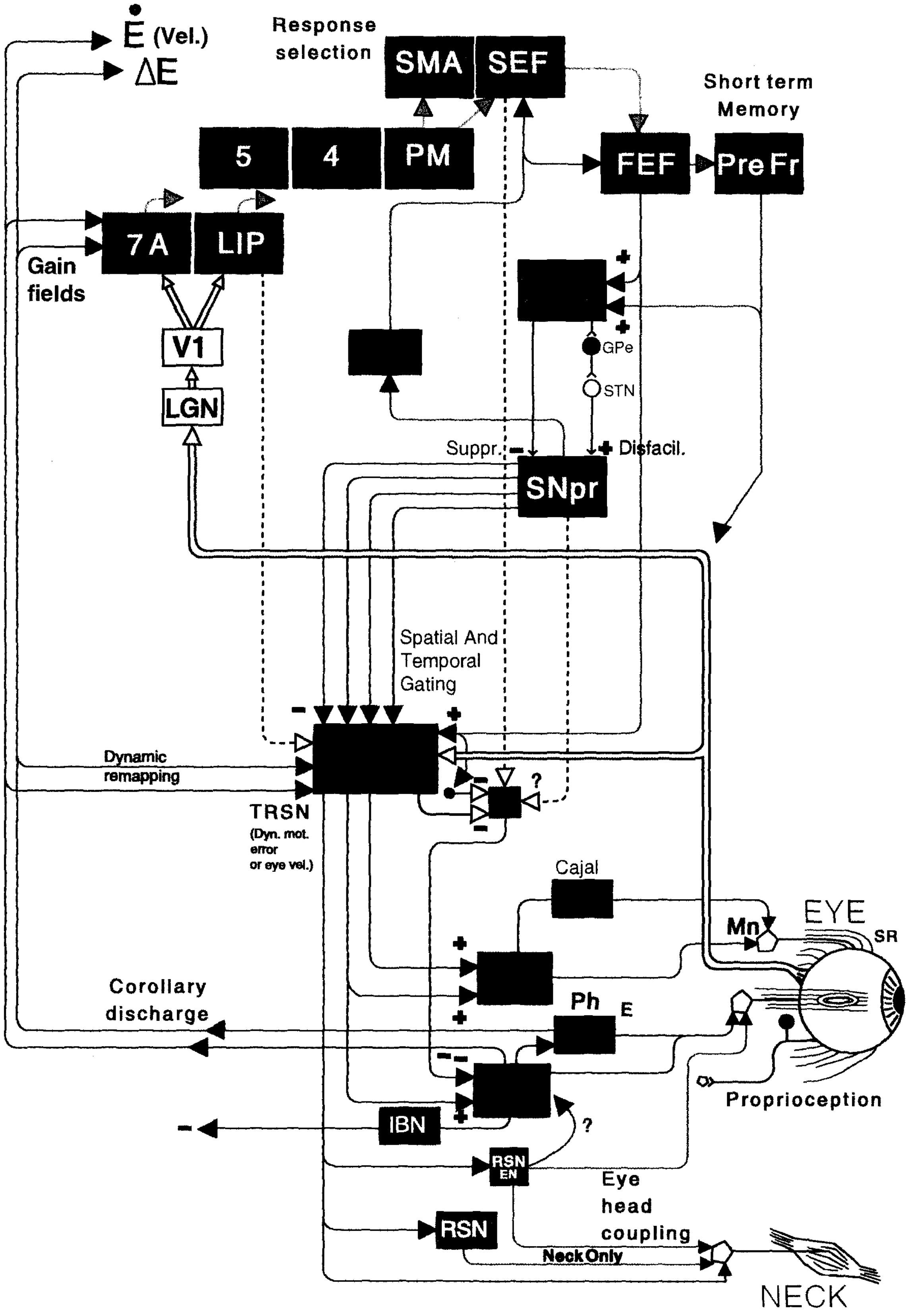
But the gating process is even more complex and subtle. Recent discoveries have shown that, in parallel to this 'selection by suppression' mechanism involving the caudate and SN, a second cascade of inhibitions and excitations produces a selection. This pathway which goes through the sub-thalamic nucleus is composed of the following neurones (see Figs. 1 and 2): an inhibitory interneuron located in the striatum which projects to the external globus pallidus (Gpe) on another inhibitory interneuron which projects in turn to the sub-thalamic nucleus. The target neuron in this structure is excitatory and projects to an inhibitory neuron in the substantia nigra which suppresses the activity in the superior colliculus intermediate layers. The action in this pathway is therefore the following: activation of the input neuron produces an inhibition of the GPe neuron which releases activation from the subthalamic neuron which increases nigral inhibition thus producing a suppression on the SC neurons. It has been shown that subthalamic neurons maintain a tonic discharge when the animal is fixating a target that anticipates a reward. Inhibition is then not only there for reciprocal inhibition, or for blockage of reflexes during voluntary action, or for selecting on line the adequate synergy, it could be used for preventing execution of movement in order to allow internal simulation of the planned movement and internal testing of its potential consequences. It also is probably essential in learning and subtle modulation of the various components of the motor system. The brain becomes like a chess player who can predict several moves ahead what may be the consequences of his actions and modify his plans accordingly.

Another very important property of these inhibitory cascades is that at each stage the presence of inhibitory interneurons allows for influences from other parts of the brain to modify the transmission. Evidence from the cerebellum, the hippocampus and the model of the inhibitory Ia interneuron in the spinal cord, which is one of the rare inhibitory neurons well studied, shows this fundamental role of inhibitory interneurons in integration of multiple inputs.

3.4. Inner loops and decision

In the introduction we have reminded the reader of our previous theoretical proposal of 'inner loops contributing to a projective mode of movement control'. This part of our theory has obtained recently some support from the discovery of the potential important functional role of such circuits as the basal ganglia-thalamo-cortical loops. This suggests that saccades are not produced by simple sequences along sensory to motor circuits but that 'internal circuits' such as the basal ganglia-thalamo-cortical loops [1] which are organised in modular loops related to several motor or behavioural functions and, as far as the 'oculomotor loop' is concerned probably play a fundamental role in the elaboration of oculomotor strategies. This concept of inner loops in which activity can be sustained provides also a new view concerning the way decision processes can be made.

The interesting contribution to our theory brought about by Hikosaka is that he has also proposed a theoretical circuit by which reward can influence the basal ganglia-thalamo-cortical loop involved in the regulation and selection of saccades. In his view the basal ganglia act as co-ordinators for the mutual interplay between the various cortical areas involved in the elaboration of a motor strategy. These areas would be functionally connected by reward-based learning. The outputs from these independent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ΔE
Response selection
SMA
SEF
Short term Memory
5
4
PM
FEF
Pre Fr
7A
LIP
Gain fields
V1
LGN
GPe
STN
Suppr.
Disfacil.
SNpr
Spatial And Temporal Gating
Dynamic remapping
TRSN
(Dyn. mot. error or eye vel.)
?
Cajal
Mn
EYE
SR
Ph
E
Corollary discharge
Proprioception
IBN
?
RSN EN
Eye head coupling
RSN
Neck Only
NECK

Fig. 2. Are the same structures activated during imagined and executed movements? Positron emission tomography picture of the CBF activation map of cortical sites during both executed and imagined voluntary saccades. The maps were obtained at two different brain levels and superimposed on his corresponding axial MRI slices. Slice levels are 56 mm (top) and 42 mm (bottom) above the bi-commissural plane. This single subject was shown a visual fixation point and was asked to perform first horizontal self paced saccades. Blood flow evaluated by standard techniques using oxygen-15 was compared with a rest condition during which the subject fixated the visual target. Colour scale represents CBF increase in pixel counts normalised by whole brain counts. R: right; L: Left. The subject was then asked to fixate the visual target and simulate mentally imagined saccades similar to the previously executed ones. Eye movements where measured by electro-oculography. This picture shows that in both cases the supplementary motor area (SMA) and the frontal eye field (FEF) were activated. The precision of the technique does not allow for a dissociation between several subparts of the SMA or FEF. (From Lang, W., Petit, L., Höllinger, P., Pietrzyk, U., Tzourio, N. Mazoyer, B., Berthoz, A., *Neuroreport*, 5 (1994) 921–924.)

Fig. 1. Schematic representation of the main levels which underly the production of orienting eye and head movements. The purpose of this diagram is not to show the detailed neuronal circuits which underlie saccade or head movement generation but to support the idea that the decision to make an orienting movement with the eye or with the head, or both, is taken through a hierarchy of parallel excitatory and inhibitory mechanisms. The eye saccade is produced by excitatory burst neurones (EBN) located in the pontine and mesencephalic reticular formation. EBN-V and EBN-H indicate the immediate premotor burst neurones which provide the velocity gaze signals to the eye. The saccadic integrator is indicated by the symbol ($\int$) only for EBN-H. Note that the information on eye displacement (ΔE) and eye velocity $\dot{E}$ is sent through ascending pathways as a corollary discharge of the premotor elements. The discharge of EBN-H is under inhibitory control from the pause neurones (P) which constitute a temporal gating device located at the immediate premotor level. Therefore the cortical and collicular circuits can be activated but the execution of the saccade is controlled by this premotor lock. Pause neurones are themselves inhibited probably by two parallel routes. One descending directly from the frontal eye fields (FEF) the second descending from the rostral pole of the superior colliculus (in the monkey). However, the exact mechanism underlying fixation is not known. A second level is represented by the superior colliculus (SC) which mediates visually guided saccades and also some saccades from memory. Intermediate layers of the SC contain tecto-reticulo-spinal neurones (TRSNs) which project to the pontine and mesencephalic saccade generators. Saccade initiation by these neurones is only possible if the tonic inhibition exerted by the substantia nigra pars reticulata (SNpr) on the SC map is suppressed. The SNpr exerts a spatial and temporal selection on this map. The SNpr is itself under inhibitory control from the caudate nucleus (Caud). In addition to this inhibitory cascade a second one which is not shown her has been found to be mediated through the sub-thalamic nucleus. The diagram also shows that the basal ganglia structures involved in orienting movement generation are part of cortico-thalamo-basal ganglia loops which probably allow internal simulation of some aspects of the movement. Cortical structures involved in eye movement generation are indicated schematically. Several structures probably involved in the internal mechanisms responsible for saccade generation and control and for reafferent information useful for the adjustment of saccade direction and amplitude are not shown (Cingulate cortex, Pulvinar etc...).

cortical areas would converge on the basal ganglia at the beginning of the learning. During learning an association between the motor convergence and the reward signals coming from the limbic system would select at the level of the basal ganglia only those combinations of cortical inputs leading to reward.

3.5. Cortical selection mechanisms

3.5.1. FEF

Although, from what precedes there are several subcortical mechanisms for the selection of saccades, it is also clear that cortical structures play an essential role in this process. In addition to the direct influence of the FEF on the local brain stem gating mechanisms through the omnipause neurones [95], the FEF can also act through the caudate-nigral-collicular inhibitory cascade. It is known from monkey recordings that the FEF contains a variety of neurones among which 'fixation neurones' [14,15,23,35,96]. It can also act through the group of neurons in the rostral pole of the SC which are active during fixation. The FEF could also contain a dual organisation, like the superior colliculus, with possible inhibitory interconnections between the neurones involved in fixation and in saccade generation. In humans the involvement of the FEF, whose location has been found in the anterior part of the precentral gyrus, has been shown in visually triggered saccades [25], simple voluntary self-paced saccades in darkness [81] as well as in imagined saccades [61] and during fixation of an imagined target [83]. In addition it is also involved in memorised sequence of saccades [9,82].

3.5.2. SMA-SEF, Pre-SMA-SEF

Another important cortical structure for the organisation of saccades is the dorso-medial frontal cortex: the supplementary motor area (SMA) is known to be important for the generation of complex sequences of movement and probably participates in the preparation of movements [59,60,104]. Within this area more precisely the supplementary eye field (SEF) described in the monkey [92], is concerned with the generation and control of eye movements. Recent studies in humans [31,32,84–86] have shown that the SMA-SEF is indeed activated during several kinds of eye movements, simple voluntary self-paced saccades in darkness [81], imagined [61] and memorised [9]; data from patients with focal cortical lesions have shown that although the FEF seems to be crucial for visually guided saccades, the SMA is essential for the generation of memory guided sequences of saccades [84]. The SMA-SEF therefore seems crucial for the organisation of complex oculomotor 'scan-paths' to either visual or memory-guided saccades. However recent anatomical studies have revealed a dissociation between a SMA proper and a pre-SMA region [101]. The precise neuronal link to the sub-cortical structures still has to be discovered but it should be remembered that an 'oculomotor' basal ganglia-thalamocortical loop involving the SEF has been described anatomically by Alexander and Strick [1].

3.5.3. Parietal cortex

In a recent set of studies we have compared, with the PET technique, voluntary simple self-spaced saccades in darkness with imagined saccades and with the reproduction, in total darkness from memory, of learned sequences of five saccades to visual targets in the horizontal plane [9]. In this last paradigm the subjects first viewed five visual targets which were aligned in the horizontal plane and were illuminated randomly in sequence. The subject had to remember this sequence and to repeat the five saccades in total darkness. This task therefore involved spatial memory and the organisation of a complex sequence of saccades. The PET activation measurements were only made during this part of the experiment, that is during the reproduction of the prelearned sequence of saccades. The interesting result is that the posterior parietal cortex, which had not been activated during any of the other saccades paradigms of self-paced executed or imagined saccades in darkness [61,81–83], was only activated during the execution of this memorised sequences of saccades task. The activation is particularly centered on the intraparietal sulcus and extends towards the superior parietal cortex. The activation was bilateral. Recently a bilateral activation of the superior parietal cortex has been described [2], during the execution of visually guide saccades although previous activation studies had not shown any activation of the parietal lobe during visually guided saccades [25]. An activation of the superior parietal gyrus and intra-parietal sulcus during the repetition of a sequence of finger movements [97] and the activation of the superior parietal cortex during the execution of hand movements in darkness [21] have also been described.

These findings suggests that an inner loop is activated to recall the remembered positions of the target in space and that the parietal cortex is activated together with other structures. Activity related to delay in an oculomotor task has been recorded by Gnadt and Andersen [34] in the intraparietal sulcus in the monkey. In humans, Pierrot Deseilligny et al. [86] have shown deficits of memorised saccades in the case of patients suffering from lesions of the posterior parietal cortex. Although we did not see any activation of the hippocampus in the PET experiments is could be suggested that this structures could be also activated and that the parieto-fronto-hippocampal circuit would be instrumental in this short term memory recall task. Recent data from Pierrot Deseilligny et al. [87] which demonstrate a strong deficit in a memorised sequence saccade task in patients with focal lesions of the medial temporal lobe support this idea.

The detailed neuronal mechanisms involved in these selection processes are not known but I would like to predict that, here again, in addition to excitatory mechanisms, inhibition will be a major component of the selection.

3.5.4. Superior dorso-lateral frontal cortex

In humans, Guitton et al. [44] showed that patients with frontal lesions have deficits in the performance of the 'anti-saccade task': in this task the subject is asked to make a saccade in the opposite direction to the location of the visual target, therefore combining a 'no-go' instruction to a decision to go in the opposite direction. Since this pioneering experiment several other results have indicated the role of the frontal and prefrontal cortex in complex decision processes of saccade generation. Patients with frontal lobe lesions show impairment in the predictive aspects of saccade generation [57]. In addition, schizophrenic patients have been shown to have deficits in anti-saccade tasks and in delayed oculomotor tasks [36,79] and high levels of 'distractibility' [58] which may be taken as an indication of a lack of capacity to select and decide for a motor strategy. However the exact location of the regions involved in these high level processes is not well defined and only recent studies using brain imagery techniques have started to bring some information concerning the function of frontal and prefrontal areas in humans.

Using the PET technique we have found an activation of the superior dorso-lateral frontal cortex during the execution of prelearned saccades sequences which was described above. In this task the subjects view five visual targets which were illuminated randomly in the horizontal plane in front of them and repeated the sequence from memory [9]. We have already discussed the fact that the parietal cortex was activated during this task. The activated area in the superior dorso-lateral frontal cortex corresponds to area 6 of Brodman rostral to the pre-central gyrus. It definitely is distinct in humans from the frontal eye field which lies in the anterior part of the precentral gyrus as mentioned above. The activation of this area has not been seen in any other types of saccades in darkness. It has, however been already found in activations studies involving prelearned sequences of movements of the fingers.

3.5.5. Pre-frontal cortex

We have seen above that non-reflexive eye saccades are therefore produced by neural mechanisms which involve several parallel loops arranged in cascade in such a way that excitatory processes are inhibited at several levels. This allows an internal simulation of eye movement even in the absence of overt saccades. Such a multilevel inhibition of the process allows spatial and temporal selection and internal predictions which are the mechanisms which give an overt impression of a unified decision. In this process the prefrontal cortex, although probably important in some higher level decisions, is only one of the areas in which decision occurs.

It is now clear that the prefrontal cortex participates in the decision to launch a movement. Evidence for this function has been recently brought by Sasaki et al. [90,91] who have recorded from field potentials in the monkey and EEG and magnetic fields in human subjects. They found 'no-go' potentials in the prefrontal cortex of the monkey in a go/no-go hand movement task with discrimination between different colours or sound stimuli. Similar no-go potentials where recorded from the human scalp.

The prefrontal cortex should, of course, be considered as a major component of cognitively driven decisions in visuo-motor exploration together with the temporal lobe [77]. This is suggested by a number of results on animals and humans. The prefrontal cortex is involved in working memory. The initial neurophysiological evidence comes from single unit data from Funahashi and his colleagues [28–30] who discovered three principal kinds of neurones: (a) neurones that register the stimulus to be recalled; (b) neurones that retain the information on line; and (c) neurones that use the information to guide the appropriate response in direction and timing. In addition a partial lesion of the dorsolateral prefrontal cortex in one hemisphere can disrupt the performance in an oculomotor delayed response task particularly under circumstances of memory guidance. The same lesion has little effect when the eye movement is guided by external cues. Therefore the prefrontal cortex may not only be involved in visual representational memory or, as suggested recently by Israël et al. in vestibular representational memory but also in the capacity to select proper sequences of motor actions. Data from Joseph and Barone [55] and more recently by Boussaoud et al. [12,13] concerning the premotor cortex indeed point in this direction.

Only future detailed electrophysiology will reveal the neuronal mechanisms underlying this selection by prefrontal cortex. It is most probable that, here again a combination of inhibitory cascades and excitation will be found.

It should be pointed out that the involvement of the prefrontal cortex in decision processes cannot be separated from other neural centres involved in the inner-loops along which spatial perception and movement control are simulated: for instance, as mentioned above, a recent PET study has revealed that during the execution of internally generated sequences of memorised saccades the parietal cortex, which was not activated by simple voluntary saccades in the dark, is activated together with the dorso-lateral frontal cortex [82].

3.6. Cingulate cortex

In addition the data we have obtained suggest that the cingulate cortex is involved in the organisation or in the control of internally generated saccades. Several recent results obtained either in the monkey or in man with imaging techniques have provided new evidence that the several sub-parts of the cingulate are involved either in the post-saccadic adjustments, or in internally generated movements [26], or in cognitive tasks involving internally taken perceptual decisions. We could therefore suppose that the cingulate cortex is an essential station of the structures involved in «internal loops» in which movement or action are simulated either during or in absence of execution. However more detailed experimental work is necessary to understand the role of the various parts of the cingulate cortex.

4. Conclusion: do imagined movements utilise the same structures as executed movements?

According to our theory which proposes the idea that the brain is a simulator whose capacities for anticipating the future consequences of action have improved during evolution, the same central neural networks should be involved both in imagined and executed movements. Motor imagery would not be a special process but only the manifestation of the normal internal simulation which accompanies the planning and execution of movements. In order to test this hypothesis we have conducted an experiment in which subjects were asked to produce saccades to imagined targets. This work leads to the conclusion that the SMA, FEF and cingulate cortex were activated during this tasks and that apparently the same parts of these structures were active. This results is in good agreement with the work by Decety et al. [19,20] on imagined movements. However the precision of PET does not allow us to exclude the possibility that discrete areas within these regions, or even different types of neurones are activated during these different tasks. In fact only experimental results on monkey neurones will be able to settle the question. Recent PET data [101] suggest that the pre-SMA would be involved during mental rehearsal or imagination of finger movements and the SMA proper during executed movements thus proposing a dissociation between the different areas involved in imagined versus executed movements. The role of the pre-SMA in motor planning and selection has also been confirmed in humans by a functional MRI study (Deiber et al. 1995, Human brain mapping, Suppl. 1, 310).

Obviously more empirical data concerning the detailed neuronal mechanism at cortical level is needed before a definite theory can be proposed. My personal feeling is that these questions will only be solved if we can apply at cortical level the morpho-functional approach that has been employed for the brain stem and basal ganglia in order to define in well identified neurons the participation of excitation and inhibition in these processes.

Several questions need also to be answered. One of them concerns the origin of the information about the consequences of imagined or preplanned actions because this information is necessary for the anticipation of the outcome of intended actions. The problem is therefore to know if some of the feedback loops which carry reafferent information about the executed action can be used by the ‘projective mode’. The role of structures such as the pulvinar and the posterior cingulate cortex have been suggested as mentioned above. It would be, however, interesting to know if their is a mechanism to simulate at higher levels the lower (motor) level operations or if mental simulation of a movement requires the activation of the premotor structures.

If, as believed by several authors, the brain stem contains internal models of the eye plant, imagined eye movements could be simulated by activating all the network but the pause neurons would just prevent the final executory level.

My suggestion is that there is not a simple dichotomy between imagined and executed movements. The present theory says that there is a hierarchical organisation using inhibition as a main mechanism, which allows gating of the execution at different levels of its organisation. This hierarchical gating is necessary because each movement is not made in isolation but is the result of a complex interplay of many dynamic processes that we have only started to understand.

5. Note added in proof

Two recent papers pertaining on the questions discussed here have brought evidence of the possible involvement of the basal ganglia and motor cortex in imagined movements. P.J. Dominey et al. (*Neuropsychologia* 33, 727–742, 1995) have found imagined finger movements of the affected hand in hemi-parkinson patients were slower than imagined movements of the non-affected hand. A. Sirigu et al. (*NeuroReport* 6, 997–1001, 1995) have found the same result in a patient with a restricted lesion of the primary motor cortex.

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