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Seeing and Acting at the Same Time: Challenges for Brain (and) Research

Minireview

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Traditionally, studies of the visual system of nonhuman primates have investigated neurons while the animal fixates a target in a static environment. Clearly, this is not what our everyday life is like; neither the environment nor we are stationary while we act in our world. On the contrary, we constantly move our eyes or limbs. Here we review a number of recent studies describing the brain in a more realistic mode of operation.

A number of seemingly trivial problems have to be solved for an everyday process such as finding the latest issue of *Neuron* on a bookshelf and grabbing it for reading. First of all, the eyes scan the scene to find the journal. During each eye movement, the whole visual scene sweeps across the retina at high speed, and after every eye movement, the images of the books on the shelf occupy a new position on the retina. Consciously, neither the motion nor the displacements are perceived: the world is stable. After having localized the "target," we have to reach for it. This is anything but trivial, since the reference frame in which the target is encoded—the retina—is different from the effector's reference frame—the hand. Several elegant recent studies have overcome some of the technical difficulties inherent to studying the brain in an active, exploratory mode that is more akin to everyday life. These results have contributed greatly to our knowledge of how the visual system, and the posterior parietal cortex (PPC) in particular, represents space during scanning of a visual scene and during the preparation and execution of a movement.

Scanning movements change the position of the world's objects on the retina and induce retinal smear, but both go unnoticed. Helmholtz suggested that the perceptual stability in the presence of eye movements could rely on an internal monitoring of an ongoing or planned eye movement (Helmholtz, 1867). Later on, von Holst, Mittelstaedt, and Sperry put this suggestion in a cybernetical context and coined such an internal monitor an "efference copy" or "corollary discharge" (Sperry, 1950; von Holst and Mittelstaedt, 1950). Sommer and Wurtz (2002) recently identified a possible neuronal analog of this corollary discharge in the macaque brain. In a first experimental step, Sommer and Wurtz demonstrated that neurons in the mediodorsal nucleus of the thalamus (MD) receive input from saccade control areas of the superior colliculus and project away from the motor systems toward saccade planning systems in the frontal eye fields (FEF). These MD neurons fire just prior to saccades. In a second experimental step, Sommer and Wurtz inactivated the MD nucleus and asked the animal to perform a double-step saccade task. In this paradigm, two visual targets are briefly presented, and the monkey is trained to saccade to the targets sequentially. Both targets disappear prior to saccade onset.

If the animal plans the two saccades in eye-centered coordinates, the saccade plan for the second target is invalid once the first saccade has been made. The metrics of the first saccade must therefore be taken into account to complete the second saccade to the right spatial location. Thus, an internal monitoring of the completed first saccade—a change of reference frame—is necessary. Sommer and Wurtz showed that muscimol inactivation of the MD nucleus causes specific errors in the double saccade task: the end-points of the second but not the first saccade are shifted in the direction of the retinal vector during target presentation (Figure 1A). This is consistent with the hypothesis that the MD thalamic nucleus keeps track of the ongoing eye movements and thereby effectively updates the internal spatial reference frame. Interestingly, Figure 1B shows that the first saccade, before inactivation of the MD, shows a vertical offset. In itself this finding is not new (Gnadt et al., 1991), but what is remarkable in this context is that this error in the first saccade is not corrected in the second saccade. This means that, at least in total darkness, the saccade planning and updating mechanism does not rely on the *actual* eye position but, rather, on the *intended* eye position, i.e., the motor plan. This fits well with previous reports on the saccade-related activity in the superior colliculus (SC), which show that these cells respond to the planned, not the actually executed, saccade. Other areas, such as the FEF, can overrule SC planning (Schlag-Rey et al., 1992) and may therefore also carry a representation of the actual eye movement. This could explain why inactivating the corollary discharge signal in the MD only causes about 20% of the expected error in the second saccade: other areas, including the FEF, could contribute the remaining 80% of eye position information. Tian et al. (2000) recently claimed that the FEF stores not just single saccades, but complete sequences of saccades. This provides further evidence for the controlling role of the FEF in complex eye movement tasks. Whether such sequences are planned in relative coordinates—obviating the need for a change in reference frame—or that planned sequences are updated within the FEF (possibly with signals arising from the SC and/or the MD) remains to be seen.

A saccadic corollary discharge signal such as that emanating from the MD thalamus could instruct the visual system to suppress its sensitivity and ignore upcoming retinal stimulation (Figure 2A). Psychophysically, this so-called *saccadic suppression* has been shown to lead to a 10-fold reduction in contrast sensitivity (Burr et al., 1994). Yet, vision is not completely abolished during saccades. First of all, humans' sensitivity

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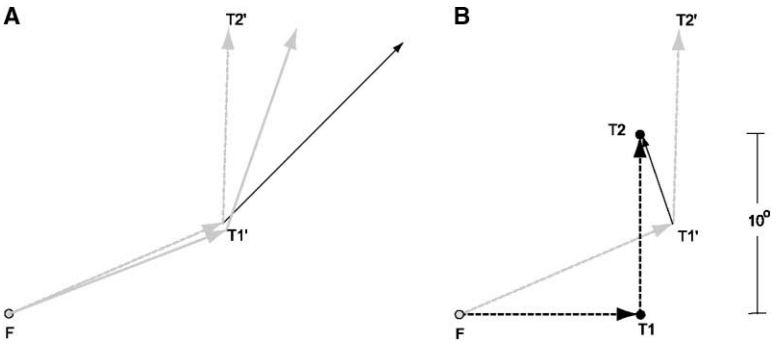

Figure 1. Double-Step Saccades

(A) Monkeys make saccades from a fixation point (F) to two remembered targets: first to T1′, then to T2′. The dashed gray lines show the average saccades with an intact MD. The solid gray lines show the performance with an inactivated MD. The first saccade (to T1′) is unchanged, but the second saccade is too far to the right, as if the monkey's knowledge of the rightward movement due to the first saccade was impaired. Sommer and Wurtz report that, on average, the effect of inactivation is about 19% of what would be expected if the first saccade were completely ignored when planning the second saccade (this situation is represented here by the solid black line). (B) A closer look at the saccades *before* inactivation. The monkey was instructed to make saccades to T1 and T2. Its first saccade, however, is inaccurate and shows an upward bias (T1′). If the monkey had access to the actual position of the eye, one would expect the second saccade to correct for the error in the first saccade and follow a trajectory similar to the solid line (possibly combined with an additional error component). Instead, the monkey saccades to T2′, following a vector that is very much like the vector T1–T2. This seems to indicate that the monkey's saccade plan assumes that the eye is at T1, suggesting that the saccade planning center has access to the *intended* rather than the *actual* saccade.

for stimuli typically processed by the magnocellular motion pathway is much more reduced than sensitivity for isoluminant stimuli typically processed by the parvocellular form pathway (Burr et al., 1994). Second, even motion can be perceived intrasaccadically if the stimulus properties are carefully chosen (Castet and Masson, 2000; Ilg and Hoffmann, 1993).

Whether changes in perception around the time of saccades are attributable to passive changes in retinal stimulation caused by the saccade itself or to an active extraretinal process that prepares the visual system to ignore saccade-induced stimulation is a topic of ongoing debate. Castet et al. (2002) argued that changes in the retinal input alone are sufficient to explain changes in perisaccadic perception. They first showed that a stationary low-spatial frequency grating, briefly flashed during the *first* half of a saccade, is perceived to move against the direction of the saccade. Second, they showed that this percept of motion is much reduced—even abolished—when the grating remains visible (and stationary) for a brief period after the saccade. Because the extraretinal parameters (the saccade itself) do not change between these two conditions, this experiment demonstrates that (passive) changes in the retinal input play an important role in the suppression of intrasaccadic motion perception. In this view, the presence of a stationary stimulus after the saccade masks the motion present during the saccade. On the other hand, Castet et al.'s data also show that a brief stationary stimulus, presented entirely intrasaccadically but in the *second* half of the saccade, is not perceived to move. In retinal terms, the only difference between these two conditions is that the first has an increasing velocity profile, the second a decreasing profile. To our knowledge there is no evidence to support the view that this retinal difference would result in a percept of motion in the former but not in the latter case. In our view, this difference in motion perception together with the stimulus-type specific reduction in contrast sensitivity (Burr et al., 1994; Diamond et al., 2000) point to the influence of an extraretinal mechanism.

Thiele et al. (2002) studied the neural basis of an extra-

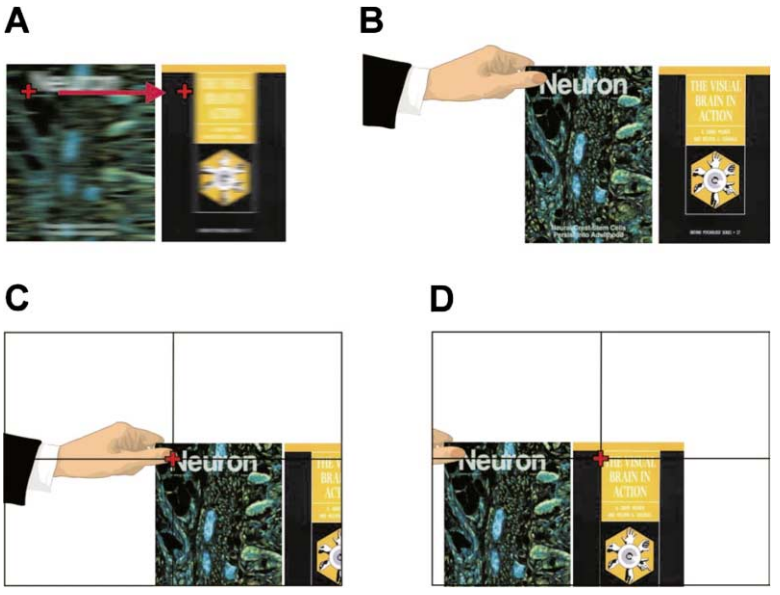

Figure 2. Vision during Eye and Hand Movements

(A) Retinal image during fast scanning eye movements. The saccade, as indicated by the red arrow pointing from one fixation location to the next, induces retinal smear, which perceptually goes unnoticed. (B–D) Reaching for an object as seen within different reference frames. (B) indicates the reaching as seen in an allocentric reference frame. (C) and (D) show the identical scene within an eye-centered reference frame (the red "+" sign indicates the fovea). The fixation location (+) changes between (C) and (D), while the reaching movement toward the book is the same. In (C), the origins of the eye- and hand-centered frame of reference are identical; in (D), they are different. In other words: the motor signals for controlling the reach are identical in (C) and (D), while the visual signals differ significantly.

retinal process of *saccadic suppression* in the macaque. They compared the response of neurons in areas MT and MST in two conditions. In the first condition, the monkey makes saccades across a structured background; hence its saccades create retinal motion. In the second condition, the monkey fixates a central target while the structured background is moved across the retina with a velocity profile identical to that of a saccade in the first condition. The retinal stimulation is identical in the two conditions; hence, any changes in the cells' responses must be due to extraretinal processes. Thiele et al. found that 35% of cells reverse their preferred direction of motion during saccades. They suggested that these reversed motion signals cancel out the motion signals arising from the nonreversing population and thereby lead to a reduced awareness of retinal motion. Such a competitive interaction between opposing motion signals is supported by the data of Qian et al. (1994), who showed that transparently moving objects cancel out each other's motion signals if they are in close spatial proximity. Thiele et al. also discuss another subset of cells: about 25% of cells respond when the background is moved but not at all during the saccade. A reduction in the response of some cells and the competitive interaction between other cells could be the reason why we do not observe the retinal stimulation that our eyes create while scanning the world around us; it is convincing evidence for an extraretinal neural mechanism of saccadic suppression.

A corollary discharge signal, similar but not necessarily identical to that in the MD thalamus, would likely be involved in transforming the ever-changing retinal position of objects to a stable percept of position. This process of coordinate transformations is normally flawless, as witnessed by the convincing perceptual stability of the world in the presence of about 200,000 eye movements per day. Only when objects are flashed briefly before or during a saccade can one observe cracks in this perceptual stability; such objects are mislocalized. This so-called perisaccadic mislocalization offers a tool to study the processes underlying perceptual stability (for a review, see Ross et al., 2001). Several authors have suggested links between perisaccadic mislocalization and the dynamic shape and position of receptive fields in various cortical areas. Duhamel et al. (1992), for instance, showed that some neurons in the lateral intraparietal area (LIP) respond to the presentation of stimuli at locations in space that will become the RF location of the cell after completing a saccade. Hence, such neurons shift their visual RFs to the new location even before the eyes have started to move. Similarly, Tolias et al. (2001) found that cells in V4 shift and shrink their receptive fields perisaccadically. As these studies did not explicitly address how these neurons represent space, the link with the psychophysics of perisaccadic mislocalization remains tentative. In a recent study, Krekelberg et al. (2003) showed that neurons in MT and MST accurately represent the position of flashed bars during fixation but that this representation is disturbed in the temporal vicinity of a saccade. They speculated that this disturbance is caused by the attempt of the visual system to suppress the visual motion signals caused by the saccade. In this view, perisaccadic mislocalization is a (undesirable) side effect of the (desirable) saccadic suppression. An important point all three studies make is that neurons' receptive fields, and thereby their representation of space, are not static entities but that they change around the time of a saccade to deal with changes in relevant reference frames and behavioral demands.

Coordinate transformations and changes in reference frames are equally important when visual spatial information is used for motor control. Let's assume we have localized the latest issue of *Neuron* on the shelf—now, how do we reach for it? The image of the target is encoded in retinal coordinates, while the movement of the arm must be encoded in the arm and hand reference frame. A recent paper may have an answer to the question. Buneo and colleagues (2002) trained their monkeys to make reaching movements during steady fixations. In the experiments, they systematically varied the initial location and the target location of the hand and the fixation location. This results in conditions that are identical in eye, hand, or body coordinates, or identical in both hand and eye or hand and body coordinates. As an example, for a given hand position, reaching for the journal on the shelf could require a hand movement up and to the right, regardless of whether one fixates the journal itself or the book standing next to it (Figures 2B–2D). In retinal coordinates, however, these movements differ. The former condition involves a movement toward the fovea; the latter does not. Buneo and colleagues recorded neuronal activity in parietal area 5 and showed that neural responses are most similar if the reach is the same in both hand and eye coordinates. In other words, given their stimulus configuration, there exist reaching movements with identical trajectories within the hand and the eye reference frame that, in turn, lead to the most similar neuronal responses.

This implies that the coding for visually guided, goal-directed hand reaching movements in area 5 of the monkey PPC is neither eye nor hand centered but in an intermediate frame of reference. Such intermediate representations may be preprocessing stages on the way to a representation in a single reference frame in other areas, but it is becoming increasingly difficult to interpret mixed reference frames as the exception rather than the rule. Theoretical studies in fact have shown that intermediate encoding schemes may be an optimal way to combine information arising from multiple frames of reference. Deneve et al. (2001) modeled coordinate transformations with networks of basis function neurons. In this context, a basis function neuron is a unit that responds only to stimuli in a fixed and restricted range of positions. In other words, it has a classical, retinocentrically fixed receptive field, and spikes from this unit are interpreted as evidence for the presence of a stimulus at the center of the cell's receptive field. This is an encoding assumption that is implicit in many studies: it presumes a labeled-line code, which appears to be violated in some areas across saccadic eye movements. Given this assumption, however, Deneve et al. showed that their networks provide a near-optimal way to implement coordinate transformations. Moreover, they showed that feedback between neurons that use different reference frames leads to an encoding in intermediate frames of reference. Given the ubiquity of feedback connectivity in cortical networks, this seems a reasonable hypothesis and one that could conceivably be

tested with an inactivation study in a prototypical sensorimotor region such as area 5.

Studies in awake monkeys on spatial action and perception have given us inspiring new insights into how the brain copes with the challenges posed by seemingly trivial everyday processes such as locating and reaching toward an object. Yet, this is only the first step toward a full understanding of the neural processes underlying sensorimotor transformations, and we have pointed out some of the issues that are still unresolved. It is promising, however, that with today's knowledge it is already possible, for example, to control artificial reaching devices with real neuronal data from, among others, PPC neurons (Taylor et al., 2002; Wessberg et al., 2000). The current level of technical sophistication and the increasing variety of methods in neuroscience allow us to study the brain in an ever more realistic mode of operation. We can now combine technical feasibility studies and theoretical insights with neural circuitry data from awake behaving monkeys and imaging studies in humans that demonstrate similarities and dissimilarities between the species. Eventually, these combined approaches should lead to a better understanding of how the brain manages to solve the challenges posed by everyday life.

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