The Saccadic System: A Neurological Microcosm

Familiarity can breed contempt: perhaps it is precisely because the saccade is the commonest movement we make – about three every second of our waking lives – that we rather take it for granted. Yet, apart from being a movement of extraordinary speed and elegant precision[1,2] (fig. 1), it not only determines absolutely what we are allowed to see, but precedes and prepares for nearly every directed action that we make. Research over the last couple of decades has demonstrated in detail the involvement in saccadic control of nearly every level of the brain, from the simple neural circuits in the brainstem reticular formation that ensure the saccade's remarkable technical performance, to neurons in frontal eye fields that help decide whether to look at one thing or another[3,4]. As a result we have a more detailed understanding of the saccadic system, in the sense of being able to relate structure and disorder of structure to quantitative measurements of function, than of any other sub-system of the brain. Because saccades are stereotyped movements, small deviations may carry immense clinical significance. As a result, recent technical advances (in making micro-miniaturised oculometers that store data for subsequent analysis by lap-top) have begun to turn this neurophysiological knowledge into clinical utility, inaugurating what may perhaps turn out to be a new era of genuinely *quantitative* neurology[5].

The saccadic hierarchy

There is an intrinsic three-fold hierarchy in any motor act, that can be summarised as *what, where, how*: recognition of a target, and decision; localisation and proprioception; and creation of the detailed patterns of forces needed for execution. This general principle of motor organisation is particularly clearly seen in the saccadic system[2,3] (fig. 2). At the lowest level are the neural circuits in the prepontine and mesencephalic reticular formation, close to the oculomotor nuclei, that generate the highly specific temporal patterns of firing by which the oculomotor neurons move the eye so precisely and rapidly to their new position. Above them, the colliculus primarily has the task of converting information about the visual location of an object into an appropriate command to the brainstem that will move the gaze to the same location; in this it is supplemented by the cerebellum and has assistance from the cortex. But in the real world we are seldom presented with just a single potential target: we must choose between many, and some will have more significance than others. This choice – deciding what to look at – is a function that culminates specifically in the frontal eye fields. All of these hierarchical levels have immense diagnostic potential; for instance, saccadic slowing characteristic of disorder at the lowest level may be a very early indicator of neurodegeneration[6]. But in this review there is only space to concentrate on the highest level, where recent work has used the stereotyped precision of saccades to discover a great deal about how cortical areas make saccadic decisions[7,8].

Latency: the measurement of decision

The two lowest levels of the saccadic hierarchy are in principle all that is needed to generate a saccade that lands accurately and swiftly on a visual target. In a laboratory situation, with single targets presented in the dark, that would be fine. But the real world is full of interesting stimuli competing for our attention. While the collicular level can localise visual targets, what it cannot do is *recognise* them, or evaluate their behavioural significance, for which the cortex appears to be necessary. Consequently, we find that the collicular mechanisms are tonically switched off by descending, ultimately cortical, inhibition, and only permitted to carry out their function when the higher processes of decision are complete. As a result, we have *procrastination.* The time between presenting a stimulus and starting to make a response – the saccadic latency – is far longer than would be expected from the speed of visual transduction, nerve conduction and synaptic action. Reaction time is decision time, and studies of how this latency varies with changing stimuli and circumstances – and in neurological disorder – have yielded much information about how these decision mechanisms work. The result is something called the LATER model: as well as recalling the procrastination the name stands for Linear Approach to Threshold with Ergodic Rate. This succinct but perhaps cryptic expression implies the existence of decision units, whose activity represents the system's degree of belief in different possible targets; at rest , their activity represents prior probability or expectation, and as sensory evidence comes that supports the belief, their activity increases linearly until it reaches a threshold, the point where it is so overwhelm-

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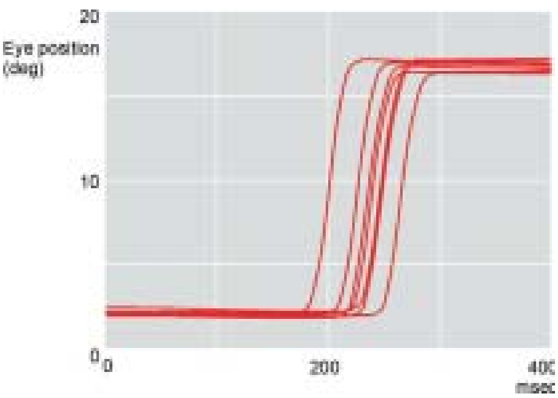

Figure 1.
A set of seven human saccades evoked by sudden movement of a target 15 deg to the left, showing that although these very stereotyped movements are rapid in the sense that the velocity of the eye is many hundreds of degrees per second, there is a long latency before the movement starts at all, that varies randomly from trial to trial.

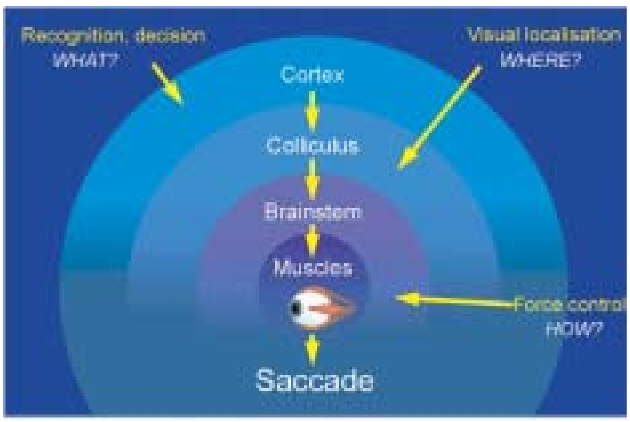

Figure 2.
The saccadic hierarchy. At the highest level, a target must be recognised and a decision made as to whether it is worth looking at; this decision gates the intermediate level, at which information about the target's location is translated into selection of an appropriate saccadic metric; and this in turn activates brainstem circuitry that elaborates the complex patterns of neural firing that throw the gaze efficiently and rapidly on to the target, as in figure 1.

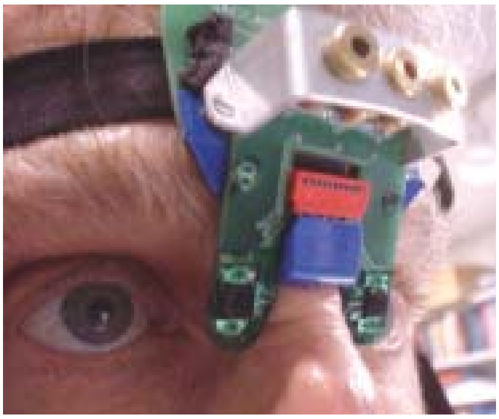

Figure 3.
A miniature, non-invasive saccadometer in use. In this prototype, stimuli are projected on to a convenient surface by the three miniature lasers at the top; a system of infra-red emitters and detectors monitors the ensuing saccades, the information being analysed and stored in a separate, tiny microprocessor unit which can subsequently communicate with the user's computer through an infra-red link.

ingly probable that action is justified, and initiated[9]. Such a system can be regarded as an 'ideal' decision device, in the sense that it makes maximal use of information to alter its estimated probabilities through an essentially Bayesian mechanism.

LATER seems to be applicable to all reaction times, whether saccadic or manual, and inaugurated by visual or auditory or even tactile stimuli, and provides quantitative predictions of what happens when expectations alter, when information is only partially available, or when a subject is under pressure to respond more urgently[10]. A well-known feature of latency is that it varies randomly from trial to trial, and this randomness seems to be created 'deliberately' by the brain. Because many such units, corresponding to different possible actions, normally race against one another, the winner determining the response that is finally selected, this randomness in timing results in randomness of choice, perhaps in order to make our behaviour unpredictable, and perhaps also to generate exploration and creativity[11,12].

Recordings from the frontal eye fields in monkeys have revealed a population of saccadic movement-related neurons whose activity is very similar to what was predicted by LATER[13]. Before a saccade, firing frequency rises steadily for 100-200 msec before the start of a saccade, the movement being initiated when the activity reaches a fixed threshold level; the rate of rise varies randomly from trial, in correspondence with the variability in the latency itself. LATER-like rise-to-threshold behaviour can be seen in many areas of the cortex in advance of motor responses, and may well represent something quite fundamental about how the cortex works.

Future developments

An attractive aspect of LATER is that the performance of the eye in terms of latency can be summarised essentially by just two numbers, which are in turn directly related to the parameters of the model itself. They represent the fundamental parameters that must be defined for any decision system: for example, whether speed is more important than accuracy, the relative weight to be attached to present rather than past information, and the degree of creativity (randomness). In the brain, these parameters clearly need to be regulated in some way, and an exciting possibility is that they might possibly be related to the several ascending systems – noradrenergic, serotonergic, histaminergic - that innervate cortex relatively diffusely from below[14,15]. The reason for having so many has always been a puzzle: if all they do is cause 'arousal' one would surely be enough. We hope soon to be able to establish whether defects in these systems do indeed cause the quantitative changes that LATER would predict. If so, the fact that miniature non-invasive devices for measuring eye movements (fig. 3), requiring practically no skill in setting up, will very soon be available at little cost and could revolutionise the diagnosis and monitoring of neurological impairment.

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For a case report on vertical supranuclear gaze palsy, see http://acnr.co.uk/case%20report.htm

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