view of the debate about what microsaccades, and saccades in general, contribute to visual processing. Ko et al.\textsuperscript{1} made the insightful argument that the value of microsaccades should be most apparent, not when a task such as needle-threading was nearly completed, but rather in the few seconds prior, when visual comparisons across small distances were most critical. In Ko et al.\textsuperscript{1} version of a needle-threading task (Fig. 1b), the ‘needle’ was a vertical bar with a narrow ‘eye’ displayed on a computer monitor. The ‘thread’ was a thin horizontal bar, located a half degree from the needle and moving toward it either at a slow, constant speed or (in a replication of previous conditions\textsuperscript{6}) under the subjects’ control. Ko et al. replicated previous results\textsuperscript{6,7}, finding that the frequency of microsaccades was smaller (by a factor of two) at the very end of the trial than at the beginning.

Ko et al.\textsuperscript{1} then repeated the experiment, this time allowing the subject to adjust only the thread’s vertical position and ending each trial when the thread was a scant 7 min of arc from the needle, when critical visual comparisons between thread and the eye of the needle were still very much underway. Saccades did not drop out of the eye movement pattern over time, but instead became smaller. By the end of trials (but before the thread intersected the needle), the frequency of occurrence of saccades smaller than 20 min of arc, which had been initially low (0.6 per s), increased to the level found during maintained fixation on stationary targets (about 1 per s). An increase in frequency was also found for a population of even smaller saccades (\textlessthan;10 min of arc); however, saccades this small were rare during either threading or fixation (0.2 per s).

Further analysis showed that the saccades were not simply random shifts of the line of sight, or movements designed to produce retinal image transients, but rather reflected the strategies of the task. Microsaccades (<20 min of arc) were made to look back and forth between needle and thread. In addition, any adjustments to the position of the thread were more likely to occur just after a microsaccade was made to look from the needle to the thread than after other possible transitions. After an adjustment in thread position, microsaccades were more likely to be directed to the thread (perhaps an attempt to evaluate the effect of the adjustment) than to the needle. These findings suggest that microsaccades are part of an active looking strategy, incorporating and reflecting the goals and plans of the task.

Ko et al.’s findings\textsuperscript{1} are important because they show that microsaccades are used precisely the way large saccades are, namely, to bring the line of sight to visual details that are crucial for the immediate task. These findings are unexpected because when visual details are of sufficiently high contrast, not obscured by crowding from neighbors and separated by less than half degree on the retina, it should be possible to perform the task without saccades. A judiciously chosen central fixation location should have provided the vantage point needed to evaluate the relative position of the critical details (needle and thread) and permit the appropriate adjustments. Further research using controlled, rather than spontaneous, fixation behavior should elucidate whether microsaccades (specifically, those smaller than 15 min of arc) are actually necessary or helpful in accomplishing the present task. Ko et al.’s results\textsuperscript{1} deal not with necessity, but with spontaneous behavior. Given the alignment task, the subjects preferred to make saccades. Why? What was the benefit of this strategy?

The same question can be raised about any saccade, regardless of size, when objects and details are large or vivid enough to be resolved using the visual periphery. Why bother to look around when vision is already good enough? One intriguing possibility is that the limitations that prompt the use of saccades in an environment where all the visual details are easy to see are cognitive, rather than visual. Perhaps we can only make one decision at a time. If so, saccades, be they micro or macro, are doing something in addition to improving spatial resolution. They are transforming the visual scene into a sequence of discrete views that focus our attention, decisions and plans on only one detail at a time\textsuperscript{8}. Ko et al.’s experiment\textsuperscript{1}, which deals with the smallest of voluntary human movements, sheds light on the larger connections between vision, thinking and action that underlie real-world activities.

How hard is the CNS hardware?

Martin E Schwab

A study in this issue reveals gene expression differences between neurons that do, and those that do not, show recovery-associated growth after stroke. The differentially expressed genes may provide potential therapeutic targets.

Stroke hits unexpectedly, like lightning, striking the farmer in a field during a hot summer’s day or the recently retired manager preparing for a stress-free life of enjoyment. Large strokes leave the sufferer hemiplegic and frequently, when the motor speech area is also affected, unable to speak, even when comprehension of language and cognitive abilities are intact. Recovery after large strokes is often very limited and quality of life is severely affected; many inhabitants of health care homes are, in fact, stroke victims. In this issue of Nature Neuroscience, Li et al.\textsuperscript{1} find that a vigorous growth response occurs in spared neurons around the lesion and investigate the molecules mediating this growth. Outgrowth of new fibers and the formation of new connections over large parts of the motor and sensory cortex may provide the substrate for the establishment of new circuits that compensate for lost functions during the process of rehabilitation.

Ruptured blood vessels (hemorrhagic stroke) or aggregates of platelets and blood cells (thrombi) that clog important cerebral blood vessels (ischemic stroke) lead to local tissue destruction in the brain in a few hours. The destruction process is complex and can only be halted, in the case of clogged vessels,
by very early intervention with thrombolysis; that is, the injection of an enzyme into the bloodstream that dissolves the thrombus2. Currently, only about 10% of stroke victims can profit from this therapy, often because victims do not reach a hospital with an appropriate stroke unit early enough. Prognosis and recovery then depend on the location and extent of the stroke lesion3,4. If motor areas are affected, then either slight weakness and impairments (paresis) or complete paralysis (hemiplegia) occur on one side only, resulting in paralysis of the opposite side of the body (hemiplegia). For large strokes, recovery is often minimal. This is very different for small-sized strokes, which mostly have a good prognosis and allow for extensive or full-scale recovery of lost functions5. The only therapy available today is training and physiotherapy during the rehabilitation phase. Many studies have suggested that training must be very intense over a prolonged time period to be effective6. Depression, which often accompanies stroke, or insufficient health insurance to cover the costs of an intense rehabilitation program, can severely restrict the rehabilitation process.

What really happens in the brain during rehabilitation remains largely unknown, but is a topic of great interest for basic neuroscience as well as for clinical investigations. Shifts in regional brain activity patterns, including motor and sensory maps, are seen in human stroke victims during rehabilitation using modern imaging techniques3,4. In animal models, the sprouting of dendrites and axons of nerve cells around the lesion and in the opposite (intact) hemisphere have been seen5,7,8 (Fig. 1). Neuronal growth factors or factors released by implanted stem cells could enhance these growth processes8. Similarly, the functional blockade of neurite growth inhibitory factors, in particular the potent growth and regeneration inhibitor and CNS wiring pharmacological blockade of the IGF receptor NgR1 also decreased map expansion after the stroke. Similarly, pharmacological blockade of the IGF receptor and the proteins Lingo-1 and NgR1, two components of the receptor complex for the neurite growth inhibitor Nogo-A, Notably, suppression of the nuclear factor ATRX by RNA interference in stroke-affected rats led to a substantial reduction in the motor map expansion seen after the stroke. In contrast, inactivation of the growth inhibitory Nogo receptor constituents NgR1 or Lingo-1 induced massive enhancement of cortical sprouting in reaction to stroke lesions.

Although manipulation of the growth factor IGF and the growth inhibitory Nogo pathway produced expected results, the nuclear protein ATRX is especially noteworthy for its supposed mechanism of action, chromatin remodeling13,14. ATRX was found to be associated primarily with heterochromatin in cell nuclei. It has a zinc finger domain and a DNA-dependent ATPase domain. ATRX is especially notewor.

In summary, fiber tracing and biochemical readouts of the growth process, in particular the insulin-like growth factor (IGF), the Nogo receptor complex subunit Lingo-1 and the nuclear regulatory factor ATRX.
of rats and mice, even at an advanced age. These expanded networks can act as a substrate for functional recovery provided that the new connections are stabilized via use and training. However, much remains to be learned about possible restrictions. With regard to anatomy, can map shifts occur between forelimb, hindlimb and head maps? With regard to functional subfields, can the pre-motor area fully substitute for the primary motor field? Can an intact left cortical hemisphere compensate for the injured right part of the brain? In addition, time windows for therapeutic interventions and optimal training procedures need to be taken into consideration. The unraveling of key players in the underlying molecular mechanisms opens the door for new pharmacological interventions for enhancing the structural plasticity of the CNS hardware and thereby increase the chance of forming new circuits to reestablish lost functions.

COMPETING FINANCIAL INTERESTS

The author declares no competing financial interests.