NATURE

100 YEARS AGO

Recent researches by Surgeon-Major Ronald Ross have shown that the mosquito may be the host of parasites of the type of that which causes human malaria. Ross has distinctly proved that malaria can be acquired by the bite of a mosquito, and the results of his observations have a direct bearing on the propagation of the disease in man. Dr. P. Manson describes the investigations in a paper in the *British Medical Journal,* and sums them up as follows: – The observations tend to the conclusion that the malaria parasite is for the most part a parasite of insects; that it is only an accidental and occasional visitor to man; that not all mosquitos are capable of subserving it; that particular species of malaria parasites demand particular species of mosquitos; that in this circumstance we have at least a partial explanation of the apparent vagaries of the distribution of the varieties of malaria. When the whole story has been completed, as it surely will be at no distant date, in virtue of the new knowledge thus acquired, we shall be able to indicate a prophylaxis for malaria of a practical character, and one which may enable the European to live in climates now rendered deadly by this pest.

From *Nature* 29 September 1898.

50 YEARS AGO

"Thomas Jefferson Among the Arts" – Thus we find Jefferson the revolutionary, workman, writer, thinker, toiling ever and anon to establish culture, both abstract and material, in his youthful America. To him there was no difference between 'pure' and 'applied' (whether art or science); all was for the benefit of mankind, and the pursuit of the good. Naturally, this led to some strong likes and dislikes, short shrift for Plato and Samuel Johnson, to mention but two. Love of contrast is characteristic; formal Palladian architecture, surrounded by 'serpentine' gardens, as if to say "Oh Western Wind, blow soft and kind" upon the exceedingly solid and uncompromising stone buildings he admired and advocated. The author of the Declaration of Independence is entitled to such light and shade in his dealings with contemporary events.

From *Nature* 2 October 1948.

signalling cascade that is dependent on SAP (and probably on fyn, a member of the src tyrosine kinase family) to one that depends on SHP2. Put more generally, Sayos *et al.* propose that SAP controls the signal-transduction pathways initiated by interactions between SLAM molecules at the interface between T and B cells.

Why should the impairment of SAP, an inhibitor of SLAM-triggered T-cell activation, inhibit the T-cell response against EBV-transformed immunoblasts? The answer will come from clarification of the SLAM pathway, of the interactions between T cells and EBV-infected B cells, and of SAP-dependent T-cell inhibition. EBV-transformed B cells express SLAM at a high level, and are also professional antigen-presenting cells; that is, they stimulate T cells to proliferate and generate both $CD4^+$ and $CD8^+$ effectors targeted against EBV proteins involved in growth transformation. Even a seemingly minor disturbance in SAP may perturb the finely tuned interactions between the different effectors, with disastrous consequences. Eventual apoptosis of the activated, but SAP-defective and therefore dysregulated EBV-specific T cells, is one of the obvious possibilities.

Epstein–Barr virus is unique in being both an inhabitant of B cells and an active player in the B-cell system, especially in the interactions between the EBV-infected immunoblast cells and T cells. That might explain the curious fact that XLP patients have a selective defect in their T-cell response to these immunoblasts but not to cells infected with other viruses, and that they seem to be more prone to EBV-associated disease than are patients with other inherited immune deficiencies. Conceivably, regulation of the SAP–SLAM pathway may also differ with age. If so, it might help explain why primary EBV infection remains silent in most small children and usually causes mononucleosis only in adolescents and young adults.

The identification of the *XLP* gene, alias *SH2D1A* or *SAP*, and its signalling function opens the way to a better understanding of the highly sophisticated immune response against EBV-transformed cells. It may improve the diagnosis of a severe but enigmatic disease with variable manifestations, and it may also in time lead to treatments. □

George Klein and Eva Klein are at the Microbiology and Tumor Biology Center, Karolinska Institute, PO Box 280, S-171 77 Stockholm, Sweden.
e-mail: Georg.Klein@mtc.ki.se

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Neurobiology

See and grasp

Nikos K. Logothetis

To be able to grasp and manipulate objects, we need to know not only their location, but also their shape, orientation and size. Visual information about such properties determines the anticipatory posture of the hand and fingers during reaching, and is critical for controlling skilled actions such as precision grip[1]. But the neural representations of shapes may be different from the representations that mediate the visual control of action. For example, although object recognition relies on representations that do not vary with changes in orientation, location and size, to act on these objects we probably need representations that are sensitive to just such changes.

On page 500 of this issue, Sereno and Maunsell[2] address the questions of how object- and space-related information is integrated, and how the brain uses the invariant representations that underlie visual perception to guide our geometry-specific grasping. In primates, the perception of objects and space seems to be mediated by two neural pathways, which are functionally distinct and anatomically segregated[3–5] (Fig. 1). Although both emanate from the primary visual cortex, one then stretches to the temporal lobe (ventral pathway), and the other to the parietal lobe (dorsal pathway)[3]. Sereno and Maunsell now suggest that there may be visual shape representations in both of these visual pathways, some directly suitable for visually guided action. Recording from the posterior parietal cortex of monkeys — an area thought to be involved in spatial vision — they find that neurons in the lateral intraparietal area, one of the functional areas of the parietal cortex, respond selectively to images of simple, two-dimensional shapes.

Previous studies[6,7] showed that neurons in the parietal lobe of monkeys are sensitive to shape. Monkeys were trained to reach and grasp real, three-dimensional objects, either immediately after the object was presented or after a delay period of several seconds during which the object could not be seen. Posterior parietal neurons were found to be selective to both the visual appearance of simple, geometrical solids, and the monkey's short-term memory of them. Moreover, most of these cells showed shape-

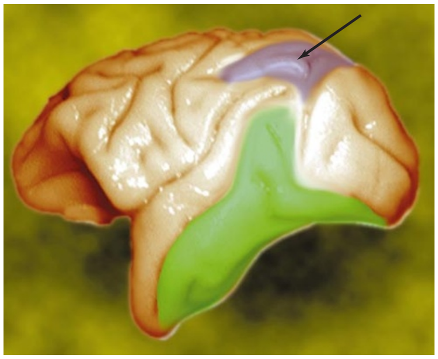

Figure 1 **Lateral view of the macaque brain. The purple and green areas show cortical regions that are involved in processing spatial and object information, respectively. The area reported by Sereno and Maunsell lies within the intraparietal sulcus, shown by the arrow.**

selective activity, even when the monkey was required to refrain from grasping the object. Nonetheless, in all of these experiments the monkeys were trained to manipulate the test objects and, presumably, had developed the representations required for their hand manipulation through both visual and somatosensory information.

What makes the findings of Sereno and Maunsell remarkable is that their monkeys were not involved in a hand-manipulation task, and they could not touch the stimuli (two-dimensional images of objects). In fact, the animals were trained only to perform a simple fixation task or a visual delayed match-to-sample task. During the fixation task, the monkeys looked at a screen, holding their gaze on a central spot, while a shape was presented within the receptive field of the recorded neuron. During the delayed match-to-sample task, the animals fixated a central spot and, shortly afterwards, a sample shape was superimposed on the spot. This was then replaced by three shapes equidistant from the fixation spot, and the monkeys had to make an eye movement to the test shape that matched the sample shape for a juice reward. Surprisingly, many of the recorded parietal neurons — just like the temporal or prefrontal cells reported by other investigators — showed differences in activity as different shapes were presented during the fixation task. Some also showed shape selectivity during the delay period of the match-to-sample task.

Why should shape be represented in the posterior parietal cortex? Our perception of shapes is probably mediated by neurons in the temporal lobe. Although lesions in this area of the brain severely interfere with pattern perception and recognition, lesions in the parietal lobe only affect spatial vision (our sense of where things are), leaving pattern vision intact[3]. Most neurons in the temporal lobe respond selectively to simple or complex visual patterns, including views of human and monkey faces, indicating that this region is critical in shape perception. Shape selectivity is also found in areas of the prefrontal cortex. These are interconnected with the visual areas of the temporal lobe, and are thought to mediate the working memory for visual objects[8].

Neurons in the temporal lobe tend to be position and size invariant; that is, they lack properties that are critical for manipulating objects by hand. Although no data are available, shape selectivity in the posterior parietal cortex may turn out to be specific for the size range of objects that an animal could possibly manipulate. Shape selectivity in the parietal cortex may also be specific for orientation with respect to a reference frame centred on the viewer or on some other object — a property that is rarely seen in the responses of temporal neurons. On the other hand, selectivity to material properties of objects, such as colour and textures, would be meaningless for a system that underlies hand-manipulation of objects, but essential for certain recognition tasks. So the existence of separate temporal and parietal shape representations may be partly due to the different output requirements of the visual system, as neuropsychological studies also suggest[9].

Finally, based on the neuronal properties of the posterior parietal cortex, it has been suggested that this region of the brain is the main area that mediates visuospatial attention[10,11] or, alternatively, an animal's intention to reach a particular point in space[12]. The data presented by Sereno and Maunsell indicate that at least some areas of the parietal cortex may be important for switching attention or instigating an intentional movement, not only to particular locations, but also to particular objects that are targets for either action or identification. Shape- and location-triggered attentional or intentional shifts are bound to require neurons that discriminate shapes to some extent. □

Nikos K. Logothetis is at the Max Planck Institute for Biological Cybernetics, Spemannstrasse 38, D-72076 Tübingen, Germany.
e-mail: nikos.logothetis@tuebingen.mpg.de

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Daedalus

Psychic misperceptions

In Everett's 'many worlds' view of quantum mechanics, the complete multidimensional Universe can be divided into many vector subspaces. Each subspace is a physically real 'parallel world'. Quantum-probability paradoxes neatly disappear. Schrödinger's famous cat, whose life hangs on one random quantum event, lives in some of the Everett worlds, but dies in others.

Clever, says Daedalus; but not clever enough. Why should the Universe divide so neatly into perfect physically real worlds? By choosing a different set of orthogonal vectors, you could divide it just as validly into worlds whose quantum states were hopelessly mixed. Their inhabitants would be like Schrödinger's cat before it is observed: neither alive nor dead, but in a ghostly, non-physical, quantum superposition of these states.

So Daedalus sees the complete Universe as a set of physically real Everett worlds, embedded in a matrix of quantally mixed, physically non-real, ghostly worlds. He identifies this mystic matrix with the spiritual world of ghosts, telepathy, and so on. Indeed, it may act as a telepathic channel for messages from other Everett worlds. This theory explains the deplorably unreliable nature of mystic insights, telepathic intuitions and so on. They may in fact refer to some other world.

But how to tell? Daedalus reckons that a complementarity principle must apply. To sustain the correct probabilities of its quantum states, a live Schrödinger cat in one world implies a dead one in another; a successful lucky chance in one world must fail in another. Daedalus recalls a study of intuition in business executives. Successful ones scored significantly better than chance; but failing ones scored worse than chance. Clearly, says Daedalus, these perverse 'anti-psychics' were, sadly for them, tuned to another world. So Daedalus plans to seek out such rare and gifted individuals among bankrupt businessmen, failed spiritualists and inspired losers of all kinds. He will then look for statistical agreements among their hopeless fantasies. Tantalizing glimpses of some other Everett world may emerge.

Although this world will probably be very close to ours in the universal 'holospace', Daedalus can see no way of exchanging material as well as ideas. He does wonder, however, whether its inhabitants find extra socks in the wash, but suffer mysterious losses of wire coat-hangers.

David Jones