NEUROLOGICAL DISEASES

Getting the measure of stroke

When attempting to treat stroke, it pays to know the nature of the beast. Acute stroke consists of an evolving infarction — an area of brain tissue that is damaged beyond repair — surrounded by an 'ischaemic penumbra', which, although threatened, can potentially be rescued by restoring blood flow to the affected area. But brain 'reperfusion' with thrombolytic agents carries with it the risk of haemorraghic complications, and is effective only in those cases in which there is a penumbra to save. So, how to tell when to use it? A study published in the *Annals of Neurology* now shows how a new version of X-ray computed tomography (CT) can be used in acute stroke patients to decide whether reperfusion will be effective, and also to predict the final infarct size and expected clinical progression.

Stroke diagnosis has relied on the use of CT for more than 30 years, but this study uses a modern variant, perfusion CT, that can generate brain images at a much faster rate. Perfusion CT can be used to monitor the passage of injected CT dye through the brain, and therefore to create maps of cerebral blood volume and cerebral blood flow — measures that correlate with the size of the infarct and the affected penumbra.

The technique was applied to 22 adult stroke patients at the time of emergency-room admission, and was found to be highly predictive of the cerebral infarct size measured three days later by magnetic resonance (MR) imaging, which is the accepted best method at present for detecting the area of long-term damage. Furthermore, the initial size of the combined cerebral infarct and penumbra defined by the admission perfusion CT correlated better with various standard assessments of

NEURODEGENERATIVE DISORDERS

The comeback of immunization

The idea that immunization against amyloid-β (Aβ) could be an effective therapy against Alzheimer's disease (AD) suffered a significant setback earlier this year after reports of inflammatory reactions in patients that took part in an initial clinical trial. Although the cause of the inflammation remains unknown, this observation prompted many critics to argue that the days of immunization as a possible AD therapy were over. But as two recent papers from the laboratories of David Holtzman and Steven Paul show, we still have a lot to learn from the use of anti-Aβ antibodies, which might compel us to reconsider their diagnostic and therapeutic potential.

In the first paper, DeMattos *et al.* measured the plasma concentration of Aβ before and after the administration of an anti-Aβ antibody to transgenic mice that expressed a human form of the amyloid precursor protein, and tried to correlate this with the brain amyloid burden (an index of the amount of Aβ that is present in the brain). As is the case in people with AD, the authors found no correlation between the basal plasma levels of Aβ and brain amyloid burden. However, the plasma concentration of Aβ increased 24 hours after a single antibody injection, and there was a strong correlation between the new level of Aβ and brain amyloid burden. In other words, plasma levels of Aβ after the injection were predictive of the brain amyloid burden. As the brain accumulation of Aβ in people with AD precedes the onset of cognitive impairments and neuronal loss, this approach could lead to the development of a diagnostic tool for people at risk.

In the second paper, Dodart *et al.* found that a similar acute administration of the antibody reduced the memory deficits that had previously been reported in the transgenic mice, without altering the brain amyloid burden. As they detected Aβ/antibody complexes in the plasma and cerebrospinal fluid of the mice, the authors propose that the memory improvements might be due to sequestration of soluble Aβ from the brain.

Although we can only speculate on the implications of these findings for patients with Alzheimer's disease, both studies converge on the idea that the clearance of Aβ from the brain is a dynamic process, and that the use of anti-Aβ antibodies provide us with a useful window through which we can examine this phenomenon.

Juan Carlos López

clinical status than did the delayed MR measurements. Interestingly, perfusion CT also seems to allow the identification of tissue within the penumbra that can be salvaged by reperfusion, and so can be used to guide the choice of therapy.

The main hurdle for the development of drugs for stroke is the difficulty of organizing large-scale clinical trials. Importantly, these new findings might pave the way for the use of perfusion CT in monitoring the effects of neuroprotective drugs in individual patients, therefore allowing small Phase II efficacy trials.

Adam Smith
Editor, Nature Reviews Drug Discovery

References and links

ORIGINAL RESEARCH PAPER Wintermark, M. *et al*. Prognostic accuracy of cerebral blood flow measurement by perfusion computed tomography, at the time of emergency room admission, in acute stroke patients. *Ann. Neurol.* **51**, 417–432 (2002)

References and links

ORIGINAL RESEARCH PAPER
DeMattos, R. B. *et al*. Brain to plasma amyloid-β efflux: a measure of brain amyloid burden in a mouse model of Alzheimer's disease. *Science* **295**, 2264–2267 (2002) | Dodart, J.-C. Immunization reverses memory deficits without reducing brain Aβ burden in Alzheimer's disease model. *Nature Neurosci.* 8 April 2002 (10.1038/nn842)
FURTHER READING Selkoe, D. J. Alzheimer's disease: genes, proteins, and therapy. *Physiol. Rev.* **81**, 741–766 (2001)
Encyclopedia of Life Sciences:
http://www.els.net/
Alzheimer disease

VISUAL PROCESSING

Switching sides

As you read this page, glance around your office or watch the world go by the windows of your train, your eyes are constantly moving. Rather than smoothly scanning a scene, they jump from one detail to another in rapid movements called saccades. Even though the visual system is usually very sensitive to movement, we are normally unaware of these saccades — despite the fact that they cause the entire visual scene to move quickly across the retina. New results, obtained by recording from motion-sensitive areas of the monkey visual system during saccades, point to one possible mechanism.

Although some researchers have suggested that the human visual system might simply be insensitive to the very fast movements of the visual scene that are induced by saccades, others argue that this is not the case, and that there must be an active mechanism for suppressing perception during saccades. Indeed, psychophysical studies show that perception of certain features is suppressed during these eye movements. Thiele *et al.* looked for neuronal correlates of this suppression by recording from individual neurons in the middle temporal and middle superior temporal (MT and MST) areas of the monkey cortex, both of which normally respond strongly to moving visual stimuli.

They compared neuronal activity in two conditions: when the monkeys carried out a saccade, and when the monkey's eyes did not move but the visual scene was moved so that it generated the same retinal image motion as in a saccade. Most of the neurons in these areas did respond to the kind of fast image motion that occurs during a saccade, supporting the idea that insensitivity to fast motion cannot explain saccadic suppression of perception. But when the responses of these neurons during saccades were compared with responses during passive movement of the visual scene, the researchers found big differences.

Some of the neurons simply failed to respond, or responded only weakly, during saccades, even if the movement of the visual field was in the direction to which they normally responded most strongly. But another set of neurons showed even more intriguing properties. These neurons responded strongly during both saccade-induced and passive movements of the visual scene — but their direction sensitivity changed so that their preferred direction during saccades was opposite to their preferred direction during passive viewing. These neurons tended to have longer response latencies than cells that did not show such a reversal.

When the researchers looked at the population responses, rather than at single cells, they found that the presence of these 'extraretinal' cells caused the overall population response to visual motion during a saccade to be weaker, and to end earlier, than the response to externally generated movement. It seems that these responses 'cancel out' those of cells that respond normally during saccades. Thiele and colleagues suggest that these properties might also explain the distortion of external motion perception shortly after saccades.

These findings support the idea that suppression of perception during saccades is an active process that is mediated by changes in neuronal responses in motion-sensitive parts of the visual system. But they also provide a tantalizing example of cortical neurons that can change their tuning properties rapidly to reflect the context of their input. Such flexibility could add a whole new layer of complexity to cortical function.

Rachel Jones

References and links

ORIGINAL RESEARCH PAPER Thiele, A. *et al.* Neural mechanisms of saccadic suppression. *Science* **295**, 2460–2462 (2002)
FURTHER READING Ross, J. *et al.* Changes in visual perception at the time of saccades. *Trends Neurosci.* **24**, 113–121 (2001)