**Cognitive neurophysiology**

# The lifeblood of language

*John C. Marshall*

IT WOULD be useful, to put the matter mildly, if we could see what the human brain was doing when the brain was doing it. And it would be yet more valuable to be able to visualize the neuronal substrate of complex abilities that can be fractionated into simpler, independently assessed stages. For the first time, Marcus Raichle's team has now successfully wedded an advanced brain-imaging technique for measuring blood flow within defined cortical regions to an information-processing model of the steps involved in some basic language functions. This work, reported by Petersen *et al.* on page 585 of this issue[1], shows how cognitive theory and current medical technology can converge on a unified psychobiology of lexical processing.

The story begins somewhat obliquely. In 1890, Roy and Sherrington observed[2] that the onset of generalized epileptic seizures, provoked by synchronized hyperactivity of nerve cells, was rapidly followed by substantial swelling of the brain. This swelling, they conjectured, was due to increased blood-flow. And they were accordingly led to postulate the existence of "an automatic mechanism by which the blood supply of any part of the cerebral tissue is varied in accordance with the activity of the chemical changes which underlie the functional action of that part."

The basic hypothesis turned out to be correct, and by the 1960s, technological developments allowed the functional landscape of the human brain to be plotted *in vivo* by measurement of regional cerebral blood flow (rCBF). A radioactive isotope, xenon-133, that attaches to red blood cells was introduced into one of the main arteries that supply the brain's nutritional requirements; a gamma-camera could then monitor simultaneous radioactivity counts from different brain regions. And these counts could in turn be transformed into measurements of rCBF that reflected the differential activation of brain areas when the conscious patient (or normal volunteer) is actually engaged in a particular mental task[3].

If the data from the gamma-camera are further processed in a computer, then images can be displayed on a colour monitor in which different hues are assigned to different levels of blood-flow. David Ingvar, one of the pioneers of rCBF methodology, has therefore termed such flow-charts "cerebral ideograms" of mental activity[4].

In general, early studies of speech and language processes using the xenon-133 technique supported the classical views of localization of function that had been derived from investigation of the effects of focal damage to the left hemisphere of the brain. For example: in neurological patients without focal tissue damage, speaking aloud activates auditory cortex,

*Watching the working brain.*

the primary (rolandic) mouth–tongue–larynx area and the supplementary motor area; silent reading activates the visual-association area, the frontal eye field, supplementary motor cortex and the foot of the third frontal convolution (Broca's area)[5]. There were, however, some surprises for traditional neuropsychology; most notably, increased flow in right-hemisphere areas that, when damaged, do not typically provoke aphasic impairment[5]. This finding should alert us to the possibility that inhibition, as well as excitation, requires energy.

Such studies promised considerable insight into the neurophysiology of language processing but were subject to several technical limitations: poor spatial resolution of adjacent brain areas; imprecision of anatomical localization due, in part, to attenuation of radiation from structures deeper in the brain; and poor temporal resolution due to the slow clearance curve for $^{133}$Xe. Equally critically, these investigations used multi-faceted tasks that 'lit up' very large regions of the cortical mantle.

By contrast, Raichle's team[1] has devised a set of interrelated behavioural and imaging techniques that are rapidly overcoming the inadequacies of previous work. Positron emission tomography (PET) can image rCBF by reading the spatio-temporal distribution of injected radionuclides with short half-lives (oxygen-15, for example). As each individual radiation dose is low, repeated measurements can be taken from the same subject performing different tasks. Although the spatial resolution of adjacent point sources by PET is currently poor (1.0 cm at best), a single point source can be localized with excellent accuracy (5 mm or better).

Hence, if experiments are designed so that each new behavioural task adds a further processing requirement to the previous one, rCBF measurements from the simpler task can be subtracted to obtain a precise image of the successive stages of the more complex task. Raichle's group initially validated the subtraction method by imaging the retinotopic map within human visual cortex[6]; it is now extended[1] to help resolve a longstanding controversy about visual word recognition and reading aloud.

The first models of reading, proposed by nineteenth-century neurologists[7], explicitly claimed that all reading for meaning was mediated by the cortical centre for auditory speech processing. Lesions that impaired the ability to read (and write) centred around Wernicke's area and the angular gyrus (in the left posterior temporo-parietal region), areas that are known to be crucial to the analysis and comprehension of speech. This model dominated the interpretation of both normal and pathological reading until the mid-1970s. LaBerge thus categorically states[8] that "written material must be coded into phonological form to be comprehended." The model was challenged, however, by the discovery[9] of patients who could read words aloud (albeit with numerous semantic para-

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