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The neurobiology of language and verbal memory: observations from awake neurosurgery

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Abstract

Neurosurgical operations under local anesthesia provide a unique opportunity to investigate the neurobiology of human cognition. We have studied the cortical organization of language and verbal memory in this setting, using two different techniques: electrical stimulation mapping and extracellular microelectrode recording of activity of individual neurons. The two techniques provide very different perspectives. Stimulation mapping identifies brain areas that are essential for a behavior, while changes in neuronal activity can occur in non-essential regions. Stimulation mapping identifies multiple discrete areas in perisylvian cortex of the dominant hemisphere as essential for a function, with separation of areas for different aspects of language including naming in two languages, different semantic classes, naming compared to reading, and language from verbal memory. There is substantial individual variation in the location of these essential areas, variability that in part relates to subjects age, gender and verbal abilities. Neurons changing activity with language or verbal memory are widely distributed, in both hemispheres. However, individual neurons usually change activity with only one function, including naming in only one of two languages, only naming or reading, or with recent verbal memory encoding but not identification of similar items. A few lateralized changes in neuronal activity have been identified, including a predominance of inhibition in dominant hemisphere with naming, and polymodal memory responses in dominant hemisphere, unimodal in nondominant. Specific neuronal populations have been identified that are related to different aspects of memory, that differentiate correct from incorrect identification or memory performance and differentiate learned from unlearned associations, with some evidence of differences in neuronal activity related to subjects' ability.

Keywords: Stimulation mapping; Verbal memory; Awake neurosurgery

Investigation of the neurobiology of human cortex during awake neurosurgery has a long tradition. Initially those investigations used cortical electrical stimulation, with the first use of that technique to evoke motor responses in awake humans following shortly after the demonstration of electrical excitability of motor cortex in non-human animals (Bartholow, 1874). The most widely known application of this technique to study human cortical function is that of Penfield during awake neurosurgery for epilepsy. Penfield noted two different effects of applying an electric current to the human cortical surface: evoked behavioral

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changes and interference with ongoing behavior. In his work, evoked effects of stimulation included motor-sensory, visual and (rarely) auditory responses from primary cortices, and the interpretive and experiential responses from association cortex (Penfield and Jasper, 1954; Penfield and Perot, 1963), though the experiential responses are now known to appear only when the current evokes an afterdischarge propagated to medial temporal structures, suggesting that they represent epileptic phenomena (Gloor et al., 1982). The more common effect of stimulation of association cortex at currents below afterdischarge thresholds was interference with ongoing activity. Penfield used this effect on object naming to map representation of language (Penfield and Roberts, 1959). The author's group subsequently demonstrated that the relation of a resection to sites where stimulation repeatedly interfered with naming predicted whether a resection would or would not result in a language deficit (Ojemann, 1983; Haglund et al., 1994a). Thus stimulation identifies cortex with functions that are 'essential' for that behavior at that time. The studies of the author and his associates of the cortical organization of language and verbal memory using this technique are one portion of this review.

A separate tradition utilized the opportunity provided by awake neurosurgery for recording of activity of individual cortical neurons through microelectrodes. Initially these studies were directed at determining patterns of activity of 'epileptic' neurons, to compare to neuronal recordings in experimental animal models of epilepsy (Ward and Thomas, 1955; Calvin et al., 1973). However, awake neurosurgery for epilepsy also often provides access to cortex that does not show evidence of epilepsy electrophysiologically and is histologically normal. Microelectrode recording in that cortex during appropriate behavioral measures provides an opportunity to determine correlates of human cognition in relatively 'normal' neurons. That opportunity as utilized by the author and his colleagues is also summarized in this review. Neuronal activity provides a different perspective on functional cortical representation than that provided by stimulation mapping. Neuronal activity changes that correlate with a behavior do not necessarily indicate activity 'essential' for the behavior, only that it 'participates' in the behavior. Several other techniques applicable to the intraoperative investigation of the neurobiology of cognition also indicate activity the 'participates' in a behavior, including optical imaging of the intrinsic signal, the subtle swelling of neurons when they are active (Haglund et al., 1992), and electrocorticographic correlates (Fried et al., 1981; Ojemann et al., 1989a). The changes in oxygen extraction and blood flow that are the basis for functional magnetic resonance imaging also indicate 'participating' but not necessarily 'essential' activity. There is no a priori reason that techniques that identify 'participating' or 'essential' areas should identify changes in the same cortical regions or that the cortical representations with the different 'participating' techniques should be identical; those are empirical questions.

1. Electrical stimulation mapping

Utilizing the electrical stimulation mapping technique during naming that identifies 'essential' brain regions for language, the author and his associates demonstrated that sites where stimulation repeatedly interfered with naming were often localized to focal areas of dominant hemisphere cortex of approximately 1 cm^2, frequently with one such site in perisylvian inferior frontal cortex and several others in temporoparietal cortex. Nondominant cortex does not show such sites. The exact location of these sites in the left language dominant hemisphere was found to vary substantially across the patient population. Variability was particularly evident in temporoparietal cortex. This variability was partly related to patient's gender and preoperative verbal abilities as measured by the verbal IQ (VIQ). In addition to having a somewhat different pattern of localization, patients with lower VIQs had a larger surface area from which naming interference could be evoked (Ojemann et al., 1989b). When the sites of naming interference were determined in children 4–16, overall fewer sites were found in those who came to operation before 9, compared to older children, who had fewer sites than those who came to operation as adults. This may represent an effect