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INTRODUCTION

The Investigation of Lexical Semantic Representation in Alzheimer's Disease

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The study of lexical semantic representation is central to an understanding of brain and language. In Alzheimer's disease, neuropathological alterations consistently involve neocortical areas in which lexical semantic information is represented, and patients with this common dementing disorder evince priminent lexical semantic disturbances. General issues concern the establishment of new semantic memories, the manner in which meaning is represented within the lexicon, the retrieval of semantic information from the lexicon, and the relation between lexical semantics and nonlinguistic cognitive processes. Studies of lexical semantic representation in patients with Alzheimer's disease are especially informative in considering all but the first of these key issues.

Studies of language have long commanded center stage in the quest to understand how specific neural substrates and operations determine the form, content, and product of cognitive processing. The basic function of language is to allow a speaker to convey propositions whose meaning can be comprehended by an intended recipient. The fact that this interaction occurs at all presupposes that meaning (particularly including lexical semantics) is in some way represented in an accessible manner within complementary neural structures possessed by both participants in this linguistic transaction. From this perspective, lexical semantic representation can be viewed as fundamental to a study of brain and language.

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ALZHEIMER'S DISEASE AS A MODEL FOR LEXICAL SEMANTIC IMPAIRMENT

Are patients with Alzheimer's disease an appropriate population in which to explore the semantic lexicon? Alzheimer's disease is the most prevalent form of dementia, but after all one might choose to study healthy subjects or other clinical groups. Using functional neuroimaging modalities, cognitive processing could be investigated, for example, in volunteers with no brain injury whatsoever. It is apparent, however, that the language disintegration that accompanies brain pathology can provide unique insights into the structure of language complimentary to—and not readily obtained from—neurolinguistic, neurophysiological, or neuroanatomical investigations of normal subjects.

One might also investigate patients with other brain disturbances, and whether Alzheimer's disease—more so than these other disorders—is a useful model for the study of lexical semantic representation requires additional consideration. Neuroscientific heirs of Broca and Wernicke have tended to focus on language deficits resulting from stroke, tumor, trauma, and other focal lesions of the cerebral hemispheres, both as a matter of convenience and also because the interpretation of clinical–pathological associations appeared to be more transparent. However, because of diaschisis and because of unrecognized collateral damage (e.g., diffuse axonal shearing in closed head injury or remote pressure effects from tumors, hemorrhage, or penetrating missile wounds of the brain), focal lesions rarely produce discretely circumscribed disruptions. Diaschisis also occurs with cerebral infarction, ostensibly the form of brain injury most conducive to analyses of brain–behavior relationships. Moreover, infarction is necessarily confounded by the nature of the lesion. It can directly affect only neural tissues lying within or between specific vascular distributions, and one can study in relative isolation only those neuronal constituencies that happen to be gerrymandered into delimited vascular districts.

Alzheimer's disease, while fraught with its own anatomical ambiguities, nevertheless represents an enticing model of central nervous system dysfunction upon which to base a study of lexical semantic representation. Despite individual variation and occasional jarring exceptions, the pathological alterations of Alzheimer's disease within the cerebral hemispheres follow a fairly predictable time sequence and affect neuronal subsets within fairly predictable regions of the brain (Kemper, 1994). The patho-anatomical consistency may be at least as great as that for ischemic stroke such as, for example, that affecting the upper or lower division of the left middle cerebral artery. In Alzheimer's disease, medial temporal structures are implicated early. Neocortex is involved next, with posterior (temporal–parietal) association cortex altered to a greater extent than frontal association regions. With the exception of olfactory cortex, primary motor and sensory cortical areas are relatively spared until late in the disease course. Left and right cerebral hemispheres are usually affected in parallel and usually to comparable extents.

Another striking feature of Alzheimer's disease pathology is the extent to which interneuronal connections are affected. A massive loss of dendritic arborization is evident in Golgi preparations that reveal individual neuronal processes to their full extent (Scheibel, Lindsay, Tomiyasu, & Scheibel, 1975), and more recent studies confirm an impressive loss of cortical synaptic markers (Alford, Masliah, Hansen, & Terry, 1994). One generalization, then, is that Alzheimer's disease represents a progressive illness of cortical neuronal disconnection (Morrison et al., 1986), which has a predilection for posterior neocortical association areas. This deafferentation may be transsynaptically mediated, and pathology may thus be most evident in interconnected pathways (Samuel, Henderson, & Miller, 1991), including those neural systems involved in semantic representation.

Virtually all patients with Alzheimer's disease show language changes, with naming disturbances being especially prominent (e.g., Bayles & Tomoeda, 1983; Williams, Mack, & Henderson, 1989). Naming—for example, visual confrontation naming—is a complex multi-step process that involves perceptual identification, lexical semantic retrieval, phonological access, and activation of a motor articulatory sequence. These processes can be disrupted at linguistic and nonlinguistic levels (Henderson, 1995). However, most naming errors in Alzheimer's disease occur within a lexical semantic domain (e.g., Martin & Fedio, 1983; Chertkow & Bub, 1990; Hodges, Salmon, & Butters, 1991). The distributed anatomy of semantic memory representation involves neocortical association areas, particularly areas adjacent to the classic perisylvian language zone in so-called posterior transcortical regions (Henderson, 1995). As posterior neocortex is heavily invested with pathological changes of Alzheimer's disease, it is not surprising that lexical semantic disruption is prominent in this disorder.

The justification for the study of lexical semantic representation in Alzheimer's disease thus becomes straightforward: Alzheimer's disease is a common disorder; pathological changes of Alzheimer's disease consistently affect brain regions in which lexical semantic information is believed to be represented; and lexical semantic disturbances are readily discerned in most patients with this illness.

GENERAL RESEARCH ISSUES

From cognitive and neuronal perspectives, there are four general issues in the study of lexical semantic representation: (1) What are the processes by which semantic information comes to be stored in the lexicon? (2) How is meaning represented within the lexicon (i.e., what is the nature of the semantic lexicon)? (3) How is lexical semantic knowledge accessed and retrieved? (4) How do other cognitive operations affect these lexical semantic processes?

The first question, on the laying down of semantic memory, is not often broached in studies of Alzheimer's disease patients, nor has it been well

studied in other patient populations. It is likely that early neural events implicate the same medial temporal (hippocampal, parahippocampal, entorhinal) structures essential for the establishment of episodic memories (Squire, 1992). Because this temporal lobe region is affected so severely in Alzheimer's disease patients (Hyman, Van Hoesen, Damasio, & Barnes, 1984), the establishment of semantic memory (as opposed to the representation/storage of semantic knowledge) could be studied only in incipient cases. However, future investigations in such mildly affected persons, at a time when critical neocortical association areas are still largely spared, could indeed yield insights into the process of semantic memory formation.

More typically, as reported in each of the ten articles of this issue of *Brain and Language,* research in Alzheimer's disease has focused on the second, third, and fourth questions. In this dementing disorder, concepts and associations appear to dissipate and lexical boundaries to erode. At the extreme, comprehension is altogether lacking and residual utterances are altogether bereft of meaning. From subjects' performance deficits during this process of linguistic dissolution, it becomes possible to consider the nature of the semantic lexicon, ways in which semantic memories are accessed and retrieved, and types of nonlinguistic operations (e.g., attention or visual perceptual processing) that might impact lexical semantic competency and performance. Resultant observations are germane not only to Alzheimer's disease but inferentially to normal cognitive functions as well. A related controversy in Alzheimer's disease is the extent to which production and comprehension impairments observed during the early to middle course of the illness reflect a partial loss of lexical semantic information. An alternative or complementary perspective is that these deficits can be understood as a disruption in semantic organization or as a processing deficit (e.g., impaired access to an otherwise intact lexicon). Advocates of each contention are supported by data reported in this journal issue.

REFERENCES

Alford, M. F., Masliah, E., Hansen, L. A., & Terry, R. D. 1994. A simple dot-immunobinding assay for quantification of synaptophysin-like immunoreactivity in human brain. *Journal of Histochemistry and Cytochemistry,* **42,** 283–287.

Bayles, K. A., & Tomoeda, C. K. 1983. Confrontation naming impairment in dementia. *Brain and Language,* **19,** 98–114.

Chertkow, H., & Bub, D. 1990. Semantic memory loss in dementia of Alzheimer's type. What do various measures measure? *Brain,* **113,** 397–417.

Henderson, V. W. 1995. Naming and naming disorders. In H. S. Kirshner (Ed.), *Handbook of neurological speech and language disorders.* New York: Dekker. Pp. 165–185.

Hodges, J. R., Salmon, D. P., & Butters, N. 1991. The nature of the naming deficit in Alzheimer's and Huntington's disease. *Brain,* **114,** 1547–1558.

Hyman, B. T., Van Hoesen, G. W., Damasio, A. R., & Barnes, C. L. 1984. Alzheimer's disease: Cell-specific pathology isolates the hippocampal formation. *Science,* **225,** 1168–1170.

Kemper, T. L. 1994. Neuroanatomical and neuropathological changes during aging and dementia. In M. L. Albert & J. E. Knoefel (Eds.), *Clinical neurology of aging,* 2nd ed. New York: Oxford Univ. Press. Pp. 3–67.

Martin, A., & Fedio, P. 1983. Word production and comprehension in Alzheimer's disease: The breakdown of semantic knowledge. *Brain and Language,* **19,** 124–141.

Morrison, J. H., Scherr, S., Lewis, D. A., Campbell, M. J., Bloom, F. E., Rogers, J., & Benoit, R. 1986. The laminar and regional distribution of neocortical somatostatin and neuritic plaques: implications for Alzheimer's disease as a global neocortical disconnection system. In A. B. Scheibel, A. F. Wechsler, & M. A. B. Brazier (Eds.), *The biological substrates of Alzheimer's disease.* San Diego: Academic Press. Pp. 115–131.

Samuel, W. A., Henderson, V. W., & Miller, C. A. 1991. Severity of dementia in Alzheimer's disease and neurofibrillary tangles in multiple brain regions. *Alzheimer Disease and Associated Disorders,* **5,** 1–11.

Scheibel, M. E., Lindsay, R. D., Tomiyasu, U., & Scheibel, A. B. 1975. Progressive dendritic changes in the aging human cortex. *Experimental Neurology,* **47,** 392–403.

Squire, L. R. 1992. Memory and the hippocampus: a synthesis from findings with rats, monkeys, and humans. *Psychological Review,* **99,** 195–231.

Williams, B. W., Mack, W., & Henderson, V. W. 1989. Boston Naming Test in Alzheimer's disease. *Neuropsychologia,* **27,** 1973–1079.