

Abnormality of Semantic Network in Patients with Alzheimer's Disease

Evidence from Verbal, Perceptual, and Olfactory Domains^a

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ABSTRACT: A series of studies was initiated to model the organization of semantic memory in Alzheimer's disease (AD) patients using multidimensional scaling (MDS) and Pathfinder analyses. The resulting models (cognitive maps or semantic networks) embed studied stimuli in a coordinate space or network where distances between points are assumed to reflect psychological proximity between items. The organization of semantic networks in verbal and sensory domains were modeled based upon the frequency of the subject's choice of two concepts as most alike. Results suggested that while the organization of concepts in the semantic networks of AD patients was primarily based upon a concrete perceptual dimension in both verbal and olfactory domains, those of normal controls subjects were predominantly organized by an abstract conceptual attribute. Also, networks of AD patients were more complex and chaotic than normal, that is, they consisted of more unnecessary connections and of atypical strengths of association between concepts.

It is often assumed that semantic knowledge is organized as a complex network consisting of concepts or representations that are related through serial and/or parallel associations.^{7,16} Within the network, concepts that share many attributes are more highly associated, or more closely related, than those that share few attributes.⁶ For example, the concept *dog* is strongly associated with the concept *cat*, because they share such attributes as being living creatures, four-legged animals, domestic pets, meat eaters, furry, and relatively small in size. In contrast, the concepts *dog* and *sky* are only weakly associated, at most, since they do not share any obvious salient attributes. Alzheimer's disease (AD) is a progressive dementing disorder with prominent neuropathology in those cortical association areas of the frontal, temporal and parietal lobes¹⁹ that are thought

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to be integrally involved in the neural network underlying semantic knowledge.^{10,11,20} Thus, a disorganization of semantic knowledge might be expected as the disease progresses. In the present paper we will describe a series of studies that has directly explored the impact of AD on the integrity of the semantic network. These studies employed various graphic scaling techniques^{15,18} to model the organization of semantic memory in AD patients in different domains: namely, verbal, perceptual and olfactory categories. The goal is to see how the organization of semantic knowledge in various domains might be altered by the neocortical deterioration that occurs in the disease.

The series of studies has used multidimensional graphic scaling analyses (MDS) and the Pathfinder analysis to explore the underlying structure of data generated by AD patients on various semantic memory tasks. In general, MDS analysis generates a graphic representation of the data based on some measurement of the relative degree of association (*i.e.*, closeness or proximity) between concepts in semantic memory. The resulting models represent the concepts under study within a coordinate space where the distances between points are assumed to reflect the psychological *proximity* between the respective items in an internal *semantic network* or *cognitive map*.^{6,7}

The Pathfinder analysis⁸ was also applied to examine the number and strength of the associations comprising the semantic network. This analysis systematically constructs a model of the semantic network that consists of nodes representing concepts, and links representing the connections between concepts. It has been proposed that individuals who possess sufficient knowledge in a particular domain to evaluate the degree of association between concepts will develop a clear and concise network composed only of relevant connections, while those who never developed this degree of knowledge, or who have lost knowledge they once possessed, will tend to organize concepts in a relatively chaotic way with many unnecessary adjunct connections.

The triadic comparison task was used in most of our studies to obtain the proximity (*i.e.*, strength of association) between concepts. In the task, subjects were told to choose, from among three concepts, the two that are most alike. All possible combinations of concepts from a given set, taken three at a time, were presented. This procedure produced a proximity score reflecting the strength of association for each pair of concepts in relation to all of the other concepts in the test, that is, how frequently those two items were chosen as most alike. The proximity scores were subjected to an MDS analysis, which produced cognitive maps for AD patients and elderly normal control (NC) subjects. In addition to the cognitive maps for the two groups, the proximity data were used to calculate for each individual subject a quantitative measure of the relative importance of the various dimensions for categorizing concepts (*i.e.*, dimension weights) and a measure of the degree of reliance on one or more of the dimensions (*i.e.*, skewness index).

In a study examining the organization of semantic knowledge for category 'animals',² a set of 12 high-frequency animal names were utilized in a triadic comparison task that was administered to AD patients and NC subjects. The results of an MDS analysis of these data showed that the cognitive maps of AD and NC subjects were best represented by three dimensions that appeared to correspond to domesticity (*i.e.*, wild vs domestic), predation (herbivore vs carnivore) and size (large vs small). Although a three-dimensional solution provided the best spatial representation of the semantic network of both AD and NC subjects, several significant alterations were evident in the semantic network of the AD patients. First, AD patients focused primarily on concrete perceptual information (*i.e.*, size) in categorizing animals, whereas control subjects stressed abstract conceptual knowledge (*i.e.*, domesticity). Second, a number of animals that were highly associated and clustered together for NC subjects were not strongly associated for patients with AD. Third, patients with AD had significantly lower skewness indexes than the NC subjects, indicating that they were less consistent in utilizing

the various attributes of the animals (predation, domesticity and size) for categorization. When the semantic networks of the AD patients and NC subjects were further explored by performing Pathfinder analyses, the results showed that semantic networks of the AD patients, when compared with those of the NC subjects, were characterized by abnormal strengths of association between usually weakly related concepts and by a large number of unnecessary adjunct links.³

It should be noted that these results are not likely to be a consequence of random responding by the AD patients (due to a lack of attention or an inability to follow instructions), because virtually identical results were obtained when the patients were tested again with the same procedures five to seven days later.² Furthermore, these findings could not be task specific, since similar results were obtained when the proximity between concepts was estimated for each subject from the sequence of their responses on a category fluency task in which they generated names of animals for one minute.¹

In contrast to the semantic network models generated for the AD patients, the models generated by MDS and Pathfinder analyses for patients with Huntington's disease (HD) and patients with a circumscribed amnesic syndrome did not differ significantly from those of their age-matched control subjects in terms of the number of dimensions employed, the strength of associations, or the number of common links between concepts. Unlike AD patients, HD patients and amnesic patients have little or no damage in neocortical association areas, and neither group has significant semantic memory dysfunction. Patients with HD are demented, however, and have a general retrieval deficit that arises from their prominent basal ganglia atrophy. Amnesic patients usually have relatively contained temporal lobe or diencephalic damage and have an isolated episodic memory impairment. The acquisition of normal semantic network models for these patient groups provides evidence that factors such as general cognitive decline, deficiencies in retrieval processes, or impaired episodic memory have little impact on the nature of the cognitive map generated by these multidimensional analyses of data from semantic memory tasks. Thus, the distorted cognitive map of the AD patients most likely reflects semantic memory disruption that may arise from extensive damage to the association cortices.^{10,11,20}

The observed disruption in the integrity of the semantic network in patients with AD increases as dementia progresses. A study examining the relationship between semantic network disruption and the severity of global dementia in patients with AD⁴ revealed a significant negative correlation between various measures of the integrity of the semantic network and the severity of dementia as measured by the Dementia Rating Scale (DRS).⁹ Another study demonstrated that the integrity of the semantic network seems to be predictive of the subsequent rate of global cognitive decline in AD patients.⁵ A highly significant correlation was found between AD patients' similarity indices generated from Pathfinder analyses (*i.e.*, how similar their networks is to normal), and their subsequent global cognitive decline as measured by changes over one year in their scores on the DRS. Given that semantic knowledge may be stored in a distributed fashion within the association cortices,²⁰ these results suggest that early evidence of semantic network abnormalities in AD patients may serve as a marker for the susceptibility of these cortical regions to further deterioration and a resulting increase in the severity of global dementia.

Given the success of the scaling methods for depicting some aspects of the underlying nature of the organization of semantic knowledge in the verbal domain for AD patients, we recently applied these techniques to the study of the organization of their semantic knowledge in various sensory domains.¹⁴ In an initial study, we examined the organization of AD patients' semantic knowledge in the domains of colors and odors. Because our previous studies suggested that AD patients focused more on concrete per-

ceptual than abstract conceptual information in categorizing verbal concepts, it was hypothesized that the semantic network of perceptual information (*i.e.*, colors) should be relatively intact. On the other hand, evidence from an olfactory threshold task¹² and an odor recognition memory task¹³ indicates that AD patients have an olfactory deficit. It was, therefore, anticipated that the semantic network of odors in patients with AD would be abnormal as compared with that of NC subjects.

The findings from this study showed that the semantic networks of NC subjects and AD subjects in the color domain were almost identical, and that the cognitive maps of colors generated for both groups were consistent with a wheel of color.¹⁷ In the odor domain, in contrast, the cognitive maps of NC subjects and AD patients were significantly different, particularly in terms of the primary dimension used to categorize odors. That is, while NC subjects utilized the characteristic of edibility and fruitiness in categorizing the odor stimuli, AD subjects stressed only the fruitiness attribute. Given that the attribute of edibility seems to be relatively more abstract than that of fruitiness, this finding was consistent with that obtained within the animal category. The AD patients seem to focus more than NC subjects on the relatively more perceptual attribute in processing both verbal and olfactory information. In addition, given that AD patients demonstrated a relatively intact cognitive map of colors, but not of odors, these results suggest that there may be domain-specific impairment of semantic memory in patients with AD.

Taken together, the results of the studies reviewed in this paper provide strong evidence that the organization of semantic knowledge is abnormal in patients with AD, particularly in the verbal and olfactory domains. This abnormality appears to be primarily manifested as a conceptual deficit, since AD patients were found to rely strongly on concrete perceptual characteristics in categorizing both verbal and olfactory concepts, and the organization of their semantic knowledge in a predominantly perceptual domain (*i.e.*, colors) was found to be normal. The abnormality observed in AD patients' networks is not likely to be due to nonspecific factors such as global cognitive impairment, episodic memory impairment, or a deficiency in retrieval processes, since HD patients who have a general retrieval deficit and were as severely demented as AD patients, and the amnesic patients with episodic memory deficits as severe as those of the AD patients, had normal semantic network models. It is also important to note that of these three patient groups, only AD patients develop semantic memory dysfunction, and only AD patients develop significant neuropathological changes in the cortical association areas. Because AD is a progressive disease with the pathological changes primarily focused in cortical areas, this group of patients is a unique population for studying the relationship between cortical deterioration and alterations of the organization of semantic knowledge. Further studies using scaling and other cognitive techniques to examine the semantic networks of these patients in different sensory and verbal domains will help further our understanding of the specificity of the organization of semantic knowledge in the association cortices.

REFERENCES

1. CHAN, A. S., N. BUTTERS, J. S. PAULSEN, D. P. SALMON, M. R. SWENSON & L. T. MALONEY. 1993. An assessment of the semantic network in patients with Alzheimer's disease. *J. Cognit. Neurosci.* 5: 254-261.
2. CHAN, A. S., N. BUTTERS, D. P. SALMON & K. A. MCGUIRE. 1993. Dimensionality and clustering in the semantic network of patients with Alzheimer's disease. *Psychol. Aging* 8: 411-419.
3. CHAN, A. S., N. BUTTERS, D. P. SALMON, S. A. JOHNSON, J. S. PAULSEN & M. R. SWENSON. 1995. Comparison of the semantic networks in patients with dementia and amnesia. *Neuropsychology* 9: 177-186.

4. CHAN, A. S., N. BUTTERS & D. P. SALMON. 1997. The deterioration of semantic networks in patients with Alzheimer's disease: A cross-sectional study. *Neuropsychologia* **35**: 241–248.
5. CHAN, A. S., D. P. SALMON, N. BUTTERS & S. A. JOHNSON. 1995. Semantic network abnormality predicts rate of cognitive decline in patients with probable Alzheimer's disease. *J. Int. Neuropsychol. Soc.* **1**: 297–303.
6. COLLINS, A. M. & E. F. LOFTUS. 1975. A spreading activation theory of semantic processing. *Psychol. Rev.* **82**: 407–428.
7. COLLINS, A. M. & M. R. QUILLIAN. 1969. Retrieval time from semantic memory. *J. Verb. Learn. Verb. Behav.* **8**: 240–247.
8. DEARHOLT, D. W. & R. W. SCHVANEVELDT. 1990. Properties of Pathfinder networks. *In Pathfinder Associative Networks: Studies in Knowledge Organization*. R. W. Schvaneveldt, ed. : 1–30). Ablex. Norwood, NJ.
9. MATTIS, S. 1976. Mental status examination for organic mental syndrome in the elderly patient. *In Geriatric Psychiatry*. L. Bellack & T. Karasu, Eds. Grune & Stratton. New York.
10. MCCARTHY, R. A. & E. K. WARRINGTON. 1988. Evidence for modality-specific meaning systems in the brain. *Nature* **334**: 428–430.
11. MCCARTHY, R. A. & E. K. WARRINGTON. 1990. The dissolution of semantics. *Nature* **343**: 599.
12. MURPHY, C., M. M. GILMORE, C. S. SEERY, D. P. SALMON & B. R. LASKER. 1990. Olfactory thresholds are associated with degree of dementia in Alzheimer's disease. *Neurobiol. Aging* **11**: 465–469.
13. MURPHY, C. & S. NORDIN. 1996. Impaired sensory and cognitive olfactory function questionable in Alzheimer's disease. *Neuropsychology* **10**: (1), 113–119.
14. RAZANI, J. L., A. CHAN, S. NORDIN, D. SALMON & C. MURPHY. Semantic memory for olfactory and visual stimuli in patients with Alzheimer's disease and normal elderly. (In preparation.)
15. ROMNEY, A. K., R. N. SHEPARD & S. B. NERLOVE. 1972. *Multidimensional Scaling: Theory and Applications in the Behavioral Sciences*. Vol. II. Seminar Press. New York.
16. RUMMELHART, D. & J. MCCLELLAND. 1986. *Parallel Distributed Processing: Explorations in the Microstructure of Cognition*. Vol. 1: Foundations. MIT Press. Cambridge, MA.
17. SHEPARD, R. N., & L. A. COOPER. 1992. Representation of colors in the blind, color-blind, and normally sighted. *Psychol. Sci.* **3**: 97–104.
18. SHEPARD, R. N., A. K. ROMNEY & S. B. NERLOVE. 1972. *Multidimensional Scaling: Theory and Applications in the Behavioral Sciences*. Vol. I. Seminar Press. New York.
19. TERRY, R. D. & R. KATZMAN. 1983. Senile dementia of the Alzheimer type. *Ann. Neurol.* **14**: 497–506.
20. WARRINGTON, E. K. & T. SHALLICE. 1984. Category specific semantic impairments. *Brain* **107**: 829–854.