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Semantic Networks for Odors and Colors in Alzheimer's Disease

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Abstract

Objective—Impairment in odor naming ability and in verbal and visual semantic networks raised the hypothesis of a breakdown in the semantic network for odors in Alzheimer's disease (AD). The current study addressed this hypothesis.

Method—Twenty-four individuals, half patients with probable AD and half control participants, performed triadic-similarity judgments for odors and colors, separately, which, utilizing the multidimensional scaling (MDS) technique of individual difference scaling analysis (INDSCAL), generated two-dimensional configurations of similarity. The abilities to match odors and colors with written name labels were assessed to investigate disease-related differences in ability to identify and conceptualize the stimuli. In addition, responses on attribute-sorting tasks, requiring the odor and color perceptions to be categorized as one polarity of a certain dimension, were obtained to allow for objective interpretation of the MDS spatial maps.

Results—Whereas comparison subjects generated spatial maps based predominantly on relatively abstract characteristics, AD patients classified odors on perceptual characteristics. AD patients' maps did also show disorganized groupings and loose associations between odors. Their normal configurations for colors imply that the patients were able to comprehend the task per se. The data for label matching and for attribute sorting provide further evidence for a disturbance in semantic odor memory in AD. The patients performed poorer than controls on both these odor tasks, implying that the ability to identify and/or conceptualize odors is impaired in AD.

Conclusion—The results provide clear evidence for deterioration of the structure of semantic knowledge for odors in AD.

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Keywords

Alzheimer's disease; semantic networks; multidimensional scaling; olfaction; olfactory impairment

Apart from a well-documented early impairment in episodic memory in the verbal and visual domains in Alzheimer's disease (AD; Bäckman, 2008), these patients show profound degradation in semantic memory (Chertkow, Whatmough, Saumier, & Duong, 2008). Whereas there is some evidence in favor of a retrieval problem accounting for the loss in semantic memory (Rogers & Friedman, 2008), a growing number of studies indicate a degradation of the organization of semantic knowledge in AD, suggesting a break-down in the semantic networks. Support for this comes from studies of verbal fluency, in which category tasks, relying heavily on semantic networks, have been found to be more affected than letter fluency, the latter being more dependent on retrieval processes (Butters, Granholm, Salmon, Grant, & Wolfe, 1987; Cerhan, Ivnik, Smith, Tangalos, Petersen, & Boeve, 2002; Monsch et al., 1994; Monsch, Granholm, Salmon, Grant, & Wolfe 1992; Rosser & Hodges, 1994; Gomez & White, 2006). Additional support for a break-down in the semantic networks in AD is provided by studies of object-sorting by specific attributes or category membership (Au, Chan, & Chiu, 2003; Chertkow & Bub, 1990). These findings suggest that AD patients are unable to make within-category associations or gain access to specific attributes about a given concept.

Histological abnormalities in AD, such as cell loss, neurofibrillary tangles, acetylcholine-deficiency as well as decreased levels of choline are found in areas of importance for olfactory processing. It has even been argued that these regions are among those predominantly affected, and even may be the site of initial involvement in the disease (e.g., Braak & Braak, 1997; Pearson, Esiri, Hiorns, Wilcock & Powell, 1985), including olfactory receptors, olfactory bulb, anterior olfactory nucleus, piriform cortex, entorhinal cortex, and hippocampus (Christen-Zaech et al., 2003; Kareken et al., 2001; Murphy, Jernigan, & Fennema-Notestine, 2003; Price, Davis, Morris, & White, 1991; Struble, Hughes, & Clark, 1993; ter Laak, Renkawek, & van Workum, 1994). In agreement with these findings, dysfunction in episodic odor memory has been demonstrated in AD (e.g., Moberg, Pearlson, Speedie, Lipsey, Strauss, & Folstein 1987; Nordin & Murphy, 1996; Gilbert & Murphy, 2004; Sundermann, Gilbert, & Murphy, 2007). Early studies of olfaction in normal persons suggested that odors are encoded perceptually in a holistic fashion with little or no semantic or higher-level verbal processing of the odors in episodic memory (e.g., Engen & Ross, 1973). Later studies have, however, challenged this notion, and have shown that semantic factors do indeed play an important role (e.g., Larsson, 1997; Murphy, Cain, Gilmore, & Skinner 1991; Murphy, Nordin, & Acosta, 1997). Lyman and McDaniel (1986, 1990), for example, found that odors were better remembered when they were associated with their names, significant life events, or visual stimuli. The breakdown in verbal and visual semantic networks and the early olfactory dysfunction in AD raise the question whether the networks on which semantic odor memory is based may be severely affected by the disease.

In addition to episodic odor memory, AD patients perform poorly on tests of odor identification, a task which involves semantic memory (e.g., Serby, 1986; Doty, Reyes, & Gregor, 1987; Pentzek, Grass-Kapanke, & Ihl, 2007), and that cannot solely be attributed to deficit in olfactory sensitivity or lexical demands (Koss, Weiffenbach, Haxby, & Friedland 1988; Morgan, Nordin, & Murphy, 1995). These findings suggest that AD patients are unable to make meaningful verbal and nonverbal associations with odors. Since the ability to make meaningful associations is thought to be a key feature of semantic memory (Tulving, 1987) and since the representation of odors into long-term memory is semantically mediated (Lyman & McDaniel, 1990; Murphy et al., 1991; Murphy et al., 1997), the inability of AD patients to accurately relate an odor with its label may be a strong indication for a disturbance in semantic knowledge about odors. In

order to assess the organization of semantic memory for odors in AD, we applied a method that has been used effectively in another modality.

Chan and colleagues have studied the organization of verbal semantic memory in AD (Au et al., 2003; Chan, Butters, Salmon & McGuire, 1993; Chan, Butters, Salmon, Johnson, Paulsen, & Swenson 1995). Cluster analyses of associations among animals with a category verbal-fluency task revealed that these patients tended to provide related exemplars in an atypical order, in turn, producing virtually uninterpretable clusters. Multidimensional scaling (MDS) analysis, which represents similarity data in the form of spatial maps, revealed a similar disorganization in AD. These patients used the perceptual attribute of size for clustering the related animals, in contrast to control participants who used a more abstract attribute, namely domesticity. Using a triadic comparison paradigm in which participants were presented with three animal names and asked to choose the two that were the most similar, revealed similar results (Chan et al., 1993, 1995). AD patients once again associated animals based on the attribute of size, while controls used more abstract attributes (domesticity and predation). The authors concluded that AD patients are able to make perceptual associations due to an intact visual neurologic system, but unable to draw on abstract knowledge, perhaps as a result of temporal-lobe pathology. It has been postulated that the association cortices of the temporal lobes are major sites for storage of semantic memory (Butters et al., 1987; Monsch et al., 1992) and that atrophy to these regions in AD therefore would lead to semantic deterioration, particularly loss of abstract conceptual knowledge (Chan et al., 1995). Visual perceptual information, on the other hand, seems to remain relatively intact, presumably due to the fact that such information is associated with the striate which is spared in early stages of the disease (Terry & Katzman, 1983).

The aim of the present study was to adopt the same MDS technique as that used by Chan and associates (Au et al., 2003; Chan et al., 1993, 1995) to investigate the nature of networks of semantic odor memory in AD by means of similarity judgments, reflecting ability to associate related odors. It was hypothesized that due to a disturbance in semantic memory AD patients' spatial maps would appear more disorganized and less interpretable than those of healthy elderly. A color association task was included which was similar to the odor task and used to control that a potentially poor performance on the olfactory test was not solely due to difficulties in task comprehension. Considering earlier findings (Chan et al., 1993), it was anticipated that AD patients would be able to make associations among colors given that changes in perception and cognition of color are not consistent in these patients (e.g., Wijk & Sivik, 1995; Wijk, Berg, Sivik, & Steen, 1999; Neargarder & Cronin-Golomb, 2005; Warkentin, Erikson, & Janciauskiene, 2008). The abilities to match odors and colors with written name labels were assessed to investigate disease-related differences in ability to identify and conceptualize the stimuli. In addition, responses on attribute-sorting tasks, requiring the odor and color perceptions to be categorized as one polarity of a certain dimension, were obtained to allow for objective interpretation of the MDS spatial maps.

Method

Participants

Participants were twelve patients with probable AD and twelve normal, elderly controls, closely comparable in gender and age (see Table 1). The patients were selected from a pool of participants in a longitudinal study at the Alzheimer's Disease Research Center (ADRC) at the University of California, San Diego. The diagnosis was made by two independent senior staff neurologists at the ADRC, according to the NINCDS-ADRDA criteria for probable AD (McKhann, Drachman, Folstein, Katzman, Price, & Stadlan, 1984) and the DSM III-R criteria for dementia (American Psychiatric Association, 1987). The DSM III-R criteria requires memory impairment as well as impairment in two or more areas of cognition (among language,

object recognition or naming, executive functioning, motor activity) which cannot be explained by other medical or neurological factors. Alternative causes of dementia (e.g., thiamin deficiency, thyroid dysfunction) were ruled out with extensive laboratory testing (e.g., blood tests, urinalysis). Additional screening tests (e.g., CSF, EEG, EKG, CT scan, MRI) were performed when necessary.

The control participants, recruited through advertisement, were healthy, active, community-dwelling individuals who resided in San Diego County, and who were screened for dementia with the Dementia Rating Scale (DRS; a global measure of overall cognitive functioning; Mattis, 1976). The AD patients and normal controls differed significantly in DRS score, $F(1,22) = 78.7$, $p < 0.001$ (Table 1). The mean DRS score for the controls (142.8) falls within the range of mean scores (137–144) from a review of studies of normal elderly (Mattis, 1988). All participants were screened for anosmia and significant hyposmia (Murphy, Gilmore, Seery, Salmon, & Lasker, 1990); however, as would be expected, the AD patients had statistically poorer odor-detection sensitivity (dilution step 5.2) than the controls (dilution step 6.9), $F(1,22) = 4.7$, $p < 0.05$ (Table 1). It should be noted that the average dilution step for detection in the patients (5.2) is close to what is considered within the range of clinically normal (dilution step 6.0 – 9.0; Harris, Davidson, Murphy, Gilbert, & Chen, 2006). All participants were also screened for color blindness with the Pseudoisochromatic Plates (Ishihara, 1976).

Materials and Procedures

All participants were given triadic-comparison tasks, label-matching tasks, and tasks of stimulus-sorting by attribute, in that order, for both odors and colors. The triadic-comparison tasks were performed on two days and the remaining two types of tasks on a separate day. **Triadic Comparison.** Ten highly identifiable odors were used (>90% correct identification by healthy persons; Table 2) according to previous work (Murphy & Cain, 1986; Murphy et al., 1991; Murphy, Schubert, Cruickshanks, Klein, Klein & Nondahl, 2002). Natural products or extracts of these odors were placed into opaque, squeezable bottles with pop-up spouts, and presented binocularly 2–3 cm below the nose. Color stimuli consisted of ten 2.5×2.5 cm semi-glossy chips (Table 2), together forming the color wheel (Sheppard & Cooper, 1992). Every possible permutation (i.e., order and combination) of stimulus triads was presented in a fixed random order, comprising 120 odor triads and 120 color triads. Participation was divided into two sessions of approximately 1.5 hours on separate days, consisting of 60 odor- and 60 color-triadic comparisons. Each odor triad was placed in front of the participant with an order that followed the presentation order. Each color triad was pasted on a separate page in the form of an equilateral triangle. The participant was instructed to indicate the two odors or colors within the triad that were most alike, alternating between odor- and color-triadic comparisons. The basis for the similarity judgment was left entirely up to the participant. The intertrial interval was 45–60 s for both odors and colors.

Label Matching—Five- by 10-cm laminated, written name labels of the odors and colors (Table 2) were randomly placed in front of the participant for the label-matching tasks. The participant was then asked to smell an odor or look at a color and match it to the name label presented in front of him or her by placing the stimulus beneath the chosen label, being allowed to make as many corrections as desired.

Sorting by Attribute—In the attribute-sorting task, the participant was asked to sort the ten odors and ten colors (Table 2) four times each based on the dimensions (attributes) of edibility, fruitiness, pleasantness, and intensity for odors; and warmth, likeability, brightness, and red-purple for colors. The former dimensions have been shown by previous research to be important in odor perception (Schiffman, Reynolds, & Young, 1981). Even though previous research has shown that the MDS space for colors generated by healthy persons typically is represented in

the form of a color circle (Sheppard & Cooper, 1992), the color-sorting task was conducted to enable interpretations of the MDS maps if the AD patients were found not to generate a color circle. For each attribute, two 5- by 10-cm laminated, written cards (e.g., fruity and nonfruity for the attribute of fruitiness) were placed in front of the participant. After being presented with the stimulus, the participant was asked to place it in front of the most representative attribute label.

Multidimensional Data Analysis—In general, MDS analysis generates a graphic representation of the data based on some measurement of the relative degree of association (in this case similarity) between concepts in semantic memory. The resulting models represent the concept 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 (Collins & Loftus, 1975). Ten by ten matrices, created separately for odor and color data, were analyzed individually for each participant. Each number in the matrix represented the number of times two stimuli (either odors or colors) were selected as being similar. The data were analyzed using individual difference scaling analysis (INDSCAL), developed by Carroll and Chang (1970), which is an MDS technique allowing for spatial representation of similarity data. INDSCAL analysis has the unique feature of providing both individual and group configurations. The spatial map clusters the data along one or more dimensions (axis) according to their relative proximity (i.e., number of times two particular stimuli were judged to be similar).

INDSCAL does also generate two measures of goodness-of-fit for each participant, represented by R^2 and stress values. The R^2 value represents the amount of variance accounted for by each solution in a linear model. That is, it indicates the amount of variance accounted for by the estimated proximity data obtained from the spatial configuration of the actual similarity judgments. The stress value ranges from 0 (best fit) to 1.0, and is a measure of the amount of error produced by the configuration (measure of badness-of-fit), derived through a number of iterations in an attempt to find the best fit for the data. In the iterative process, individual data points are relocated in space until an optimal configuration is reached. An individual weight index, provided by INDSCAL, indicates the importance each participant places on a particular dimension, ranging from 0 (no importance) to 1.0. Finally, INDSCAL gives a skewness index which indicates the relative distribution of saliency among each dimension, indicating how consistent a participant is in using one dimension relative to other dimensions (high index refers to high consistency; Wish & Carroll, 1974).

Determination of Dimension Attributes—The present study applied an objective method (Kruskal & Wish, 1978) instead of subjective methods (e.g., visual inspection of the configuration or explanations provided by participants regarding their sorting schemes) for discerning dimension labels to interpret MDS maps. Following this method, the dimensions for odors and colors were determined by (1) calculating the ranking score for each stimulus on the sorting task based on frequency of each odor ranked as edible, fruity, pleasant, and intense, and each color ranked as warmth, likeability, brightness, and red-purple, and (2) correlating these ranking scores with the coordinate values obtained for each dimension of the spatial map, separately for AD patients and controls.

Pathfinder Analyses—Similar to MDS techniques, Pathfinder analysis reduces similarity data into interpretable and meaningful outputs (Dearholt & Schvaneveldt, 1990). However, unlike MDS analysis, Pathfinder analysis produces networks that represent the strength of association between concepts rather than configurations of the data. For the present set of triadic comparison studies, Pathfinder networks were created, with the use of the Knowledge Network Organizing Tool (KNOT; Interlink), using the pairwise similarity data. A Pathfinder network is made up of a set of nodes, which in this case represent the odor or color stimuli. The similarity

judgments made for two nodes or stimuli (either odor or color), gathered from individual subjects, are then used to determine the strength of the associations between those two nodes (or stimuli).

The level of complexity for representing the networks can be selected by adjusting two parameters. The first, the r parameter, determines the path length or the length of the connection between two stimuli judged to be similar. The r value can be set to 1, in order to examine the greatest path length (i.e., a more complex network), or it can be set to infinity, in which case the shortest length (i.e., a more simple network) can be calculated. The second parameter, the q parameter, determines the maximum number of links in the path. When q is set to $n-1$, where n =number of stimuli or nodes, a network containing the maximum number of links can be obtained. The choice of the complexity of the network is based on the theoretical and practical purposes of the experiment. For the present set of studies we were interested in learning about the networks generated by demented and normal individuals based on similarity judgments made for stimuli that affect two different sensory modalities. We were interested in generating and understanding the simplest networks (i.e., r =infinity) with the maximum number of links (i.e., $q = n-1$).

Results

Label Matching and Sorting by Attribute

Number of correct responses on the label-matching tasks are given in Table 1. A two (AD patients vs. controls) by two (odors vs. colors) analysis of variance (ANOVA) revealed main effects of group, $F(1,22) = 47.8$, $p < 0.001$, and modality, $F(1,22) = 45.4$, $p < 0.001$, and an interaction, $F(1,22) = 45.4$, $p < 0.001$. Post-hoc analyses of the interaction showed that, compared to controls, AD patients were able to correctly match fewer odors, $F(1,23) = 47.9$, $p < 0.001$, but not colors, $F(1,23) = 3.7$, n.s. The odor attributes of pleasantness and intensity as well as all four color attributes are more subjective, in contrast to edibility (correct responses: banana, chocolate, cinnamon, coffee, orange, pineapple, vinegar) and fruitiness (banana, orange, pineapple). Mean correct-classification rates, obtained from the attribute-sorting task, on edibility and fruitiness were 65% and 66%, respectively, for the AD patients, and 88%, 82%, respectively, for the controls. A two (AD patients vs. controls) by two (edibility vs. fruitiness) ANOVA revealed a main effect of group, $F(1,22) = 13.4$, $p < 0.01$, but not attribute, $F(1,22) = 0.2$, n.s., and no interaction, $F(1,22) = 0.6$, n.s. Taken together, these results imply that the ability to identify and/or conceptualize odors but not colors was affected in the AD patients.

Triadic Comparison

Odors—Using criteria from Kruskal and Wish (1978), the data for triadic comparisons were fit to a two-dimensional solution. Mean weights assigned to each dimension are given in Table 3 and suggest that AD patients placed less importance (lower weights) than the controls on each of the two odor dimensions. This is supported by results from a two (AD patients vs. controls) by two (weights for Dimension 1 vs. Dimension 2) ANOVA, revealing a main effect of group, $F(1,22) = 20.1$, $p < 0.001$, but not dimension weight, $F(1,22) = 0.1$, n.s., or interaction, $F(1,22) = 0.0$, n.s. It does also suggest that no one primary dimension was used by either group when making odor-similarity judgments. A one-way ANOVA of the skewness index showed that both groups were fairly equally consistent in each of the two odor dimensions used, $F(1,22) = 0.6$, n.s. The spatial odor configurations suggest that AD patients' data accounted for approximately half the amount of variance (R^2), $F(1,22) = 15.1$, $p < 0.05$, and generated considerably larger stress values, $F(1,22) = 4.8$, $p < 0.05$, than that of the controls (Table 3).

Spatial odor maps for the two groups are presented in Figure 1. Visual inspection suggests that AD patients clustered odors differently than did controls. For example, fruity and nonfruity edible items are closely clustered by controls but not by patients. Correlation coefficients between ranking scores and coordinate values used for objectively determining the attributes underlying each odor dimension are presented in Table 4. The results show that for controls, the first dimension correlated significantly with the attributes of edibility (0.87) and fruitiness (0.77), and the second dimension correlated significantly with pleasantness (0.71). In contrast, AD patients' first dimension correlated significantly only with the attribute of fruitiness (0.65). The patients' second dimension correlated significantly with pleasantness (0.70).

Colors—Dimension weights for color-similarity judgments (Table 3) were virtually identical for both groups. A two (AD patients vs. controls) by two (weights for Dimension 1 vs. Dimension 2) ANOVA showed no main effects of group, $F(1,22) = 0.1$, n.s., or interaction, $F(1,22) = 3.0$, n.s., but a main effect of dimension, $F(1,22) = 29.2$, $p < 0.001$. The effect of dimension suggests that both groups place a greater importance on Dimension 1 than Dimension 2. One-way ANOVA showed no differences between groups in skewness index, $F(1,22) = 0.1$, n.s., suggesting that both groups used the two dimensions with the same consistency (Table 3). Also, no differences between groups were found in the amount of variance (R^2) accounted for by the spatial configurations, $F(1,22) = 0.7$, n.s., or by the amount of error produced by the maps, $F(1,22) = 0.5$, n.s. (Table 3). These results suggest that AD patients and controls associate colors in a similar manner.

The color-spatial maps are depicted in Figure 2 and suggest virtually identical maps for AD patients and controls, and that maps for both groups represent a color circle. No significant correlation coefficients between ranking scores for color attributes and coordinate values were found for either AD patients or controls, providing further evidence that the maps represent a color circle.

Odor Sensitivity and Spatial Odor Configurations

Analyses of covariance were conducted to investigate the potential contribution of relatively weakly perceived odors in AD patients (reflected by odor thresholds) on the MDS configurations. Using odor threshold as covariate, AD patients and controls continued to differ significantly on the amount of variance accounted for by their configuration (R^2), $F(1,20) = 13.9$, $p < 0.05$, in the error produced by their configurations (stress), $F(1,20) = 5.3$, $p < 0.05$, and on weights assigned to Dimension 1, $F(1,20) = 5.7$, $p < 0.05$, although not to Dimension 2, $F(1,20) = 1.1$, n.s.

Pathfinder Analyses

With r set to infinity and q set to $n-1$, the simplest model, with the greatest number of links among nodes (stimuli) was generated. A similarity index denoting the correlation of the number of links between each subject's network (based on an individual's similarity data) and an alternate network (either another subject's data or average group data) was produced with this analysis. Thus, the common links shared by the network of one subject to another, as well as the common links shared between an individual subject and the average network of the normal controls can be captured with similarity indices. The value of a similarity index ranges from 0, sharing no common links, to 1.0, sharing the greatest common links. The significance of the similarity index (correlation between two networks) is determined by a probability value (i.e., p value).

Odors—A similarity index capturing the similarity among the networks of each possible pair of AD subjects was calculated. Thus, for example, while one similarity index represented the similarity between the networks of patient #1 and patient #2, another represented the similarity

between the networks of patient #1 and patient #3, and so on. Averaging the similarity indices calculated between every possible pair of the AD patients for odors yielded a mean similarity index of .253 (SD=.081) with less than 12% of the indices reaching a significance level of $p < .09$. Averaging the similarity indices of the normal elderly subjects yielded a mean similarity index of .340 (SD = .122), with 65% of the indices reaching a significance level of $p < .09$. A one-way ANOVA comparing the similarity indices of the AD patients and the normal elderly showed a significant difference, with the normal elderly's networks being clearly more similar to one another than the networks of the AD patients, $F(1,119) = 20.84$, $p < .0001$. When comparing the networks of the individual AD patients with the average normal elderly network, a mean similarity index of .227 was found, and the mean probability of all the correlations (i.e., p values) was equal to .316. In fact, the probability of only one similarity index reached statistical significance ($p < .05$). Additionally, the similarity indices, capturing the similarity of each AD patient's network and the mean normal elderly network, were correlated with AD patients' DRS scores to probe an association between the degree of severity of dementia and the similarity of AD patients' networks to those of normal controls. This analysis yielded a correlation coefficient of .57 ($p=.07$). In order to assess the ability of similarity indices to predict the rate of cognitive decline in AD patients, these similarity indices were also correlated with scores capturing change in DRS scores from the first year of testing and a subsequent testing year (i.e., DRS year 2 – DRS year 1). The result, a correlation coefficient of .64 ($p < .03$), suggests that rate of cognitive decline is reflected in the deviations in the AD patients' networks from those of the normal elderly.

Colors—Averaging the similarity indices of the AD patients (i.e., comparison of each individual patient's network to every other patient's network) for colors yielded a mean similarity index of .578 (SD=.151), with over 70% of the probability values of the indices reaching statistical significance. Averaging the similarity indices of the normal elderly participants for colors yielded a mean similarity index of .562 (SD=.092), with all but one of the indices reaching the $p < .05$ level of significance. A one-way ANOVA comparing the similarity indices of the AD patients and the normal elderly for colors showed no statistically significant difference, $F(1,130)=.52$, $p=.47$, suggesting that the color networks of individuals within each group are quite similar to one another.

Discussion

Past findings of impairment in odor memory and in verbal and visual semantic networks provide a foundation for the present study's hypothesis of a breakdown in the semantic network for odors in AD. Using an MDS technique, the present study provides several pieces of evidence in favor of this hypothesis. Whereas the MDS maps from the similarity judgments suggest that healthy elderly classify odors based predominantly on the relatively abstract conception of edibility, the AD patients appear to predominantly classify the odors of the present study on the perception of fruitiness. These findings are consistent with those of Chan and colleagues (1993, 1995) who found that AD patients are unable to associate concepts in the verbal domain on the basis of abstract conceptual information. AD patients' inability to utilize more abstract odor characteristics may point to changes in the structure of stored semantic memory.

Further evidence for a breakdown in the semantic networks for odors in AD derives from the contrast in grouping of odors on the spatial maps produced by MDS. Control participants produced maps that exhibit logical grouping of odors based on common attributes shared among the odors. AD patients, in contrast, generated disorganized groupings and loose associations. For example, whereas controls closely clustered banana, orange, and pineapple based on the characteristic of fruitiness, AD patients did not. Instead, orange was as closely associated with baby powder as it was with banana. AD patients also produced lower weights

on both dimensions than controls, and they generated configurations that accounted for approximately half the amount of variance and displayed considerably larger stress values.

The data for label matching and the data for attribute sorting provide further evidence for a disturbance in semantic odor memory in AD patients. The patients performed poorer than controls on both these odor tasks, implying that the ability to identify and/or conceptualize odors is impaired in AD. This agrees well with previous findings on tasks of odor identification in AD (Doty et al., 1987; Knupfer & Spiegel, 1986; Morgan et al., 1995; Murphy, 1993; Murphy, 1999; Pentzek et al., 2007; Serby, 1986).

Another important finding is that AD patients and controls did not differ in the associations displayed on spatial maps for colors. Both groups generated MDS configurations for colors in the form of a color circle, consistent with maps previously obtained from normal participants (Izmailov & Sokolov, 1992; Shepard & Cooper, 1992). The color maps suggest that the neural networks for colors are relatively intact in AD and imply that the AD patients were able to comprehend and meet the demands of the similarity judgment task.

Additional support for the idea that the semantic networks for odors produced by the similarity judgment data generated by the AD patients differ from the semantic networks produced by normal elderly participants derives from the results of the pathfinder analysis. This analysis showed that not only were the AD patients' networks for odors less similar to one another, in comparison with the similarity of the normal controls' networks, but the AD patients' individual semantic networks for odors were significantly different from the average network of the normal elderly. In contrast, pathfinder analysis performed on the similarity data for colors supports a normal representation system in AD patients. The AD patients' networks for colors did not differ from those of the normal controls, suggesting an intact semantic network for color in AD.

Modality-specific semantic deterioration has clearly been demonstrated in the past (McCarthy & Warrington, 1988). It has been suggested that there may be more than one neuronal pathway for the storage of semantic information (Marshall, 1988) and that visual information of perceptual nature relies on the striate cortex. Whereas this region is relatively intact in AD (Terry & Katzman, 1983), major neuropathological changes have been reported in the temporal lobes where a large portion of olfactory processing takes place (Braak & Braak, 1997; Price et al., 1991).

As with all studies there are some possible limitations. The AD patients and controls were not matched with respect to odor sensitivity. However, the poorer sensitivity in the AD patients alone is not likely to explain differences between the two groups' abilities to associate odors. To begin with, no persons with anosmia or moderate or severe hyposmia participated, average detection threshold for the AD (dilution step 5.2) was close to what is considered to be in the range of clinically normal (dilution steps 6.0–9.0), and detection thresholds for all participants were at concentrations at which the odors used in this study can be expected to be clearly perceived and discriminated from each other. Importantly, when odor sensitivity was covaried out of the MDS measures, the results revealed that the two groups continued to differ on the MDS measures. It can also be argued that the two groups may have differed in odor discrimination (Djordjevic, Jonas-Gotman, De Sousa, & Chertkow, 2008), which could have explained the differences in odor associations. In one study it was suggested that poor odor discrimination is at the root of the poor odor discrimination in AD patients (Luzzi, Snowden, Neary, Coccia, Provinciali, & Lambon Ralph, 2007). The AD patients in that study correctly discriminated 11 out of 16 odors but identified only 1 out of 16, suggesting that additional factors contributed to poor identification. Future studies might investigate to what extent abnormal odor associations in AD can be referred to poor odor discrimination.

Another possible limitation refers to the presentation of the odors and colors in one of the tasks, i.e., the triadic-comparison task. In each case the triad was presented before the subject simultaneously. The odors in a trial necessarily were sampled in serial, but pace-controlled by the participant. As it was for odors, the inspection of the three colors was under the control of the participant. It was possible to sample the colors simultaneously, though participants could focus on one at a time. Thus, it is possible that somewhat higher working memory demands may have existed in the odor task compared to the color task.

Finally, the order in which stimuli in a triad were sampled was under the subject's control. The extent to which the subject may have based his choice on order rather than on the stimuli themselves is not known.

In summary, the present study suggests semantic deterioration for odors in AD, since these patients differed considerably from normal, elderly persons in the way they associated odors, but not colors. Consonant with previous findings for verbal information, the present study found that AD patients tend to use perceptual characteristics of odors, whereas normal controls employ abstract characteristics when making similarity judgments. The critical role of the mesial temporal lobe in the processing of both verbal and olfactory information may underlie the commonality in deficits in patients with AD.

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Figure 1.
Spatial odor maps for elderly controls and patients with Alzheimer's disease.

Figure 2.
Spatial color maps for elderly controls and patients with Alzheimer's disease.

Table 1Gender distribution and mean ($\pm$ SD) age and scores on various tasks

	Alzheimer's disease	Elderly controls
Males/females	5/7	6/6
Age (years)	74.3 ($\pm$ 6.5)	72.8 ($\pm$ 5.5)
Dementia Rating Scale ***	119.4 ($\pm$ 9.0)	142.8 ($\pm$ 1.4)
Odor threshold (dilution step) *†	5.2 ($\pm$ 1.9)	6.9 ($\pm$ 1.4)
Odor-label matching ***	4.6 ($\pm$ 2.7)	10.0 ($\pm$ 0)
Color-label matching	9.8 ($\pm$ 0.4)	10.0 ($\pm$ 0)

*
p < 0.05.

p < 0.001.

†
Scores 6.0 and above are considered clinically sound.

Table 2

Odors and colors (Munsell Color Classification) used in the study

Odors	Colors
Baby powder	Dark purple (5P 3/8)
Banana	Light purple (10P 3/10)
Chocolate	Blue (6.25 3/12)
Cinnamon	Green-blue (10BG 5/8)
Coffee	Green (7.5G 4/10)
Nailpolish remover	Yellow-green (10Y 8/12)
Orange	Yellow (2.5Y 8.5/12)
Pineapple	Orange-yellow (8.75YR 7/14)
Vicks	Orange (10R 5/14)
Vinegar	Red (5R 4/14)

Table 3

Mean ($\pm$ SD) measures of multidimensional scaling for odors and colors. Dimensions 1 and 2 are further described in Table 4.

	Odors		Colors	
	Alzheimer's disease	Elderly controls	Alzheimer's disease	Elderly controls
Weight				
Dimension 1	0.386 ($\pm$ 0.15)	0.560 ($\pm$ 0.18)	0.701 ($\pm$ 0.15)	0.796 ($\pm$ 0.12)
Dimension 2	0.367 ($\pm$ 0.18)	0.553 ($\pm$ 0.14)	0.528 ($\pm$ 0.17)	0.458 ($\pm$ 0.14)
Skewness index	0.166 ($\pm$ 0.20)	0.227 ($\pm$ 0.29)	0.181 ($\pm$ 0.12)	0.165 ($\pm$ 0.17)
R ²	0.343 ($\pm$ 0.23)	0.667 ($\pm$ 0.18)	0.803 ($\pm$ 0.25)	0.875 ($\pm$ 0.15)
Stress	0.295 ($\pm$ 0.06)	0.238($\pm$ 0.07)	0.139 ($\pm$ 0.09)	0.123 ($\pm$ 0.06)

Table 4

Correlation coefficients between ranking scores and coordinate values of spatial maps for each odor attribute

	Dimension 1		Dimension 2	
	Alzheimer's disease	Elderly controls	Alzheimer's disease	Elderly controls
Edibility	0.16	0.87*	0.39	0.49
Fruitiness	0.65*	0.77*	0.13	0.32
Pleasantness	0.08	0.57	0.70*	0.71*
Intensity	0.55	0.06	0.01	0.28

*
p < 0.05.