Original Article

Storage, Degradation, and New Connectivity of Face-Related Semantic Memory in Alzheimer's Disease

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Abstract

Background: Excepting amnesia, impairment of other domains also hampers the activity of daily living in Alzheimer's disease (AD). Although prosopagnosia poses problem in interacting with other persons, it rarely causes problem during interaction with close relatives as known voice acts as cue for recognition. **Objective:** In a cohort of AD, we planned to study errors in recognition, naming, and assigning relationship of close relatives, to assess the type and frequency of errors and to explain with current knowledge and hypothesis. **Materials and Methods:** This cross-sectional study was conducted in Memory Clinic of Medical College Hospital, Kolkata, India, between July 2013 and June 2015. Patients were evaluated by history, general neurological examination, and neuropsychological tests. A structured questionnaire was used to assess recognition (use of honorifics) and naming defect of close relatives. **Results:** AD was diagnosed in 42 patients. Prosopagnosia was found in 14 and anomia in 6 patients. Four patients exhibited problem during conversation with close relatives. They assigned name and relation of one generation earlier to close relatives with proper recognitions. **Discussion:** We got predictive error of name and relation assignment of close relatives by one generation back with normal recognition. It can be explained by two memory traces in connection of face-visual and name (with/without relation) representation, earlier being hierarchically older and more resistant to wearing. **Conclusions:** We hypothesize that the name/relation store is orderly conserved. In AD, after degradation of part of name/relation store, a new wiring might be built up between these two traces.

Keywords: Alzheimer's disease, face identification, semantic memory, storage and degradation

Introduction

With the increase in life expectancy, dementia is becoming a leading cause of morbidity and mortality in the elderly. Degenerative (Alzheimer's disease [AD], frontotemporal dementia, and dementia with Lewy body) and vascular (vascular dementia) pathologies are responsible for the vast majority of cases. AD is the most common cause of dementia irrespective of ethnicity and geographical boundary. It is the fifth leading cause of death in Americans aged 65 years or older.[1] The most common initial presentation of AD is impairment of episodic memory. However, a minority of patients can present with posterior cortical symptoms, language disorder, or frontal lobe syndrome.[2] Memory-onset AD will develop features of involvement of other domains such as topographical disorientation, agnosia (both object and face), language dysfunction, and behavioral symptoms as the disease progresses.

Impaired activity of daily living in AD is due to multiple factors. The most important factor is forgetfulness. However, behavioral, executive, and language problems are also quite important. Moreover, patients with AD develop difficulty in interacting with other persons. This requires recognition, proper naming of the person, and intact language function.

However, prosopagnosia (facial recognition defect) usually does not cause any significant problem during interaction with close relatives as known voice acts as a cue for proper recognition. Similarly, naming problem does not pose any problem during interaction with close relatives as naming is not required during conversation. However, some patients with AD have problem in interacting with close relatives. The reason behind this has not been explored. In this explorative study, we want to analyze this area in further detail to see whether there is any other substrate. If it is so, we would then try to understand the neuroanatomical basis of that substrate.

Materials and Methods

This cross-sectional study was conducted in the Memory Clinic of Medical College Hospital (MCH), Kolkata, India, between July 2013 and June 2015. Individuals with suspected cognitive dysfunction were referred to this specialty clinic from general neurology and psychiatry outpatient departments of MCH. Detailed history including demographic data, onset of symptoms, symptoms at presentation, nature of progression, family history, and presence of vascular risk factors were collected in a semi-structured proforma by a multidisciplinary team, after

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taking informed consent from either the patient or the guardians. A thorough general neurological examination was performed.

Anomia was defined as inability to name a person or object with retained recognition. Prosopagnosia was defined as inability to recognize the face of a person by visual means but ability to recognize with other sensory domain (e.g., voice).

For cognitive assessment, "Kolkata Cognitive Screening Battery" (KCSB),[3] which is a scale in the local language, Bengali, validated for use in a similar population, was used. The KCSB includes a 30-item screening tool, Bengali mental state examination (BMSE) which is equivalent to Mini-Mental State Examination, along with tests of attention, fluency, new learning ability using a 10-word list, and visuoconstructional ability.

Face recognition was assessed using a card with pictures of 20 famous personalities from our sociocultural background.[4] Prosopagnosia was differentiated from anomia by asking patients to elucidate the sphere of accomplishment or point out when name cue was given.

A structured questionnaire was given to the caregiver for those patients who had difficulty in interacting with relatives [Table 1].

The diagnosis of AD was reached according to the criteria for the clinical diagnosis of AD established by the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) and the Alzheimer's Disease and Related Disorders Association (ADRDA) workgroup.[5]

Laboratory investigations including neuroimaging (computed tomography [CT], magnetic resonance imaging [MRI], and single-photon emission CT scan of brain in selected cases), hemogram, blood biochemistry (renal, liver, and thyroid function tests and homocysteine level), serum Vitamin B12 level, and serology (human immunodeficiency virus enzyme-linked immunosorbent assay and Venereal Disease Research Laboratory) test were done.

Results

Out of total 120 patients of dementia, diagnosis of AD was made in 42 patients (35%). Male (n = 24) outnumbered female (n = 18). The age at presentation varied between 52 and 72 years (mean 62.83 years), total duration of illness at presentation was 1–10 years (mean 3.92 years), and the BMSE score varied from 2 to 22 (mean 12.4). Most of the AD patients started with episodic memory impairment (92.8%). Facial recognition defect (prosopagnosia) was found in 14 patients (33.3%) of AD using picture card test. We found anomia in 6 patients (14.2%).

On questioning the caregivers, it was found that most of our patients, who were found to have prosopagnosia or anomia, did not have any significant difficulty in interacting with close relatives.

Three patients with prosopagnosia and one without prosopagnosia (4 out of 42) [Table 2] exhibited a peculiar problem during interaction and conversation with relatives. They addressed their close relative with a name that is usually of a person of one generation earlier (higher). When they were asked about the relation, similarly they erred to an earlier generation (sister instead of daughter). However, it is evident from conversation (use of honorifics) that he or she could identify the person correctly [Table 3].

Discussion

Interaction with other persons including relatives is a unique character that differentiates humans from other subhuman species.

When auditory cue will not be of help (naming on seeing the photographs), the visual stimulus of face has to be perceived first and then to be recognized. If one can name it correctly, it is certain that he could recognize it. However, if there is naming error, the facial recognition might either

Table 1: Questionnaire for the caregivers to know the response of the patients during conversation with close relatives

Name of the relative and relation with the patient	Spontaneous/on questioning (after conversation started)		How he talks with him/ her (noticing the use of pronoun)	Interpretation
	Naming	Response about relation on questioning		
Example: Mr. A; son	A	Son	Appropriate (appears to be talking with son)	Normal/prosopagnosia
Mr. A; son	Could not name	Son	Appropriate	Anomia
Mr. A; son	Could not name	Brother	Appropriate	To be determined

Table 2: "Clinical features of the four patients who had difficulty in interacting with relatives"

Serial number	Age/sex	Duration of illness at presentation (years)	BMSE score	Presence of prosopagnosia	Presence of anomia
Case 1	70/male	1	12	+	-
Case 2	72/male	3	18	+	-
Case 3	57/female	2	15	-	+
Case 4	72/male	2	18	+	-

BMSE=Bengali mental state examination, +=Present, -=Absent

be incorrect (prosopagnosia) or correct (anomia). What is the proof that we could recognize it perfectly? Patients with anomia, in contrast to prosopagnosia, can tell the sphere of accomplishment on seeing the photograph and point out the picture on name cue. Patients with prosopagnosia can tell the area of accomplishment on name cue only.[4]

However, during conversation with close relatives, one takes the help of the auditory cue (voice of that relative) and that might be sufficient enough to overcome recognition defect due to primary or associative visual disorder including prosopagnosia. Thus, during conversation with close relatives, prosopagnosia does not pose any significant problem which is in accord with our finding. Similarly, patients with anomia rarely face any problem during conversation as naming is not required at that time.

What is the proof that he or she could recognize relatives during conversation perfectly? This is done by asking the name of the relative (in case of prosopagnosia) and asking the relation (in case of anomia). Another way to prove this is by speech analysis.

Speech analysis may help us understand the social relationships between the speaker and addressee. This may be done by analyzing the use of politeness markers or honorifics. The use of honorifics in Indo-Aryan languages including Bengali is rich and profuse and is an indicator of the social relationship.[6,7] For example, the pronouns for the second person address have three forms (tui/tumi/apni). The polite form "apni" is usually used for strangers, acquaintances, colleagues, and respected members of the family. The familiar form "tumi" is used between husband and wife, friends, and relatives. "Tui" is the intimate form and is used between siblings and friends. Young members of the family are addressed as either "tui" or "tumi." Consequently, if a patient addresses a person as somebody else, but his use of pronouns is compatible with the status of the person named, then it may be treated as normal recognition.

Basic face identification is done by "face" area in the midportion of the fusiform gyrus,[8,9] which is a constituent of visual unimodal association cortex. This area appears to be responsible for generic level identification of face. This information goes through ventral visual pathway[10] to access and activate multimodal associations through the heteromodal cortex of middle temporal gyrus (acting as transmodal gateway) for proper recognition of face.[11,12] The last and equally important step for proper functioning is to tag the name concerned. This is through connection between multiple semantic stores (here visual face representation and name) probably through an amodal hub.[13] Ideally, the retrieval from both the stores should be congruent to designate the proper name to the perceived face.

Two proposed mechanisms to explain the semantic deficits are degradation of the internal semantic network and failure to retrieve the information from that network.[14] Thus, if memory store of face is erased or cannot be activated, he or she will land into associative prosopagnosia. On the other hand, if memory store of name/relation is erased or cannot be activated, he or she would err in naming (anomia) and/or telling the relationship while seeing faces of that particular person in spite of proper recognition. Lesion in the amodal hub will lead to complete semantic loss.[13]

There are multiple theories for semantic memory organization. One of this is category specific (living and nonliving)[15] and other is featural (modality/attribute) specific. According to most accepted theory (sensory functional theory[16,17]), semantic knowledge is divided into anatomically distinct sensory and functional stores. Even though the sensory attributes are not single entity, they are divided into multiple attributes (e.g., sound, color, form).[18] Thus, different attributes of one single stimulus (object or face) are stored or organized in different anatomical substrates. In continuity with this concept, it had also been seen that perceptual representations of pictures had more robust connections with the visual semantic representations than the name representations.[17]

Similarly, neuropsychological evidence suggests differential access route to different components of semantic knowledge depending on the stimulus character (picture versus words)[19] during retrieval.

It has also been seen that the brain regions that involve in perceiving an object also encode its meaning.[20]

Table 3: Response about name, relation, and use of pronouns during conversation with close relatives by those four patients who had difficulty in interacting with relatives

Serial number	Relation with the patient	Naming during conversation (spontaneous/on questioning)	Response about relation on questioning (after conversation started)	How he talks with him/her (noticing the use of pronoun)
Case 1	Son	X (name of father)	Father	Appropriate for son
	Daughter- in-law	Y (name of daughter-in-law)	Wife	Appropriate for daughter-in-law
Case 2	Son	X (name of brother)	Brother	Appropriate for son
	Daughter	Y (name of sister)	Sister	Appropriate for daughter
Case 3	Husband	X (name of father)	Father	Appropriate for husband
	Nephew	Y (name of brother)	Brother	Appropriate for nephew
	Cousin	Z (name of uncle)	Uncle	Appropriate for cousin
Case 4	Son	X (name of brother)	Brother	Appropriate for son
	Daughter	Y (name of sister)	Sister	Appropriate for daughter

To summarize, different anatomical areas organize different attributes (visual attribute and name of a person) of a single stimulus (a person), and at the same time, these areas are richly connected within themselves. Retrieval of semantic memory of a person also access different routes depending on the modality of stimulus presentation (face or name of a person).

In our study, we found correct recognition (usage of proper honorifics) with improper naming tag. As this interpretation was done during conversation, the correct recognition could be due to either normal visual facial recognition or impaired visual recognition corrected by auditory cue. These two possibilities cannot be differentiated as this interpretation was done on the basis of questionnaire given to the caregivers, whose observation was during conversation between patient and close relatives. However, what is more important is that he or she recognized the relatives. Thus, it was expected that he or she should have tagged proper name to the recognized face. However, they erred in name and relation selection. This error in name and relation tag is not random, but obeys certain rule. Here, we got predictive error of name and relation tag of one generation back. We shall try to explain this unique phenomenon partially by our present state of knowledge and rest by hypothesis.

When a person is demented, he or she usually loses memory of recent events more than the past ones (Ribot's law).[21] So when a person sees his daughter-in-law, he compares the appearance of the face with his retained memory. As the age of the face corroborates with the face of a person of 30 years back, it should be either his sister or someone contemporary. He thinks that this person is matching the age and appearance of his sister (as he was dwelling in the era 30 years ago). Hence, he thinks that she should be his sister. Initially, it was thought that the temporally graded amnesia is related to episodic memory as per the standard model of memory. However, with the multiple trace theory,[22] it has been shown that temporally graded amnesia is only related to semantic memory, not to episodic/autobiographical memory.[23] If we try to explain our finding by this concept, we expect improper name, relation, as well as recognition defect (use of honorifics corroborating the perceived face). Thus, we cannot explain the predictive and differential deficit of visual facial semantics and name/relation semantics. To overcome the drawback of this concept, we are trying to explain our finding in another way.

Learning of somebody's name requires association of name with the face.[13] There are two memory traces in connection of face-visual semantic representation and name (with/without relation) representation in the neocortex. This is analogous to the concept of multiple physically separated neural ensembles of episodic memory as they are composed of different kinds of content in neocortex (e.g., sights, sounds, smells).[24] Out of these two, visual semantic memory is hierarchically older[25] and more resistant to wearing. This is corroborating with early naming problem with preserved visual memory including face in early AD. On the other hand, name store is hierarchically more recent and more prone to be degraded in dementia.

We hypothesize that the name/relation store is orderly conserved with one end for highest possible generation (e.g., grandfather, grandmother) and the other end for lowest possible generation (grandson and granddaughter). Within this name/relation trace, the more recent one would be more vulnerable to be erased or degraded, keeping the order intact. In this situation, a new wiring might be built up [Figure 1a and b] connecting the highest available store of face (visual semantic) and highest available store of name/relation. Similar type of increased functional connection had also been documented within a lobe and in prefrontal network in other studies.[26,27]

This postulation can explain this peculiar phenomenon of proper facial recognition with predictable name and relation selection error.

Conclusions

There are various peculiar phenomena found in AD. Our observation is also new and peculiar in the sense that it is predictable and indicates multiple trace theory for semantic memory. In addition, it might suggest orderly representation of semantic attributes in memory stores at least in case of close relatives. It might also suggest differential wearing of memory stores of different attributes and with temporal gradient like that of episodic memory. Thus, this observation may help us understand the semantic storage of facial identity in health and its wearing off and new connectivity in disease. Further studies are required not only to substantiate our observation,

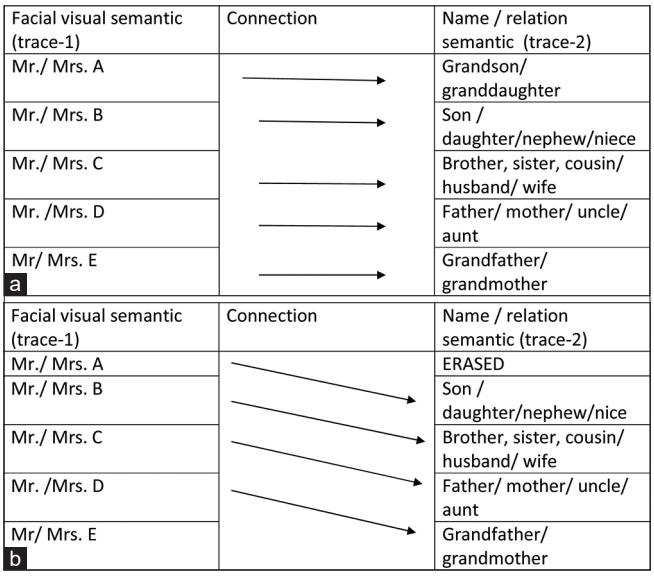

Figure 1: (a) Facial visual and name/relation semantics are separately and orderly stored with connection in between in healthy people. (b) Name/relation store is partially degraded with new connection with facial visual semantic store in disease

but also to evaluate the semantic storage of other attributes and their types of wearing off and new connectivity (if at all) in AD. This can be done by both clinical and neuroimaging (functional MRI) studies.

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Conflicts of interest

There are no conflicts of interest.

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