Animacy Effects in Fluency Task Performance in Early Alzheimer’s Disease—A Case-Control Study

Sir,

Studies pointing toward an advantage of animate words over inanimate words (animacy effect), indicative of evolutionary-based survival processing, have been noted in episodic and semantic memory functions.[1,2] Research has consistently shown that animates have a special status in various cognitive operations including perceptual, attentional, and memory processes leading to faster learning and better retention of animate words.[3-5] Evaluating the animacy advantage among patients with early dementia due to Alzheimer’s disease (AD) is thought to be intriguing since a handful of studies have reported the vulnerability of animate semantic lexicons in this population.[6,7] Given the fact that the evolutionary bias is said to enhance animate processing, it was worth exploring if it leads to increased fragility of animate concepts in pathological aging.

We relied on the Malayalam Addenbrookes Cognitive Examination (M-ACE)—based phonemic fluency and confrontational naming data collected from patients with early AD and age and gender-matched normal controls (NC) in order to delineate differences if any in the retrieval of animate and inanimate words. Patients were diagnosed based on NINDS-ADRDA (the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer’s Disease and Related Disorders Association) criteria for early AD with M-ACE scores between 60 and 75, Clinical Dementia Rating Scale <2, and minimal impairment on activities of daily living, along with a Hospital Anxiety Depression Scale performance of <7 on anxiety and depression subscales. NC were selected based on absence of subjective cognitive symptoms, M-ACE score of >85, Clinical Dementia Rating Scale 0 to 0.5, and Hospital Anxiety Depression Scale <7 on anxiety-depression subscales. Participants with a minimum of 8 years or more of formal education were selected from the study period between 2017 and 2020. Authors were not blinded to the diagnosis since data were collected via retrospective chart review.

The phonemic fluency verbatim responses for ‘P’ were classified into animate and inanimate words and the ratio of each category to total number of words generated were determined. Raw scores of animate and inanimate words in confrontation naming task were also recorded and considered for analysis. Data analysis was done using Statistical Package for the Social Sciences software version 21. Level of significance was kept at $P < 0.05$ for all analysis.

Mann-Whitney $U$ tests were used to compare age and education between the groups, which showed significant difference only for years of education, which was higher for the NC ($P = 0.01$). Spearman’s correlation coefficients of animate and inanimate scores with age and years of education (potential confounders) for phonemic fluency and confrontation naming were carried out for the total cohort. While age had no significant correlation...
with outcome scores of phonemic fluency or confrontation naming, education negatively correlated with animate words in phonemic fluency ($r = -0.296, P = 0.037$) and positively correlated with inanimate words in both phonemic fluency ($r = 0.298, P = 0.035$) and confrontation naming task ($r = 0.039, P = 0.005$) across the entire cohort. Furthermore, the numerical variables were compared between AD and NC using Mann-Whitney U test, which demonstrated significant difference between both groups. Higher mean values were noted for inanimate words over animate words among NC and AD. On the other hand, scores on confrontation naming showed better performance among NC on both animate and inanimate subsets [Table 1]. Wilcoxon-signed rank test showed statistically significant difference between animate and inanimate words for phonemic fluency task alone within NC ($Z = -3.74, P = 0.00$) and AD ($Z = -2.68, P = 0.01$).

Results revealed the following patterns: (i) AD and NC differed significantly in their performance on both phonemic fluency and confrontation naming, (ii) inanimate concepts were better retrieved in both AD and NC during phonemic fluency, however, a greater propensity for retrieval of animate items was noted among AD as opposed to controls, (iii) there was a significant positive correlation between years of education and the number of inanimate words retrieved, and (iv) confrontation naming did not favor either animate or inanimate word retrieval.

We did not observe any preference for retrieving animate words over inanimate words in both AD and NC during free recall of concepts from matured semantic systems. Our findings argue against assuming animate preferences in every dimension of adaptive memory. A similar pattern was reported in an in-depth case study of a person with AD who demonstrated significant deficits in the processing of animate items, while having spared knowledge of inanimate objects in both confrontation naming and visual knowledge tasks. Mohan et al. also did not observe any favor for animate over inanimate novel words during overnight integration or in forgetting rates. The deficit highlighted by us can be attributed to a specific loss in the knowledge about perceptual characteristics of animate objects since memory for the visual attributes of objects is conciliated by the inferior temporal lobes. Thus, our findings further assert the critical role played by temporal lobes in the processing, storage, and retrieval of animate items over inanimate ones in early dementia. Rogers et al. suggested that inanimate items can be assumed to have larger shared structures in the somatotopic representation of actions compared with animates. This extensiveness of representations could also lead to better retrieval for inanimate words.

Another observation made was the significant positive correlation between years of education and the number of inanimate words retrieved, suggesting reduced reliance on animate favored processing as years of education increased. There are prior arguments that document shift in mnemonic processing in elderly due to changes in life goals as well as prolonging for mental well-being over knowledge attainment. Aging and education may thus shift the focus from the evolutionary imprints of prey–predator roles to much higher socially driven emotional preferences and subsequent processing. It may be postulated that education and higher age may have contributed to less reliance on evolutionary-based animacy advantage in individuals with AD and NC.

However, we did observe that individuals with AD retrieved a significantly greater number of animate words when compared with NC. The significantly higher retrieval of animate objects on fluency tasks among AD with a reduced total score on both fluency and naming tasks in comparison with controls could suggest a gross compensatory strategy. Animate items are better visualized in context during the task that utilizes the semantic stores of information situated in the anterior temporal neocortex. In another sense, it can be viewed as a gradual fall back onto adaptive memory processes at the onset of a degenerative condition, wherein the individuals with AD may try to rely on the survival advantage of animate words in order to compensate for the lesser number of words, they retrieved during the fluency task.

The differences in retrieval of animate words during confrontation naming and phonemic fluency can be attributed to task-based variations. While the visual cue in confrontation naming provides easier semantic memory access, unprompted word generation makes phonemic fluency challenging. Our investigation failed to gather evidence for an animacy advantage during free recall tasks like the phonemic fluency task in both AD and NC. We deduce that education may alter the statistical significance of inanimate words in the social environment, creating a more extensive as well as resilient representation for these words over animate ones. Our findings also pointed toward the probability of gradual fall back to adaptive memory processes in individuals with AD at the onset of their degenerative condition, wherein the individuals with AD may try to rely on the survival advantage of animate words in order to compensate for the lesser number of words, they retrieved during the fluency task.

### Table 1: Between group comparisons of animate and inanimate words of phonemic fluency and confrontation naming task after adjusting for years of education

|                    | Mean (±SD)–weighted for years of education | P (Mann-Whitney U test) |
|--------------------|-------------------------------------------|-------------------------|
|                    | AD                                        | NC                      |
| PF (total)         | 9.33 (3.71)                               | 12.13 (4.16)            | <.001 |
| Animate words (PF)| 0.37 (0.21)                               | 0.27 (0.18)             | <.001 |
| Inanimate words (PF)| 0.63 (0.21)                          | 0.73 (0.18)             | <.001 |
| Animate words (CN)| 4.36 (0.96)                               | 4.91 (0.29)             | <.001 |
| Inanimate words (CN)| 4.65 (0.67)                        | 5.00 (0.00)             | <.001 |
| CN (total)         | 9.01 (1.41)                               | 9.91 (0.29)             | <.001 |

SD=standard deviation, AD=Alzheimer’s disease, NC=normal controls, PF=phonemic fluency, CN=cognitively normal.
A 17-year-old boy, born out of consanguineous marriage, presented with ataxia and hearing loss. He was referred to the Cognition and Behavioural Neurology Section, Department of Neurology, Sree Chitra Tirunal Institute of Medical Sciences and Technology, Trivandrum, Kerala, India.

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Lichtenstein–Knorr Syndrome: A Rare Case of Ataxia with Hearing Loss and Solute Carrier Family 9a1 Homozygosity

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To date, only five cases with two variants causing Lichtenstein and Knorr syndrome have been described (literature search in PubMed, Google Scholar, OMIM database). Here, we describe a novel homozygous solute carrier family (SLC9A1) mutation leading to a diagnosis of Lichtenstein–Knorr syndrome.

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