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The relationship between recall of recently versus remotely encoded famous faces and amyloidosis in clinically normal older adults

Irina Orlovsky[a], Willem Huijbers[a,b], Bernard J. Hanseeuw[a,c,d], Elizabeth C. Mormino[a,e], Trey Hedden[a,c], Rachel F. Buckley[a], Molly LaPoint[a], Jennifer S. Rabin[f], Dorene M. Rentz[a,g], Keith A. Johnson[a,c,h], Reisa A. Sperling[a,g], Kathryn V. Papp[a,g,*]

[a]*Department of Neurology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA*
[b]*Tilburg University, Department of Cognitive Science and Artificial Intelligence, Jheronimus Academy of Data Science, Tilburg, Netherlands*
[c]*Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA*
[d]*Neurology Department, Cliniques Universitaires Saint-Luc, Institute of Neuroscience, Université Catholique de Louvain, Brussels, Belgium*
[e]*Department of Neurology and Neurological Sciences, Stanford University School of Medicine, Palo Alto, CA, USA*
[f]*Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA*
[g]*Department of Neurology, Center for Alzheimer Research and Treatment, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA*
[h]*Department of Radiology, Division of Nuclear Medicine and Molecular Imaging, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA*

Abstract

Introduction: Alzheimer's disease (AD) patients exhibit temporally graded memory loss with remote memories remaining more intact than recent memories. It is unclear whether this temporal pattern is observable in clinically normal adults with amyloid pathology (i.e. preclinical AD).

Methods: Participants were asked to recall the names of famous figures most prominent recently (famous after 1990) and remotely (famous from 1960–1980) and were provided with a phonemic cue to ensure that memory failure was not purely due to verbal retrieval weaknesses. In addition, participants identified line drawings of objects. Clinically normal older adults (n = 125) were identified as amyloid β positive or negative (Aβ+/−) using Pittsburgh compound B positron emission tomography. The relationship between Aβ+/− and recall of remote and recent famous face-names and objects was examined using repeated measures analyses and general linear models controlling for demographics and media usage.

Results: When provided with a phonemic cue, Aβ+ participants recalled the names of fewer recent famous faces compared with Aβ− participants. However, recall of remote famous face-names and objects did not differ by Aβ group.

Discussion: Relative sparing of remotely learned information compared with recently learned information is (1) detectable in the preclinical stages of AD and (2) related to amyloid pathology. Both this temporal gradient and assessment of person-centered rather than object-centered semantic information may be particularly meaningful for tracking early memory changes in the AD trajectory.

Keywords: Memory; Semantic; Preclinical AD; Naming; Amyloid

1. Introduction

Memory decline is a core feature of prodromal Alzheimer's disease (AD) and AD dementia. Episodic memory, a temporally and context-dependent memory system comprised of explicit autobiographical events [1], is impacted early and preferentially [2,3]. However, semantic

*Corresponding author. Tel.: +1 617-643-5322; Fax: +1 857-307-5461.
E-mail address: kpapp@bwh.harvard.edu

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memory, a long-term memory system that is vital to the integrity of knowledge for facts, objects, and world concepts [1,4], also declines relatively early in the AD trajectory. While semantic memory is generally enriched with age [5], decline in this domain is a known feature of the AD dementia cognitive phenotype [6]. Furthermore, semantic memory may be declining concurrently with episodic memory [7] and even in the preclinical stages of AD [8]. Failure to retrieve proper nouns is the most common complaint of older adults [9], and these failures may, in some cases, represent worrisome semantic memory decline. Therefore, further characterizing changes in semantic memory may be instrumental to the early detection and tracking of AD-related cognitive decline.

A historical body of literature suggests a temporal gradient for memory loss in AD dementia, such that newly learned information is thought to be more vulnerable to disease pathology, with relative preservation of early or remote memories. This is known as Ribot's Law [10]. Famous face identification, traditionally a measure of remote semantic memory [11], is a particularly useful paradigm for exploring the temporal gradient originally described by Ribot. Task-specific demands allow for the examination of stimuli that were presumably encoded earlier versus later in life based on the period during which a famous person was prominent in the media. This paradigm has been exceptionally useful in identifying changes due to age- and disease-related memory loss for person-centered information in patients with semantic dementia [12,13], AD due to dementia [14,15], and temporal lobe epilepsy [16]. Furthermore, there is evidence that recall of famous faces is impaired in AD dementia [14], and naming of famous people is preferentially worse than naming landmarks and objects [17], in patients who satisfy diagnostic criteria for a precursor to AD dementia, mild cognitive impairment. However, it remains unclear whether this pattern is also observed at the preclinical stages of AD, where individuals show biomarker evidence of AD pathology but are otherwise clinically normal.

Therefore, the purpose of this study was two-fold. We aimed to determine whether temporally variant semantic stimuli, particularly semantic information learned relatively recently, was differentially impacted by positron emission tomography (PET) amyloid burden. In addition, we aimed to better understand whether famous face naming exhibited a similar relationship with PET amyloid outcomes compared with a traditional measure of semantic memory (i.e. object naming).

2. Methods

2.1. Sample characteristics

Our sample consisted of 125 clinically normal older adults who completed the famous face paradigm at year 6 of the Harvard Aging Brain Study. The study visit was conducted at Massachusetts General Hospital using protocols and informed consent procedures approved by the Partners Human Research Committee and Internal Review Board. Participants were deemed clinically normal at baseline on criteria including a global Clinical Dementia Rating score of 0 [18], normal Mini–Mental State Examination [19], and scores above age and education adjusted cutoffs on the 20-minute delayed recall of the Logical Memory Story [20]. None of the participants had a history of alcoholism, drug abuse, head trauma, or current serious medical or psychiatric illness. While a subset of individuals in the present study (n = 12) did obtain a global Clinical Dementia Rating score of 0.5 at their year 5 visit, none were given a research diagnosis of mild cognitive impairment at multidisciplinary diagnostic consensus meetings.

2.2. Amyloid imaging acquisition

Amyloid β (Aβ) burden was assessed using Pittsburgh compound B (PiB), a compound that binds to fibrillar amyloid, N-methyl-[11C]-2- (4-methylaminophenyl)-6-hydroxybenzothiazole [21], at baseline, year 4, and year 6. A PET scan was acquired at Massachusetts General Hospital using a Siemens ECAT EXACT HR + PET scanner. A dose of 8.5–15 mCi PiB was injected following a 10-minute transmission scan for attenuation correction. Sixty minutes of data were acquired in 3D acquisition mode following injection. PiB-PET data were processed as a distribution of volume ratio images (40 to 60-minute interval, gray matter cerebellar reference region). Mean PiB distribution volume ratio values were extracted from an aggregate of cortical regions susceptible to amyloid burden in AD including frontal, lateral temporal and parietal, and retrosplenial (FLR) cortices [22]. Participants were dichotomized on this FLR measure into Aβ+ and Aβ− groups using a Gaussian mixture modeling approach with a cutoff value of 1.2 distribution volume ratio [23]. Amyloid status was determined for majority of the participants (67%) at the time of novel semantic memory measure administration (year 6). Given slow Aβ accumulation rates, particularly in Aβ− participants [24], a subset of participants with previously acquired PiB-PET scans was classified as Aβ+/− using data from a year 4 PiB-PET scan (24%) and a baseline scan (9%).

2.3. Semantic memory measures

The famous face naming task involved selection of 24 target photographs of prominent public figures who were actively present in the media (television, sports, radio, and cinema). These faces were piloted previously on a group of healthy and cognitively normal older adults who were not enrolled in the present study, to ensure that chosen faces were familiar and well known [25]. Faces were selected based on a time period of prominence and dichotomized into remote (famous from 1960–1980) and recent time periods (1990 to present). Images of remote faces were chosen from their approximate time of prominence to ensure temporal relevance, whereas pictures of recent faces comprised images within the last three decades. All faces were presented