What's that word again? The contribution of the hippocampus to word-finding declines in aging

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Introduction

The problem: Word-finding difficulties in aging

WHAT?
- Word-finding difficulties increase as people get older, but not uniformly so:
  - Specific problems when a word is to be recalled from its meaning (e.g., naming an object, recalling someone's name)[1-4]
  - Fewer to no problems during word comprehension or reading[5-7]
  - Age-related increases in vocabulary size[8]
  - → *No study has characterized trajectory of performance across the lifespan in different lexical tasks within participants.*

WHY?
- Explanatory accounts for word-finding problems have posited age-related declines in various abilities (e.g., processing speed, executive control, perceptual problems)[9-12]
  - → *Existing theories account for some aspects of patterns, but not all.*

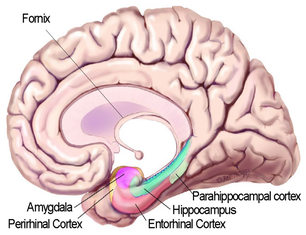
The Declarative Aging Deficit ('DAD') Hypothesis

= age-related declines in declarative memory and its neural correlates, in particular the hippocampus, lead to specific pattern of lexical declines in the learning and processing of words.

- Motivated by two lines of research:

1) Lexical abilities rely on declarative memory *(rooted in medial temporal lobe, especially hippocampus)*
- Medial temporal lobe supports both word learning and retrieval of recently-learned words (before systems consolidation)[13-17]
- Hippocampus: encoding relational (associative) knowledge (e.g., word-meaning pairs)[16,18] and retrieval via 'recollection' (e.g., recalling a word from its meaning), especially for recently-learned information[19,20]
- Perirhinal cortex: encoding of 'items' (e.g., objects, word forms) and retrieval via 'familiarity'[19,20]
- Recall requires hippocampal-based recollection, recognition can rely on recollection or perirhinal-based familiarity[19,20]

2) Declarative memory (and the hippocampus) decline with age.
- Greater learning declines when tested with recall than recognition[21-23]
- Greater declines for associations than single items[24,25]
- Striking declines for hippocampal volume[26,27]
- Less reliable declines for perirhinal cortex[28]



Predictions:

WHAT?
- Particularly strong age-related declines for lexical abilities that rely most strongly on hippocampus:
  - newer/recently-acquired words (vs. long-established/early-acquired words)
  - recall (vs. comprehension)

WHY?
- Mediation of declines through declarative memory abilities and hippocampal volume

Methods

Participants:

99 right-handed native U.S. English speakers:

	20s	30s	40s	50s	60s	70s	80s	Correlation with Age
n	20	17	7	17	21	12	5	
Sex	11 F, 9 M	11 F 6 M	4 F, 3 M	13 F, 4 M	12 F, 9 M	8 F, 4 M	5 F, 0 M	$\chi^2(6) = 5.13$, *ns*
Education (years)	15.6 (1.9)	18.2 (2.3)	17.9 (3.0)	17.4 (2.0)	18.8 (2.8)	17.8 (2.6)	15.8 (1.8)	$r = -0.21$, $p = .042$
Declarative Memory								
Recall score	0.41 (0.18)	0.33 (0.18)	0.18 (0.14)	0.31 (0.17)	0.24 (0.17)	0.24 (0.15)	0.17 (0.10)	$r = -0.38$, $p < .001$
Recollection score	0.71 (0.20)	0.66 (0.15)	0.58 (0.14)	0.56 (0.21)	0.58 (0.16)	0.50 (0.20)	0.46 (0.17)	$r = -0.39$, $p < .001$
Executive Control	66 (30)	67 (29)	59 (38)	70 (22)	70 (30)	56 (24)	52 (47)	$r = -0.13$, *ns*
Working Memory	7.0 (5.6)	8.7 (6.0)	7.3 (5.2)	2.1 (1.8)	3.4 (2.6)	2.3 (2.9)	0.8 (1.5)	$r = -0.48$, $p < .001$
Processing Speed	1166 (273)	1215 (224)	1433 (344)	1579 (343)	1694 (323)	1902 (393)	2331 (271)	$r = 0.63$, $p < .001$
Hippocampal volume*	5.90 (0.94)	5.72 (0.35)	5.77 (0.35)	5.78 (0.39)	5.53 (0.46)	5.02 (0.66)	4.80 (0.61)	$r = -0.38$, $p < .001$
Perirhinal volume*	2.03 (0.45)	1.91 (0.47)	1.78 (0.31)	1.84 (0.38)	1.68 (0.36)	2.07 (0.42)	1.93 (0.38)	$r = -0.24$, $p = .019$

Notes: Values are means per decade (standard deviations in parentheses).
*Corrected for intracranial volume; all values x 10^{-3}.

Inclusion criteria:
- No fluency in and no/little early exposure to another language (< 5 years)
- Normal performance on MoCA[29] and AD8[30]
- No more than moderate hearing or vision loss, not color-blind
- No (history of) neurological, cognitive, other learning-/language-related disorders
- At least 12 years of education (or GED)

Procedure:

Day 0:
- Screening:
  - Biographical and sociodemographic information
  - Neuropsychological testing (MoCA[29] and AD8[30])
  - Perception (vision and hearing)

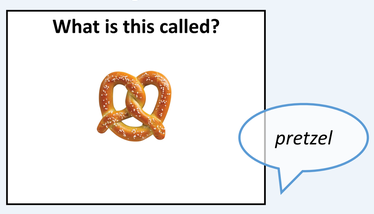
Day 1:
- Language tasks:
  - Lexical Production
  - Lexical Comprehension
- Declarative Memory[31,32]:
  - Encoding
  - Short Delay Recall
  - Short Delay Recognition
- Control tasks:
  - Processing Speed[33]
  - Executive Control[34]
  - Working Memory[35]

Day 2 ***(one week after Day 1)***:
- Declarative Memory:
  - Long Delay Recall
  - Long Delay Recognition
- MRI
  - MPRAGE (morphometry)
  - HARDI (white matter connectivity)
- Saliva sample (genetics)

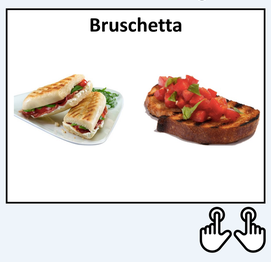
Tasks:

Language tasks

Lexical production:
Picture Naming



Lexical comprehension:
Word-Picture Matching

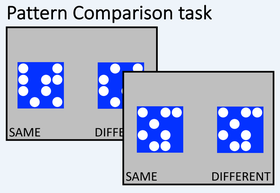


Materials for *each* task:
- 118 target words:
  - 81 established words (Oxford English Dictionary [OED] entry before 1920)
  - 37 recent words (OED entry after 1980): *sushi*, *sauna*, *yeti*, *karaoke*, …

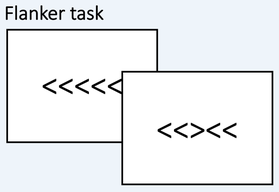
matched pair-wise for word frequency and word length

Control tasks

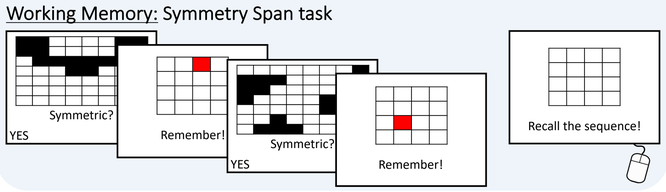
Processing Speed:
Pattern Comparison task



Executive Control:
Flanker task

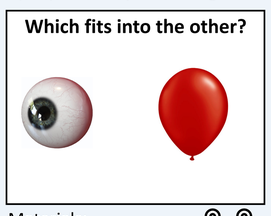


Working Memory: Symmetry Span task



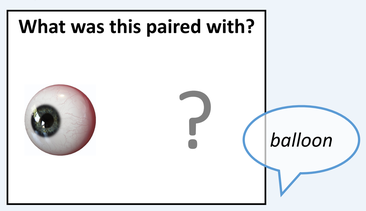
Declarative Memory

1) Explicit deep encoding



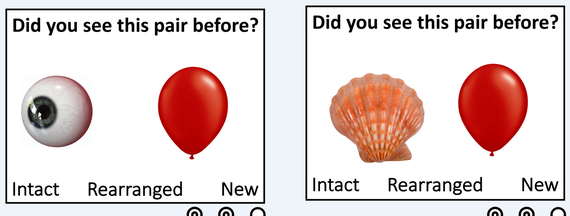
Materials:
- 72 item pairs
  - 24 tested in recall task (2a)
  - 48 tested in recognition task (2b; 24 intact, 24 rearranged (12 Day 1, 12 Day 2)

2a) Cued recall task:



Recall score = proportion correctly recalled items

2b) Recognition task:

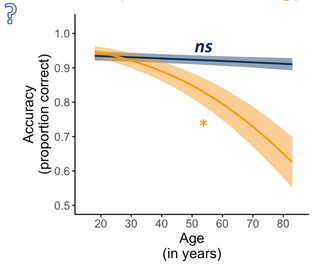


Recollection score = [proportion of intact pairs correctly endorsed as intact] *minus* [proportion of rearranged pairs incorrectly endorsed as intact]

Results

WHAT? Analyses: Generalized linear mixed-effects regression models on accuracy at Lexical Production and Lexical Comprehension, controlling for 'cohort effects' (e.g., education, sex), participant-specific differences (e.g., words not known to participants), and item differences (e.g., frequency, length).

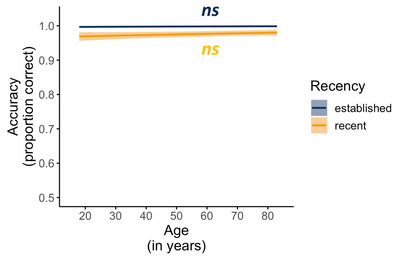
Lexical Production *(Picture Naming)*



Left:
- Interaction between Age and Recency ($z = -8.80$, $p < .001$)

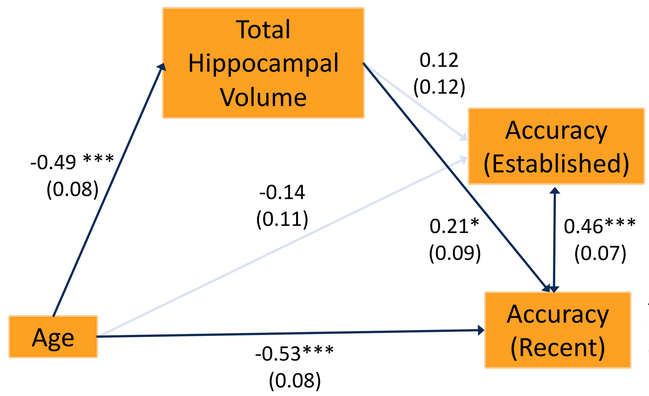
Right:
- No interaction between Age and Recency

Lexical Comprehension *(Word-Picture Matching)*



WHY? Analyses:
- A standardized structural equation model was run to test the indirect effect of total hippocampal volume mediating the relationship between age and lexical production accuracy for established or recent words.
- CFI = 1.00, TLI = 1.00, RMSEA = 0.00 (perfect fit since all variable relationships were modeled)
- Accuracy was transformed into a log-odds scale, with standardized effects being reported for all coefficients.
- Indirect effects were tested against a bias-corrected distribution of 10,000 bootstrap resamples to see if the 95% confidence interval did not contain zero.

Lexical Production *(Picture Naming)*



Age → Hippocampus → Accuracy (Established)
Indirect Effect:
β = -0.05, 95% CI [-0.18, 0.06]

Age → Hippocampus → Accuracy (Recent)
Indirect Effect:
β = -0.09, 95% CI [-0.21, -0.02]

Same pattern was obtained with Processing Speed and Executive Control also included as mediators.

Discussion

WHAT?
- Aging was associated with *specific lexical declines*:
  - Declining accuracy at producing relatively recent, but not established words
  - No age-related declines at the comprehension of (recent or established) words
  - Results held while controlling for participant-level and word-level factors

WHY?
- Relationship between age and accuracy at producing recent words is mediated by total hippocampal volume (as well as left and right volume)
- No mediation of effect of age on accuracy at producing established words

Limitations:
- Stringent inclusion/exclusion criteria limit ecological validity
- Recent words may have unusual phonotactics

Next steps:
- Analysis of contribution of hippocampal subfields, perirhinal cortex, white matter, and genetics
- Examination of role of cognitive variables (Declarative Memory, Working Memory, etc.)
- Reaction time analyses
- Examination of 'change points' across lifespan

Conclusion

WHAT?
- *Contrary to previous research,* lexical declines in aging may be specific to the recall of recent (but not established) words
- No age-related declines for word comprehension (for either recent or established words)

WHY?
- Age-related lexical declines (at recall of recent words) may be largely due to age-related hippocampal declines

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References & Acknowledgements

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