Familiarity-Related Processes and the Transentorhinal Cortex Volume: Insights into the Cognitive Functions of an Early Site of Alzheimer's Pathology

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Introduction

Neuropathology of Alzheimer's Disease appears ealy in the transentorhinal cortex (tErC)[1].

Understanding the role of this region in cognition is key for developing early diagnostic tools.

The tErC is assumed to be linked with familiarity, but it remains unclear to what aspects of familiarity, especially in aging population with neurodegenerative pathology.

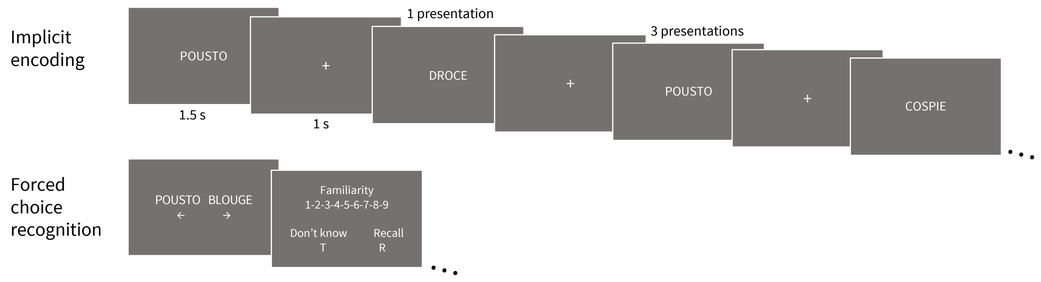
Using 3 tasks and MRI data in heterogenous aging population composed of healthy volunteers, MCI and SCD patients, we investigate:

- ***lifetime* familiarity**: gradual accumulation of familiarity with object concepts over the course of one's life[2,3]
- ***episodic* familiarity**: sense of recognizing based on a specific prior encounter[2,3]
- their additive effects and the impact of conceptual overlap discrimination

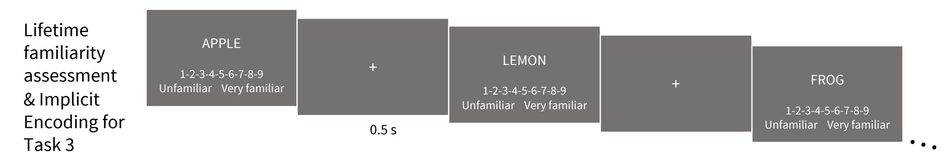
Methods

58 participants aged > 55 years old (37 healthy volunteers, 7 with Subjective Cognitive Decline, 14 with Mild Cognitive Impairment)

Task 1 - *Assessment of episodic familiarity*



Task 2 - *Assessment of lifetime familiarity*

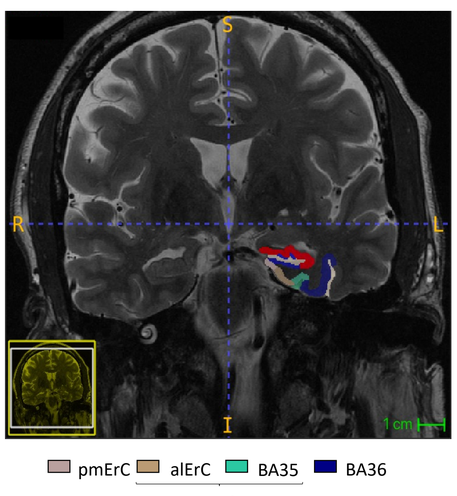


Task 3 - *Assessment of their additive effects and the impact of conceptual overlap*

		Overlap	
		High	**Low**
Target high familiarity	**Lure high familiarity**	**Apple**-Pear	**Kiwi**-Banana
	Lure low familiarity	**Frog**-Toad	**Salmon**-Dolphin
Target low familiarity	**Lure high familiarity**	**Tarantula**-Spider	**Zebra**-Cow
	Lure low familiarity	**Walrus**-Seal	**Jellyfish**-Seahorse

Structural MRI images (T1 and T2-weighted)

→ segmentation of MTL using ASHS (+ manual for alErC and pmErC).



Analyses

Task 1: ANCOVA with RM (2 numbers of presentation at encoding) on % correct responses.

Task 2: Stepwise linear regression on the adequacy (i.e., correlation) between lifetime familiarity judgements and those from a normative sample.

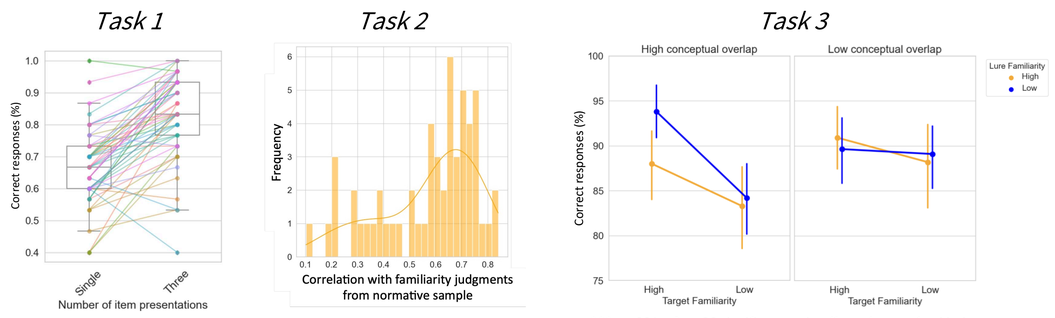
Task 3: ANCOVA with RM 2x2x2 (high or low lifetime familiarity of lure, high or low lifetime familiarity of target, high or low conceptual overlap between lure and target) on % correct responses.

For all above, covariates are:

- Age and Sex
- Volumes of left and right tErC (= alErC + BA35), pmErC, BA36, CA1, CA3, DG

Results

Familiarity performance



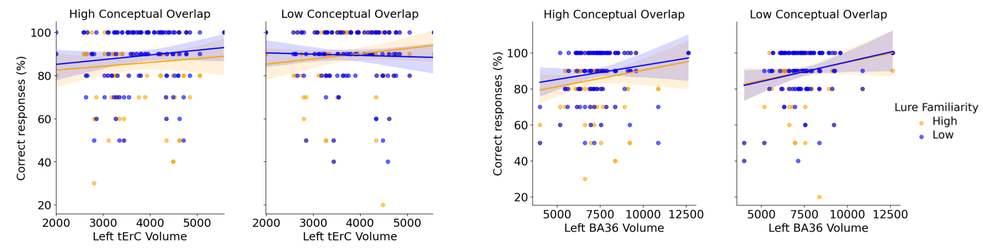
***p<.001, η^2_p = .63 significant main effect of number of presentations at encoding

All participants showed positive correlation with familiarity judgments from the normative sample (*N* = 54) and there is inter-individual variability for regression analysis with brain volumes.

*** p<.001, η^2_p = .30 significant main effect of target familiarity
*p =.02, η^2_p = .09 significant main effect of conceptual overlap
*significant interactions of conceptual overlap with target (p = .01, η^2_p = .11) and lure (p = .03, η^2_p = .08) lifetime familiarity
*p = .04, η^2_p = .08 significant triple interaction

Link between familiarity performance and volume of the tErC region

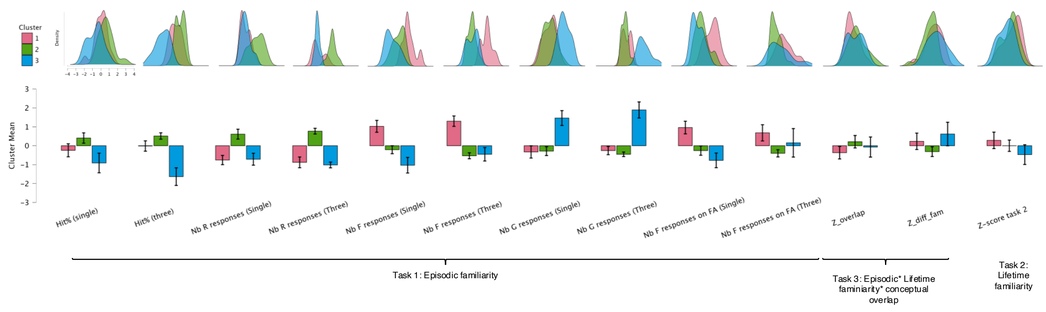
Task 1: ANCOVA with MTL brain volumes revealed no significant modulation of the performance
Task 2: Stepwise linear regression revealed no significant modulation of the performance by MTL regions volumes
Task 3: ANVOCA releaved significant triple interactions on the performance between
- lifetime familiarity of the lure, the degree of conceptual overlap and the volume of **left BA36**
- lifetime familiarity of the lure, the degree of conceptual overlap and the volume of **left tErC**

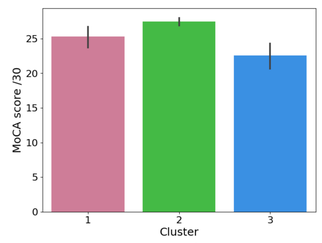


**$F(1,40)$ = 9.46, η^2_p = 0.19, p = .004

**$F(1,40)$ = 7.77, η^2_p = .16, p = .008

K-mean clustering analysis across 3 tasks & Matching with diagnosis





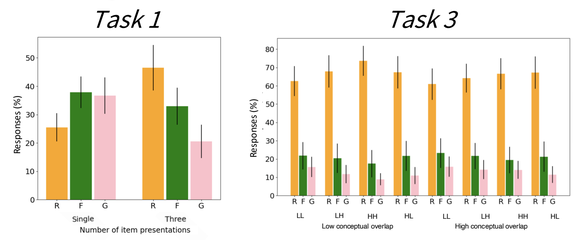
	Diagnosis			
Cluster	HC	MCI	SCD	**Total**
1	7	6	2	15
2	23	3	3	29
3	2	5	2	9
Total	32	14	7	**53**

*Kruskal-Wallis ANOVA: H(2) = 17.68, η^2 = .34 , p < .001

*$\chi^2(4)$ = 11.87, p = .018

Discussion

- Results support the link between the volume of the tErC and the familiarity decision when discriminating highly overlapping concepts is required
- Clustering analysis suggests that assessing various aspects of familiarity may help early diagnosis of cognitive impairment
- Limitation: Evaluation of representational aspect of familiarity only, not enough data to investigate the phenomenological dimension of familiarity



F: familiarity; R: recollection; G: guess

References

1. Braak, & Del Tredici (2015), *Brain*.
2. Bowels et al. (2016), *Neuropsychologia*.
3. Duke et al. (2017), *Cortex*.
4. Frick et al. (2023), *Neurobiology of Aging*.

Preprint

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