Sex Differences in Episodic Memory Performance in Healthy Older Adults with Family History of Alzheimer's Disease

Sheida Rabipour[1,2*], Sricharana Rajagopal[2], Stamatoula Pasvanis[2], *PREVENT-AD Research Group,* and M. Natasha Rajah[1,2]

[1]Department of Psychiatry, McGill University, Canada, [2]Douglas Mental Health University Institute Research Centre, Canada

INTRODUCTION

- Biological sex appears to influence Alzheimer's disease (AD) prevalence and incidence, disproportionately affecting women compared to men *(GBD Dementia Collaborators, 2019).*
- Older adults with elevated AD risk show early differences in episodic memory-related brain function, and may benefit most from early treatment *(Rabipour et al., in press).*
- Episodic memory decline is one of the earliest signs of AD *(Bateman et al., 2012).*
- Recollection (i.e., recall of contextual details) vs. familiarity (i.e., item recognition) may evolve differently in healthy aging and AD.
- **Objective:**
  To examine sex differences on whole-brain activity during episodic encoding and retrieval of items (i.e., recognition) and their spatial context (i.e., source recall), in cognitively healthy older adults with family history of AD.

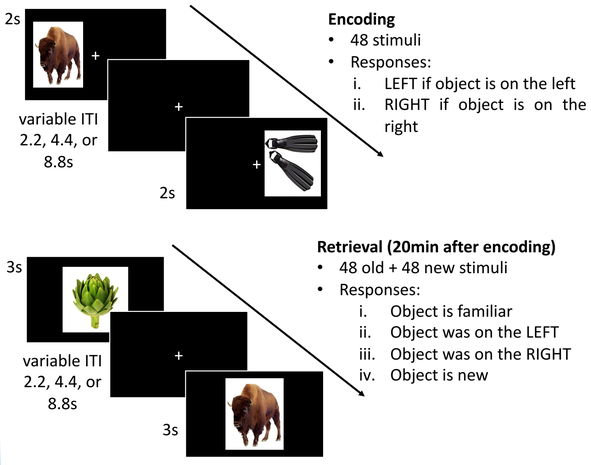
METHODS

- We analyzed baseline data from age and education matched men and women (***n* = 82, M_{age}=63.02±3.74; $M_{education}$=15.62±3.45**) who participated in the PRe-symptomatic EValuation of Experimental or Novel Treatments for Alzheimer's Disease (PREVENT-AD) study in Montreal, Canada (http://prevent-alzheimer.net).
- **Task fMRI**
  Single shot T2*-weighted gradient echo planar imaging
  TR = 2s, slice thickness = 4mm
- **Bias-corrected performance scores**
  Probability of source recall = Z(source hit) – Z(source misattribution)
  Probability of recognition = Z(recognition) – Z(false alarm)
- **Partial least squares *(McIntosh et al., 2014)***
  Brain activation levels (task PLS)
  Brain-behavior correlations (behavior PLS)

Negative saliences — Positive saliences

Response

Stimulus	"old-left"	"old-right"	"familiar"	"new"
old-left	Source Hit	Source Misattribution	Recognition	Miss
old-right	Source Misattribution	Source Hit	Recognition	Miss
new	False Alarm	False Alarm	False Alarm	Correct Rejection



Encoding
- 48 stimuli
- Responses:
  i. LEFT if object is on the left
  ii. RIGHT if object is on the right

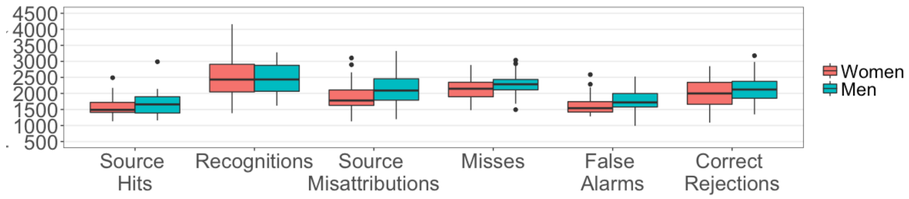
Retrieval (20min after encoding)
- 48 old + 48 new stimuli
- Responses:
  i. Object is familiar
  ii. Object was on the LEFT
  iii. Object was on the RIGHT
  iv. Object is new

RESULTS

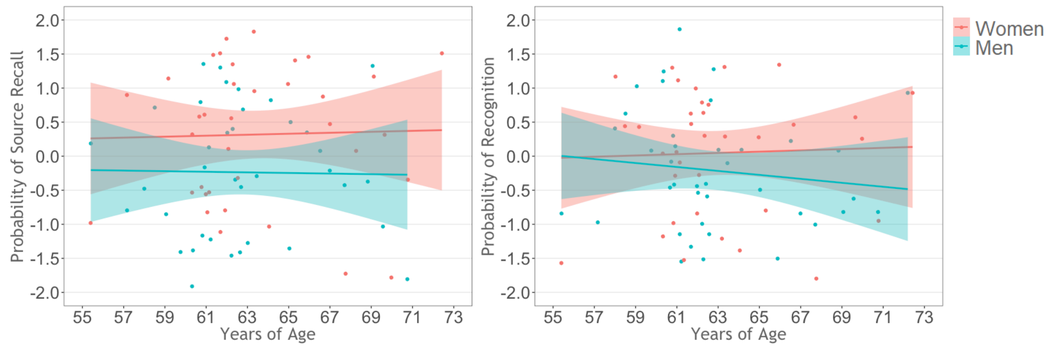
Participant Demographics

	Age	BMI	Years of Education	*APOE4 carriers*	Estimated Years to Symptom Onset	MoCA Score
Women (*n*=41)	63.13 ± 3.84	26.29 ± 4.55	15.66 ± 3.73	18 (44%)	10.97 ± 7.43	28.22* ± 1.57
Men (*n*=41)	62.92 ± 3.69	27.33 ± 3.75	15.59 ± 3.19	16 (39%)	9.46 ± 8.24	27.34 ± 1.81

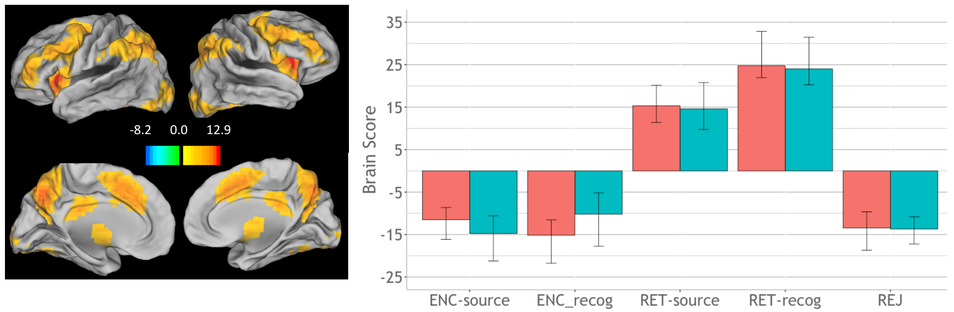
Response Times (seconds)



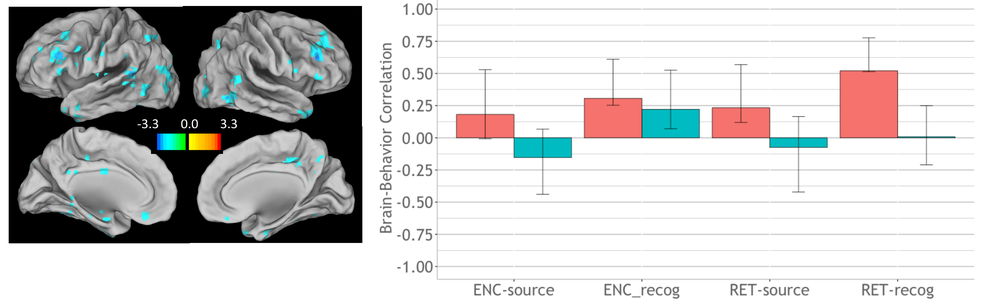
Bias Corrected Performance Scores



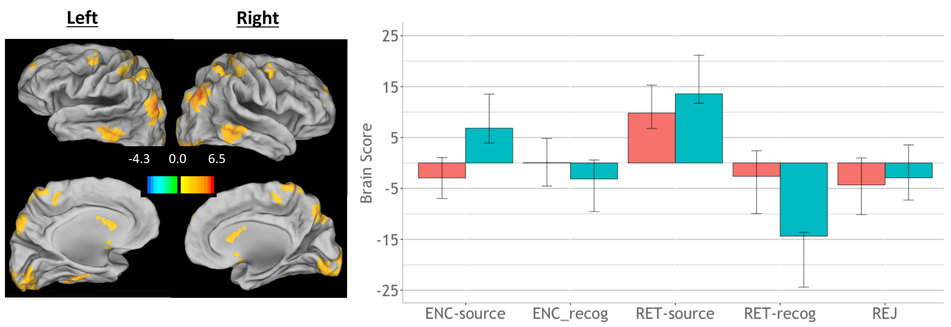
Task PLS LV1: Group Similarities in Encoding vs. Retrieval



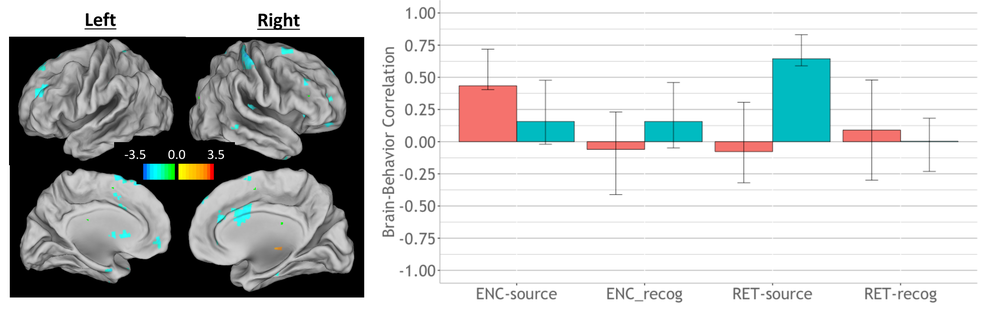
Behavior PLS LV1: Regions Supporting Episodic Memory in Women



Task PLS LV3: Group Similarities in Source Recall vs. Recognition



Behavior PLS LV2: Sex by Phase Effect for Source Recall



CONCLUSIONS

- Biological sex appears to influence episodic recollection (i.e., recall of contextual details) vs. familiarity (i.e., item recognition) in older adults with family history of AD.
- Men and women have similar episodic memory performance and task-related brain activity
  - Women tended to perform better on MoCA and source recall (*ns*), with faster response times in most categories.
- Correlations between performance and brain activity patterns differ based on sex:
  - Activation in medial and middle frontal regions is negatively associated with performance in women; no association in men
  - Activity in frontal & temporal regions is associated with source encoding in women, compared to source retrieval in men.
- Risk factors such as biological sex may influence *associations* between performance & brain activity, rather than either performance or brain activity themselves.
- Our future work will examine whether and how biological sex may influence these associations longitudinally.

ACKNOWLEDGMENTS

We thank members of the Rajah lab, the Cerebral Imaging Centre, and the StoP-AD Centre at the Douglas Institute Research Centre for their helpful feedback on this work. We also acknowledge the Fonds de Recherche Québec – Santé and Canadian Institutes of Health Research for their support of our research.

***Contact: sheida.rabipour@mail.mcgill.ca**