

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

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## INTRODUCTION

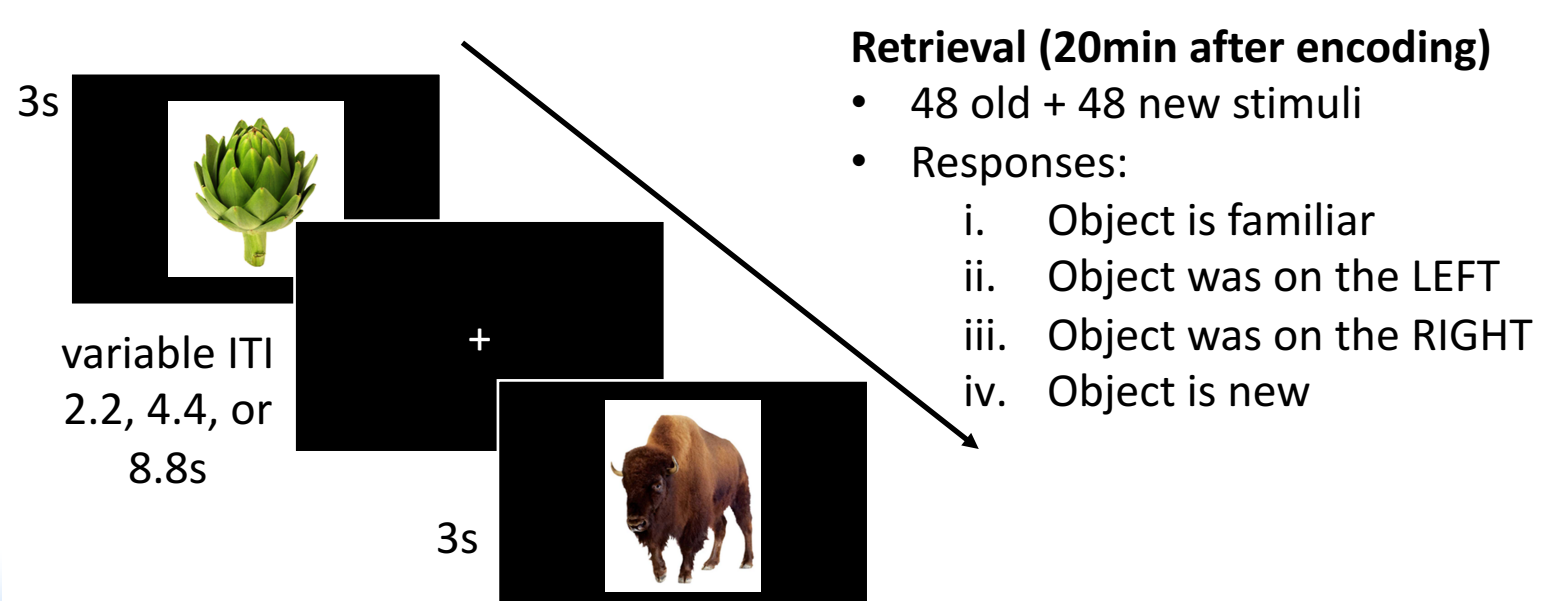
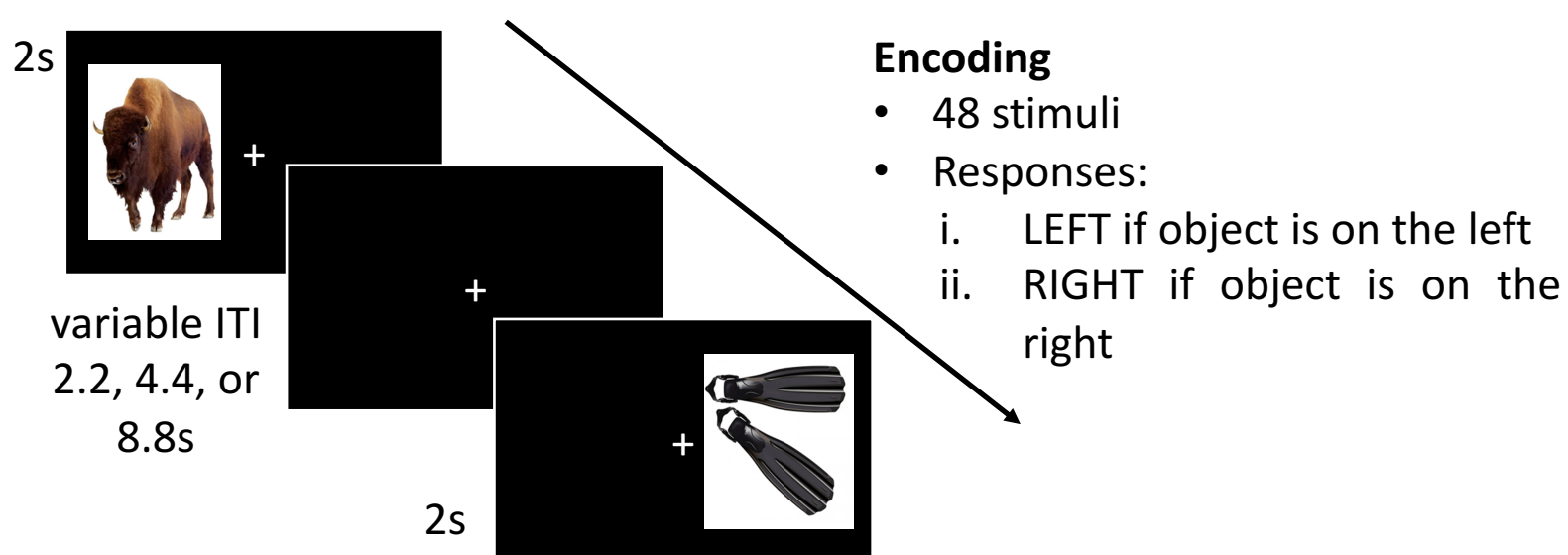
- Biological sex appears to influence Alzheimer's disease (AD) prevalence and incidence, disproportionately affecting women compared to men (*GBD Dementia Collaborators, 2019*).
- Older adults with elevated AD risk show early differences in episodic memory-related brain function, and may benefit most 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 ( $n = 82$ ,  $M_{age}=63.02\pm3.74$ ;  $M_{education}=15.62\pm3.45$ ) 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 =  $Z(\text{source hit}) - Z(\text{source misattribution})$   
Probability of recognition =  $Z(\text{recognition}) - Z(\text{false alarm})$
- Partial least squares (McIntosh et al., 2004)**  
Brain activation levels (task PLS)  
Brain-behavior correlations (behavior PLS)

		Response			
		"old-left"	"old-right"	"familiar"	"new"
Stimulus	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

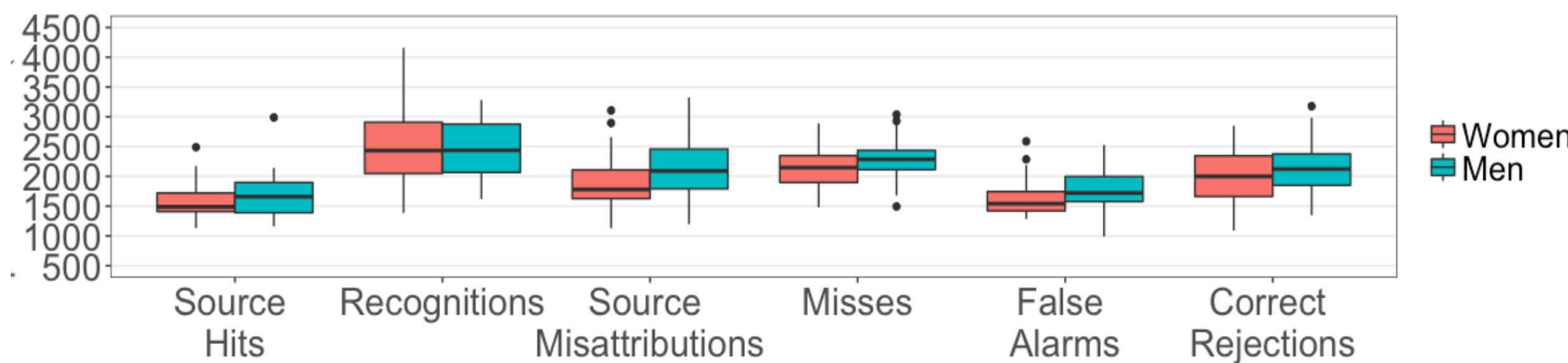


## RESULTS

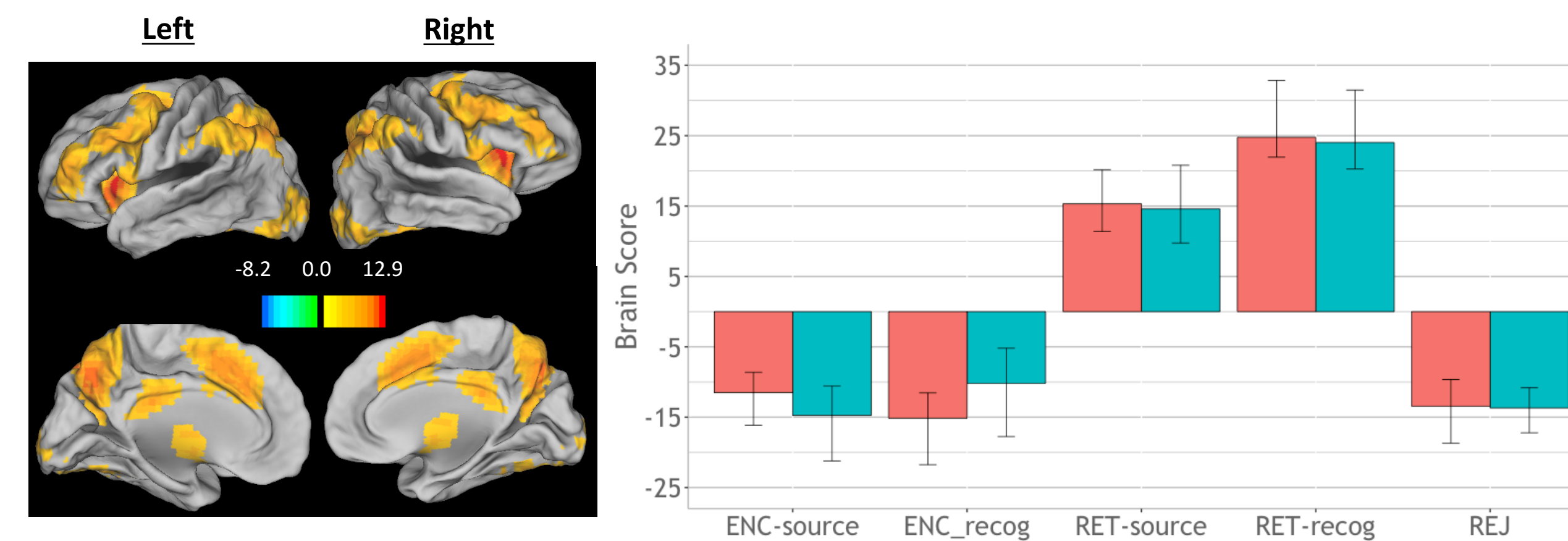
### Participant Demographics

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

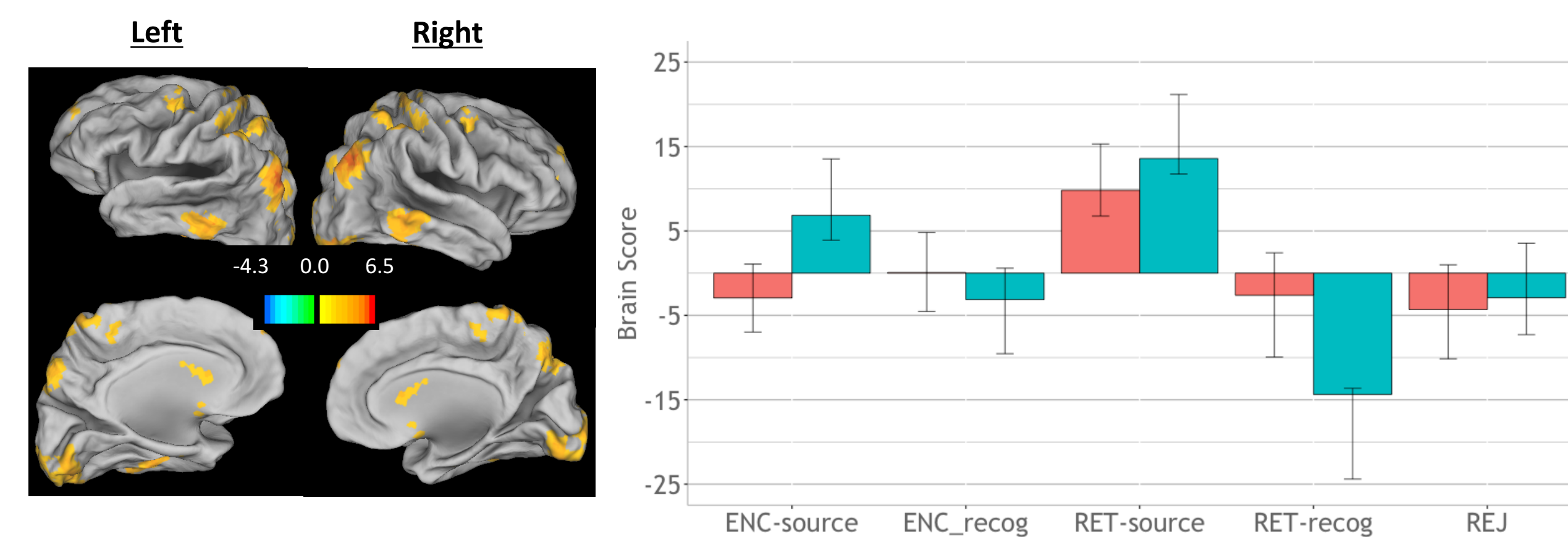
### Response Times (seconds)



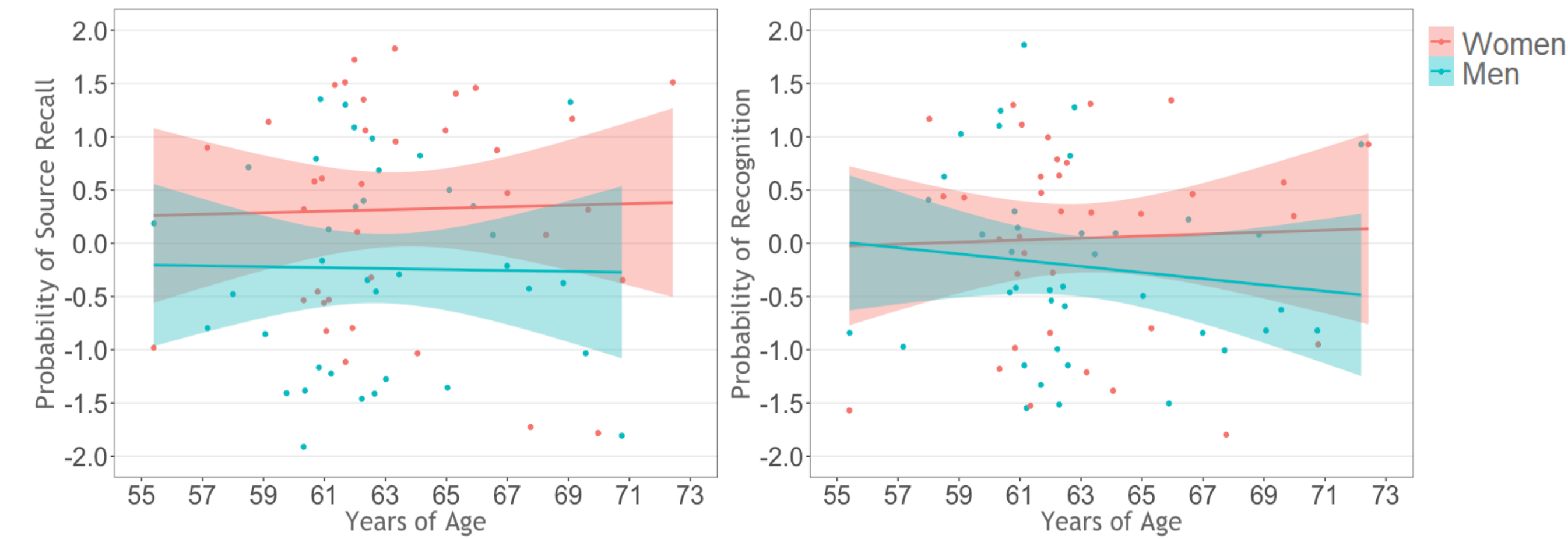
### Task PLS LV1: Group Similarities in Encoding vs. Retrieval



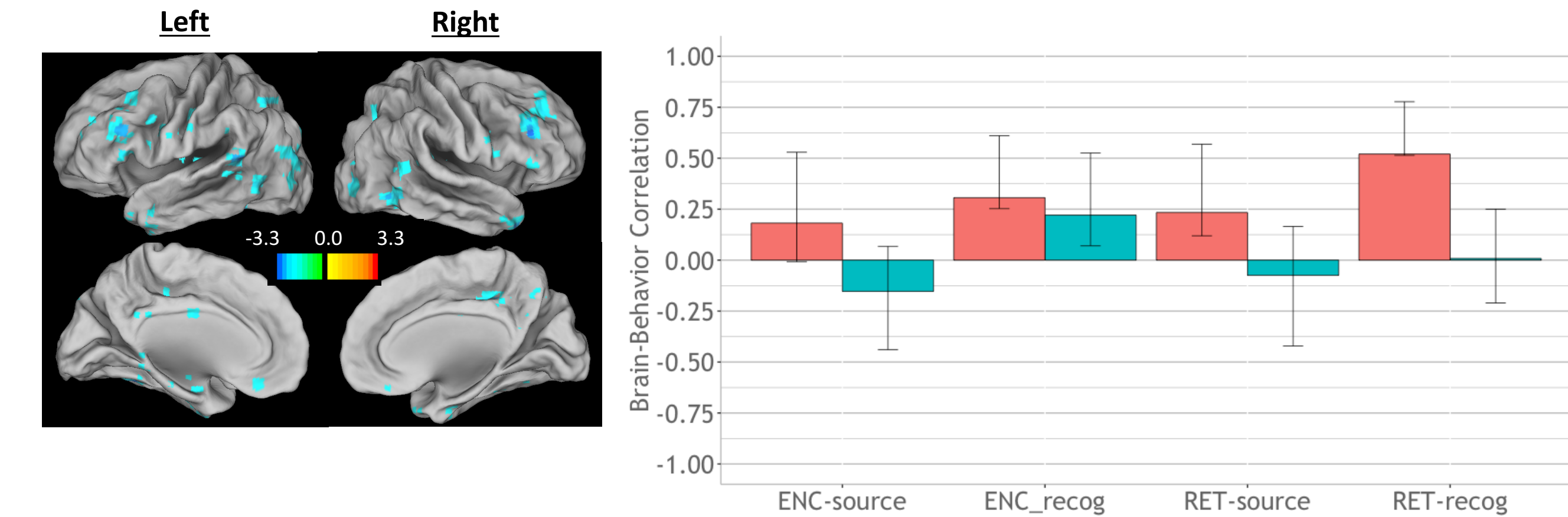
### Task PLS LV3: Group Similarities in Source Recall vs. Recognition



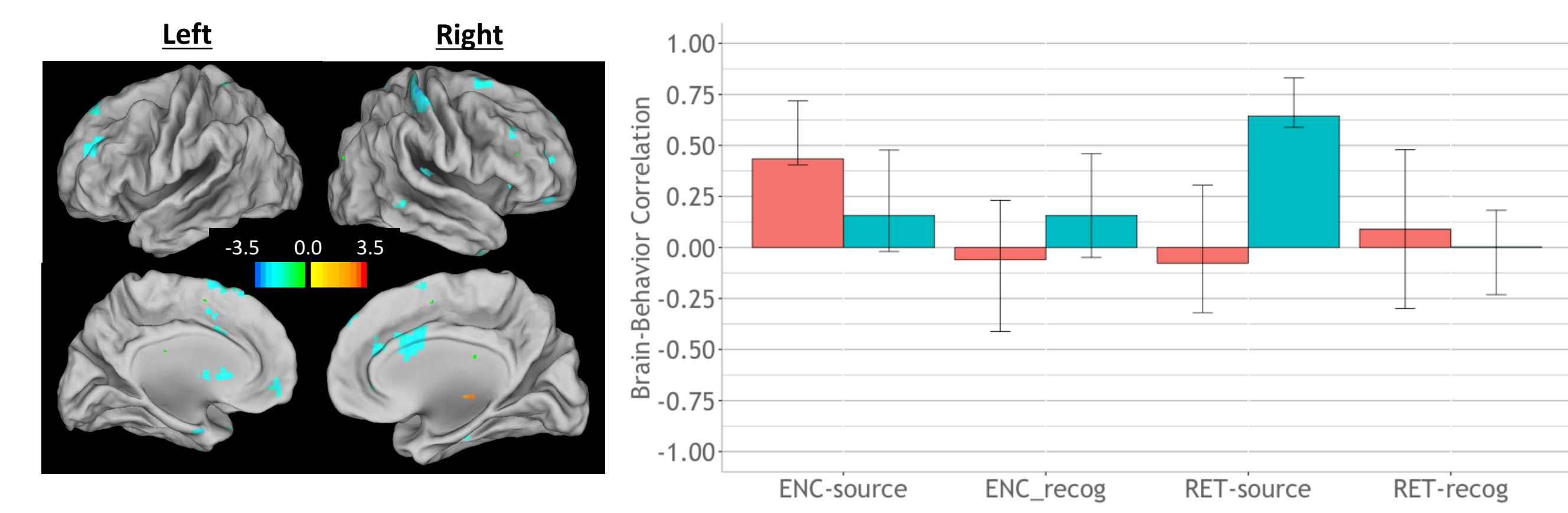
### Bias Corrected Performance Scores



### Behavior PLS LV1: Regions Supporting Episodic Memory in Women



### 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

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