#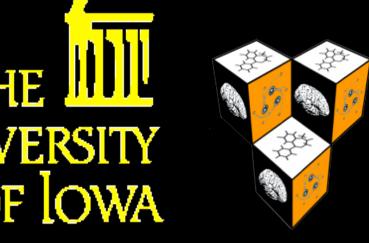 Differential contributions of medial prefrontal cortex and hippocampus to self-projection and self-referential processing

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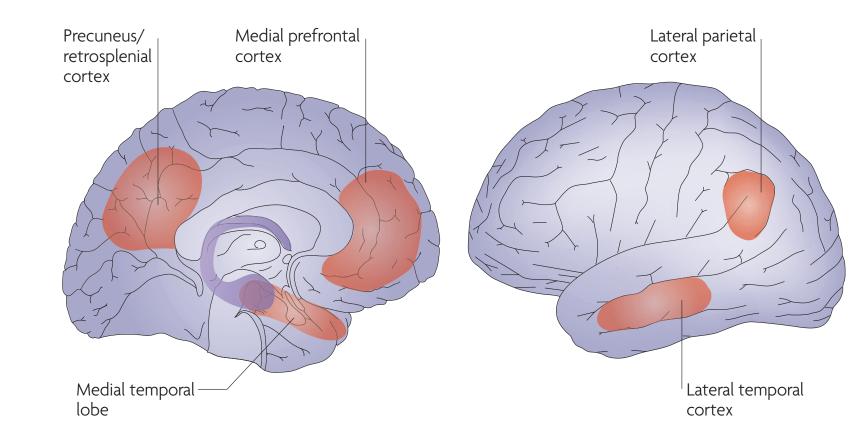
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INTRODUCTION

Recent evidence from neuropsychological and fMRI studies suggests a connection between memory for the past and thinking about the future. Its thought that we use our past experiences as the basis for our future plans and decisions.

Suggests that a **shared neural network exists** including:
- Medial Temporal Lobes
- Frontal Cortices
- Posterior Parietal Cortex

The **hippocampus** is critical for relational binding and representational flexiblity (Eichenbaum & Cohen, 2001) critical for **episodic memory** (Tulving, 1985), **spatial navigation** (O'Keefe & Nadel, 1978), and **imagination** (Hassabis et al., 2007).
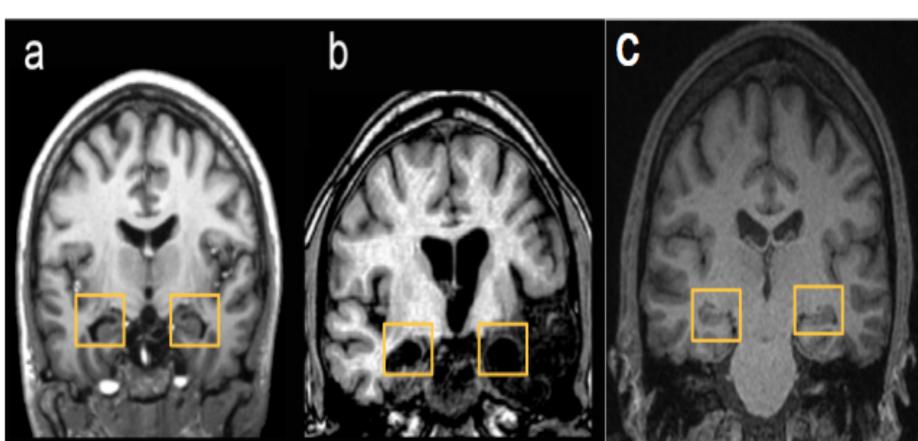
The **frontal lobes** are thought to contribute **autobigraphical memory** (Addis et al., 2004; Cabeza et al., 2004; Gilboa et al., 2004), **processing of information relevant to the self** (Craik et al., 1999; D'Argembeau et al., 2005; Fossati et al., 2004; Gusnard, Akbudak, Schulman, & Raichle, 2001; Kelley et al., 2002), and 'theory of mind' (Brunet, Sarfati, Hardy-Bayle, & Decety, 2000; Calarge, Andreasen, & O'Leary, 2003; Frith & Frith, 1999; Gallagher et al., 2000).

Here we examine if **hippocampus** and **medial frontal cortex** make distinct contributionsto **self-projection** and **self-referential processing**

METHODS

Participants

- 6 patients with hippocampal damage
- 5 patients with mPFC damage
- Inclusion criteria:
1) Minimum 3 months post onset 2) Bilateral and focal lesion 3) Adult onset lesion
- 11 healthy comparison matched pairwise to patients on sex, age, handedness
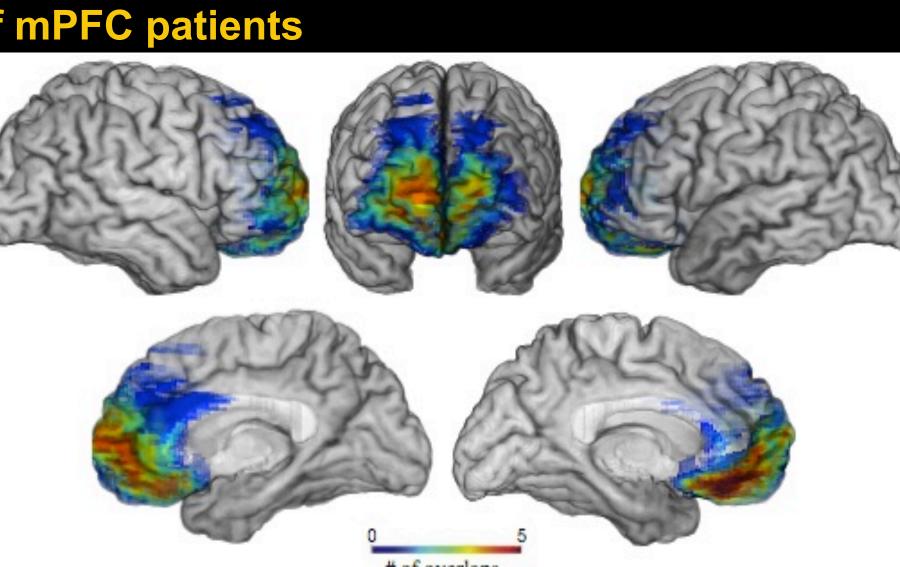
Representative hippocampal damage MRI Scans

Coronal MRI scans indicating representative hippocampal damage in a) (Anoxic 1846) and b) (HSE 1951) and an undamaged hippocampus in c) (healthy comparison)

Lesion Overlap Map of mPFC patients

The warmest color red depicts the greatest number of lesion overlaps while the coldest color represents the least.

METHODS

Patient Demographic and Anatomical Characteristics

Group	Patient	Sex	Age	Hand	Ed	Chron	Etiology
Hippocampus	1606	M	61	R	12	18	Anoxia
	1846	F	45	R	14	15	Anoxia
	1951	M	56	R	16	28	HSE
	2308	M	52	L	16	9	HSE
	2363	M	52	R	18	10	Anoxia
	2563	M	53	R	16	8	Anoxia
	Mean (SD)		53.2 -5.3		15 (1.7)	14.7 (7.6)	
mPFC	318	M	73	R	14	38	Meningioma Resection
	2352	F	64	R	14	15	SaH; ACoA
	2391	F	67	R	12	14	Meningioma Resection
	2577	M	73	R	11	15	SaH; ACoA
	3350	M	61	R	18	10	Meningioma Resection
	Mean (SD)		67.6 -5.4		13.8 (2.7)	18.4 (11.1)	

Neuropsychological Characteristics of Patients

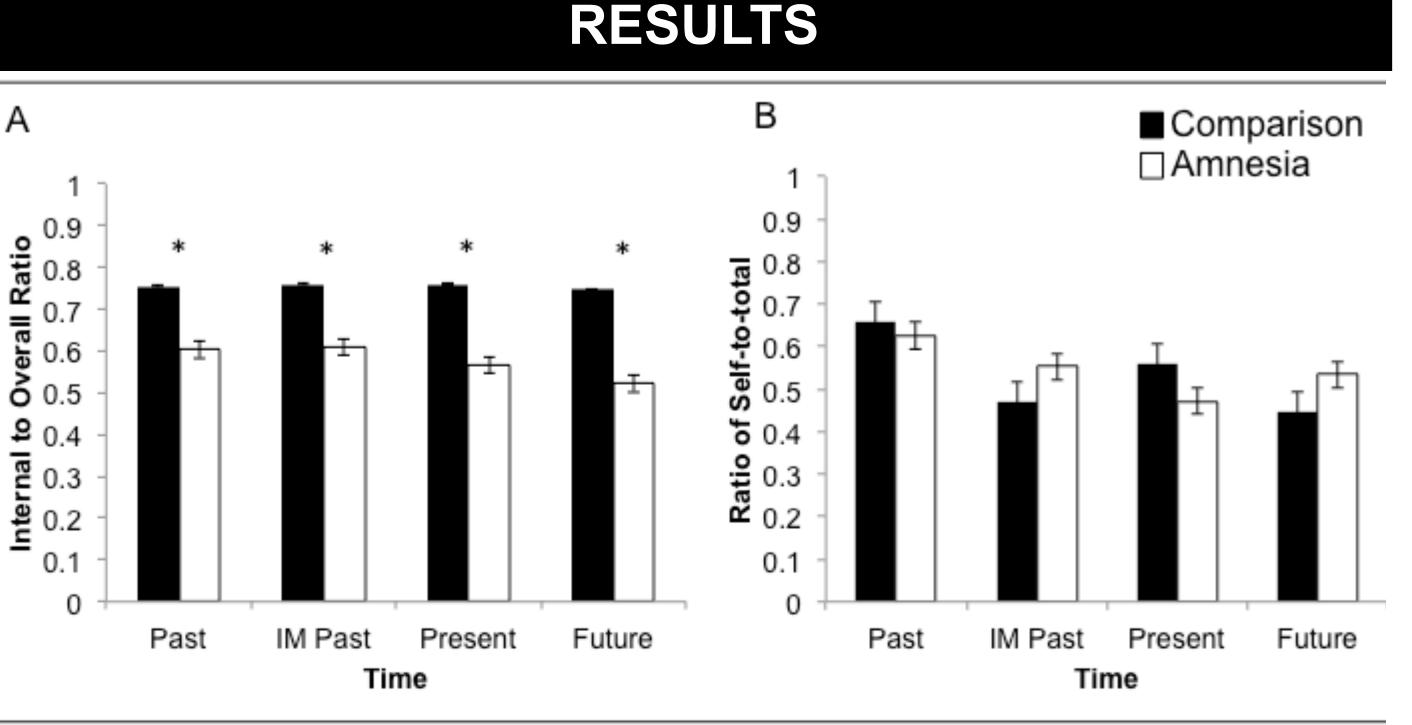| Group	Patient	WAIS-III FSIQ	WMS-III GMI	BN	TT	COWA	WCST	CFT	BDI	APP	SIP
Hippocampus	1606	91	66	32	44	43	6	34	9	No	1
	1846	84	57	43	41	24	6	28	9	N/A	N/A
	1951	106	57	49	44	40	6	32	5	N/A	N/A
	2308	98	45	52	44	24	N/A	26	0	No	3
	2363	98	73	58	44	26	6	26	N/A	No	1
	2563	94	63	52	44	36	6	36	0	No	1
	Mean (SD)	95.2 (7.4)	60.2 (9.6)	47.7 (9.1)	43.5 (1.2)	32.2 (8.5)	6 (0)	30.3 (4.3)	4.6 (4.5)	0 (0)	1.5 (1.0)
mPFC	318	143	109	60	44	54	6	36	0	Yes (-3)	3
	2352	106	109	54	44	34	6	32	1	Yes (-3)	2
	2391	109	132	57	43	59	6	34	4	Yes (-2)	2
	2577	84	96	55	44	44	0	31	7	Yes (-3)	3
	3350	118	108	52	N/A	40	6	36	3	Yes (-1)	1
	Mean (SD)	112 (21.4)	110.8 (13.1)	55.6 (3)	43.8 (0.5)	46.2 (10.2)	4.8 (2.7)	33.8 (2.3)	3 (2.7)	-2.4 (0.9)	2.2 (0.8)

Procedure

The dynamic event construction elicitation protocol was adapted from Levine et al. (2002). Participants elaborated on a mental representation in response to a neutral cue word (e.g., tree in four conditions for a total of 12 descriptions (3 per condition):
- **Past**: occurred before age 25; happened only once; autobiographical
- **Imagined Past:** occurred before age 25; plausible event that has never happened; autobiographical
- **Imagined Present**: could take place right now; plausible event that has never happened; autobiographical
- **Future**: take place in the future; a plausible event that has never happened; autobiographical
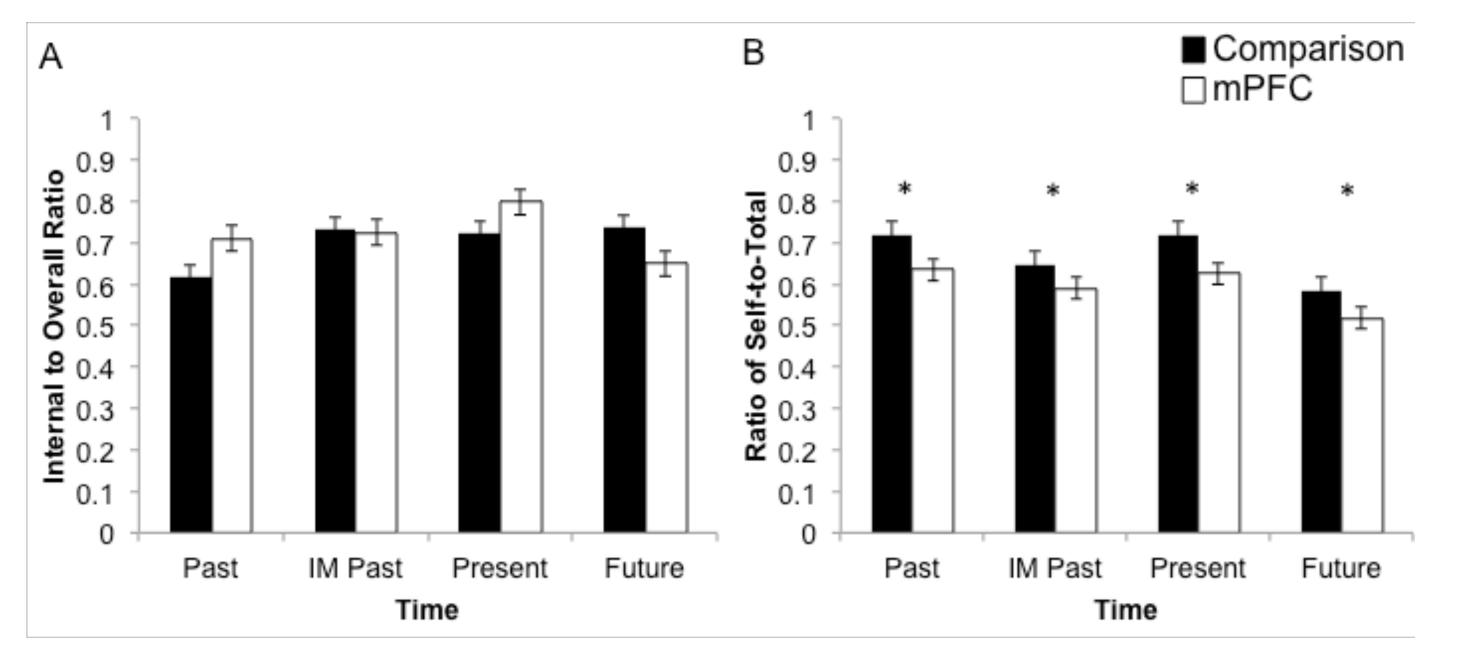
Analysis

To quantify specific aspects of the recounted memories, the Autobiographical Memory Interview Analysis protocol was used. The main event, which was specific to a time and place, was isolated and segmented into details (see table below). These details were then grouped into two overarching categories: internal and external.

Category	Description	Example
Internal		
Event	Happenings, individuals present, reactions/emotions of others, weather, clothing, actions of others, or sequences of events	I visited a lab
Place	Localization in space including countries, bodies of water, provinces, cities, streets, buildings, rooms, or locations within a room	in Iowa City
Time	Life epoch, year, season, month, date, day of week, time of day, or clock time	during the summer
Perceptual	Auditory, olfactory, tactile/pain, taste, visual, spatial-temporal, or duration of events	Outside it was hot and hazy, but inside was cool
Emotion/ Thought	Feelings, thoughts, opinions, expectations or beliefs of the subject at the time of the event	It was really challenging but I learned a lot
External		
Event	(see above description)	I also visited a museum
Place	(see above description)	In West Branch Iowa
Time	(see above description)	on a weekend
Perceptual	(see above description)	Music was playing, we could hear the carnival callers
Emotion/ Thought	(see above description)	It was fun and exciting and I was happy to be there
Semantic	General knowledge or facts, ongoing events, extended states of being, longstanding beliefs or opinions	Herbert Hoover was born in West Branch, the museum was named for him
Repetition	Unsolicited repetition of a prior detail	The music that was playing
Other	Metacognitive statements, editorializing, inferences, queries, or other information containing clauses that convey verbosity but are not related to the main event	That was a little aside

RESULTS

A) Self-projection: Amnesic patients are impaired; produced significantly fewer internal details relative to overall details indicating less "episodicness" in their narratives, $F_{(1,10)} = 19.64$, $p = 0.001$. No significant main effect of time, $F_{(3,30)} = 2.10$, $p = 0.12$, or group by time interaction, $F_{(3,30)} = 0.33$, $p = 0.805$.

B) Self-reference: Amnesic patients not impaired; no group effect on proportion of self to total references $F_{(1,10)} = 0.04$, $p = 0.84$. Significant effect of time, $F_{(3,30)} = 3.40$, $p = 0.030$) but no group*time interaction $F_{(3,30)} = 1.15$, $p = 0.346$. Follow-up: Past narratives had higher proportion of self to total references than IM Past ($p = 0.043$) and Present ($p = 0.031$).

A) Self-projection: mPFC patients not impaired; no effect of group, $F_{(1,8)} = 1.27$, $p = 0.292$, time, $F_{(3,30)} = 1.62$, $p = 0.211$, or group*time interaction, $F_{(3,30)} = 0.10$, $p = 0.96$. Comparison participants and mPFC patients produced similar ratios of internal to overall details, indicating about the same level of "episodiness" in their narratives.

B) Self-Reference: mPFC patients impaired; effect of group on proportion of self to total references ($F_{(1,8)} = 7.93$, $p = 0.023$), but no effect of time ($F_{(3,24)} = 2.01$, $p = 0.139$) or a group*time interaction ($F_{(3,24)} = 0.09$, $p = 0.967$). mPFC patients produce narratives with significantly lower ratios of self-to-other than their comparison participants.

CONCLUSIONS

These results suggest that the hippocampus and mPFC make distinct contributions to self-projection and self-referential processing. This finding, in neurological patients, is consistent with recent neuroimaging (St. Jacques et al., 2011) but at odds with another lesion study (CNS poster G106). The discrepancy between this study and the other lesion study may be due to differences in task design and patient characteristics.

Given that hippocampus and mPFC (and other neural substrates) comprise a shared neural network, future work aimed at further clarifying their individual contributions as well as their interactions in other complex behavior (e.g., decision-making, social interaction), is warranted.

ACKNOWLEDGEMENTS