

Memory Function in Children with FASDs:

Atypical hippocampal activation during associative recognition in children with FASD

FACE Research Roundtable

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& Mental Health

Memory

Memory is a way of holding onto the things you love,
the things you are,
the things you never want to lose.

~From the television show *The Wonder Years*



Summary

- Memory in FASDs
- Overview of Memory
- Previous work in our lab
 - Clinical Memory Testing
 - Structural Neuroimaging
- Recent Findings
 - Functional Neuroimaging Results



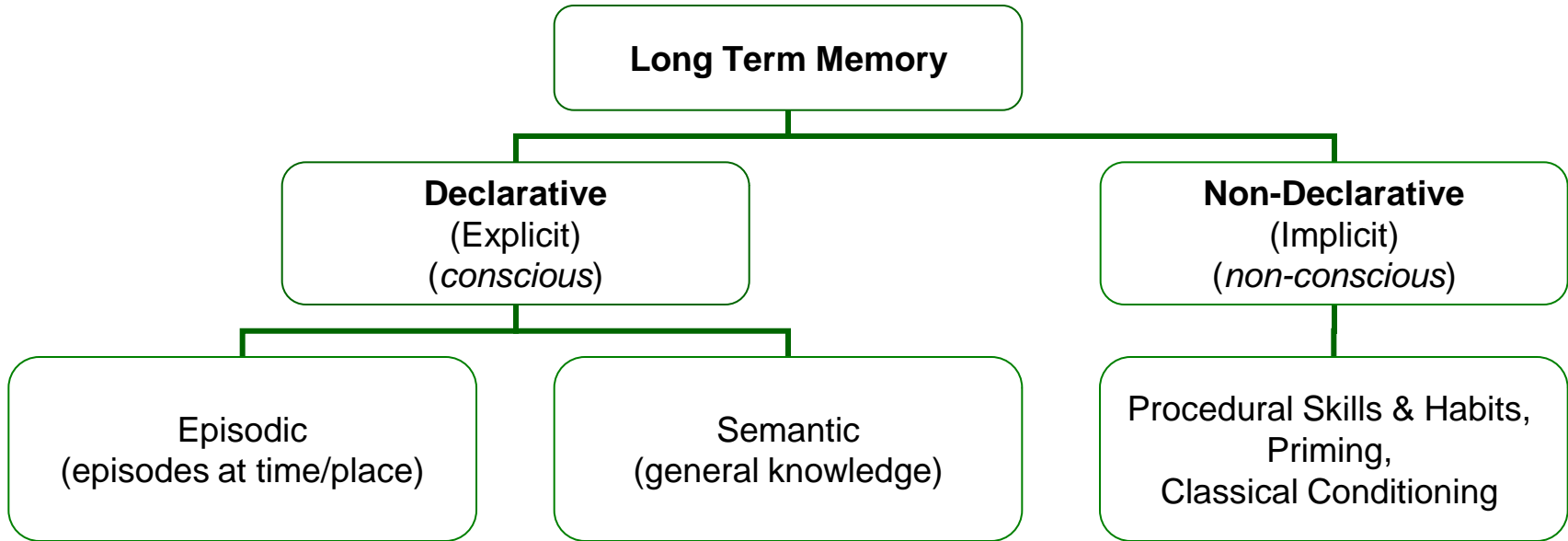
Memory Problems in Children with FASDs



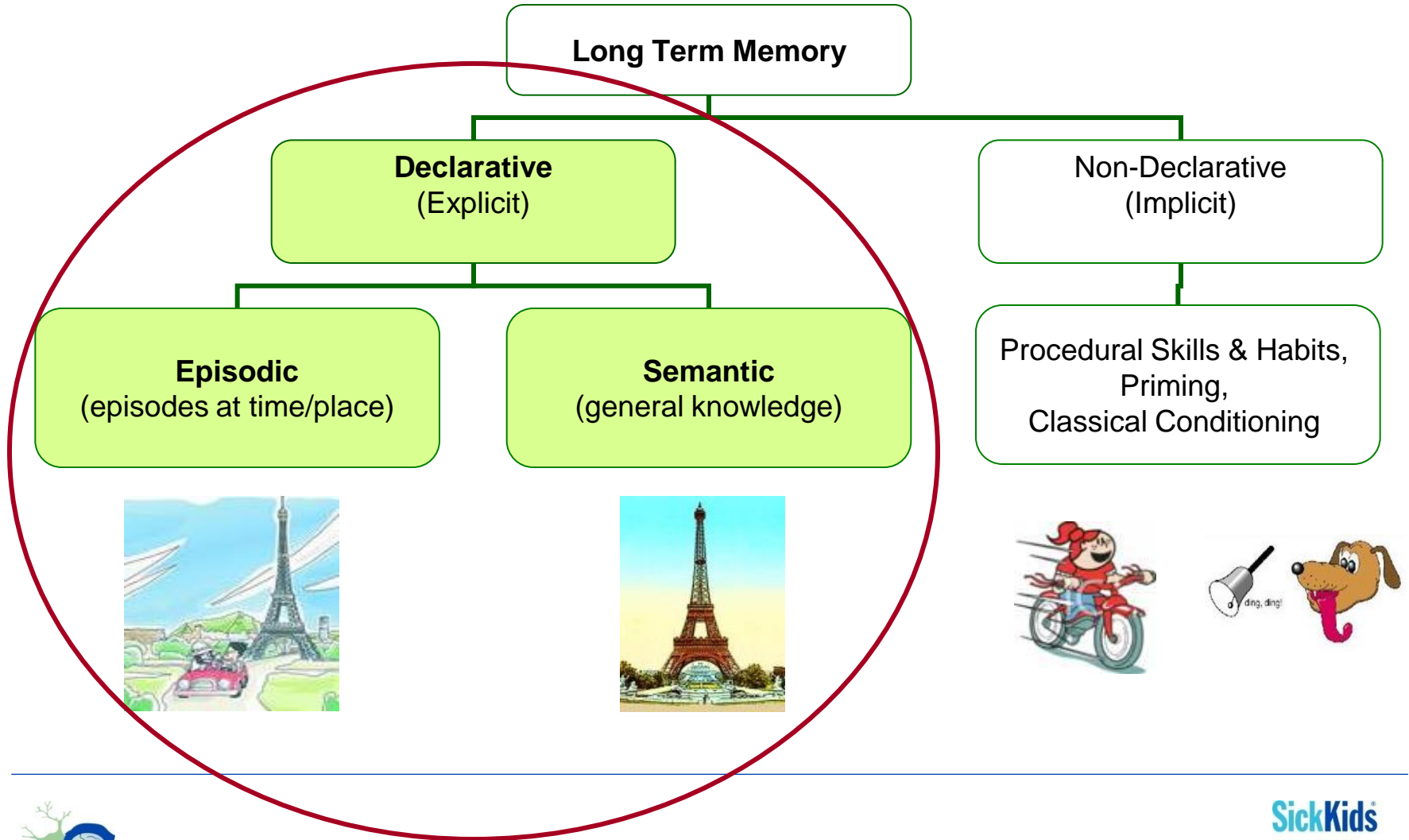
- Children with FASDs exhibit a constellation of cognitive and behavioural impairments, including memory deficits
- Memory is a domain included in the Canadian Diagnostic Criteria for FAS, partial FAS, and ARND
- The specificity of memory impairments is poorly understood
 - Understand underlying neural mechanisms
 - Will inform educational and parenting strategies
- Memory deficits may have a cascading effect on other areas of functioning such as academic achievement, adaptive behaviour, and social skills



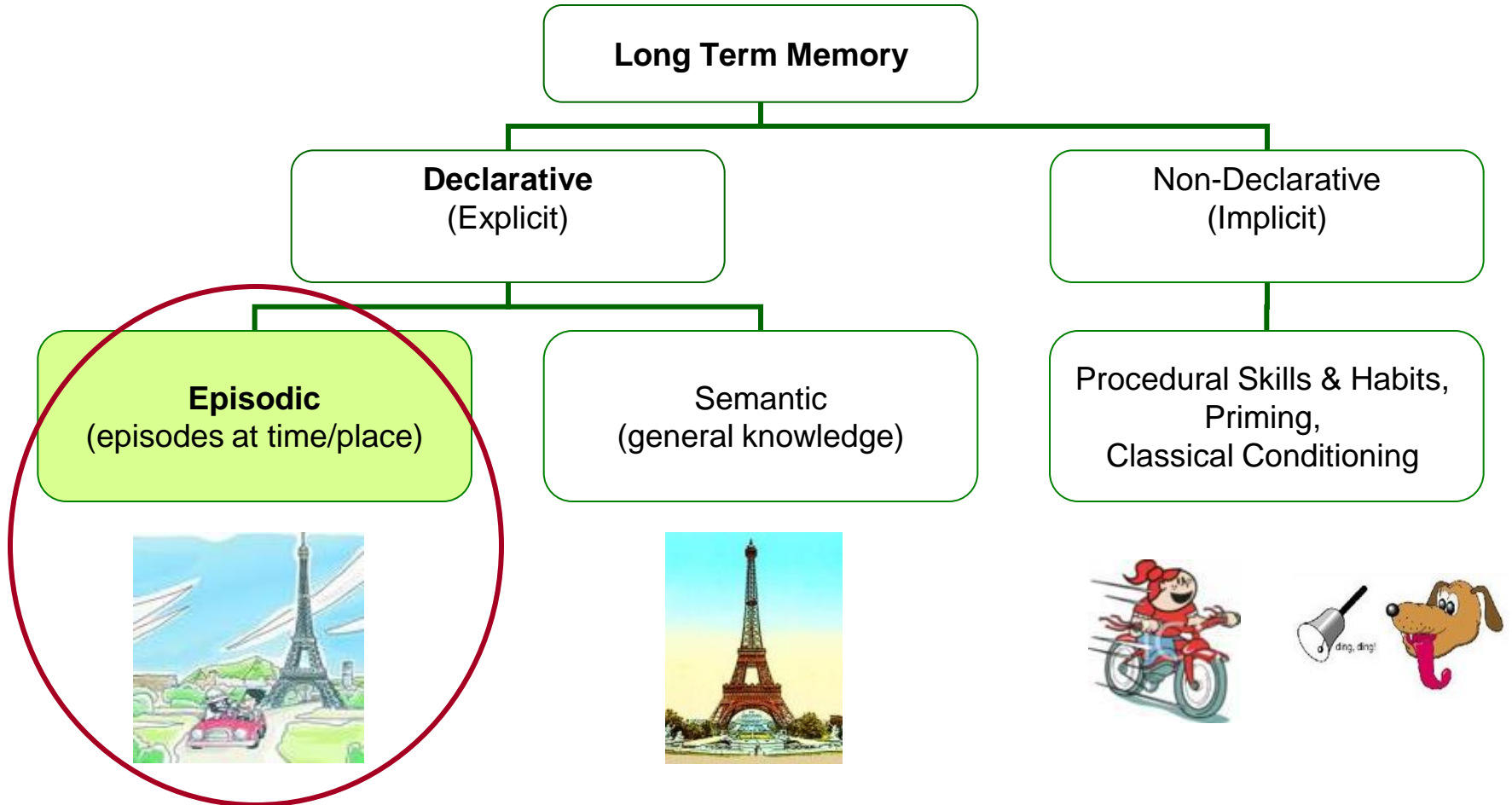
Long Term Memory



Long Term Memory



Long Term Memory Impairments in FASDs



Long Term Memory Impairments in FASDs

- Declarative memory is often found to be more compromised than non-declarative
- Declarative memory can be assessed in many ways
 - **Stage of memory:** encoding (learning) or retrieval (remembering)
 - **Type of information:** verbal or visuospatial
 - **Nature of the material:** names/stories/lists, faces/patterns/abstract figures, items/pairs of items
 - **Type of memory retrieval:** recall or recognition
 - **Timing:** short delay or long delay
- Individuals with FASDs show a wide range of declarative memory impairments



Example of Memory Impairments in FASDs

- Study in our lab compared episodic memory in children with FASDs (N=19, mean 11.9 yrs) to TDCs (N=21, mean 12.4 yrs)
- Children with FASDs significantly worse for all episodic memory measures

▪ Verbal Memory Deficits

- Stories (immediate & delay, recall & recognition BUT not recall of story themes)
- Word list recall with selective reminding
- Word pair recall
- Object name recall

▪ Non-Verbal Memory Deficits

- Dot locations (long & short delay)
- Face recognition (immediate & delayed)
- Visual selective reminding
- Abstract visual memory
- Abstract figure delayed recall
- Paired associate learning
- Delayed match to sample



Example of Memory Impairments in FASDs

- FASDs perform in clinically significant range on select tests (**low average <25th** or **borderline <9th**); all tests in the average range were <50th percentile:

▪ Verbal Memory Deficits

- Stories (immediate & **delay**, recall & recognition BUT not recall of story themes)
- Word list recall w/ selective reminding
- Paired recall
- **Object recall**

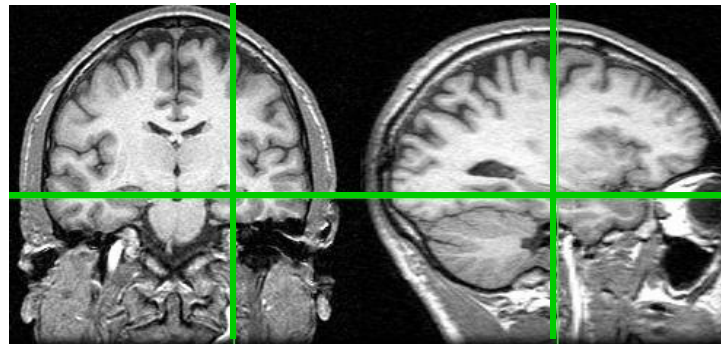
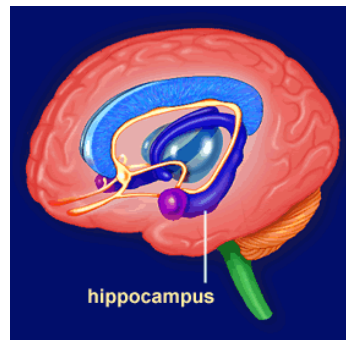
▪ Non-Verbal Memory Deficits

- Dot locations (long & short delay)
- **Face recognition (immediate & delayed)**
- **Visual selective reminding**
- Abstract visual memory
- **Abstract figure delayed recall**
- Paired associate learning
- Delayed match to sample



Why Episodic Memory Impairments?

- Prenatal exposure to alcohol has diffuse effects across the brain, although some brain regions are more vulnerable to insult than others
- The hippocampus, a small seahorse-shaped structure in the medial temporal lobes, is particularly vulnerable to the teratogenic effects of alcohol



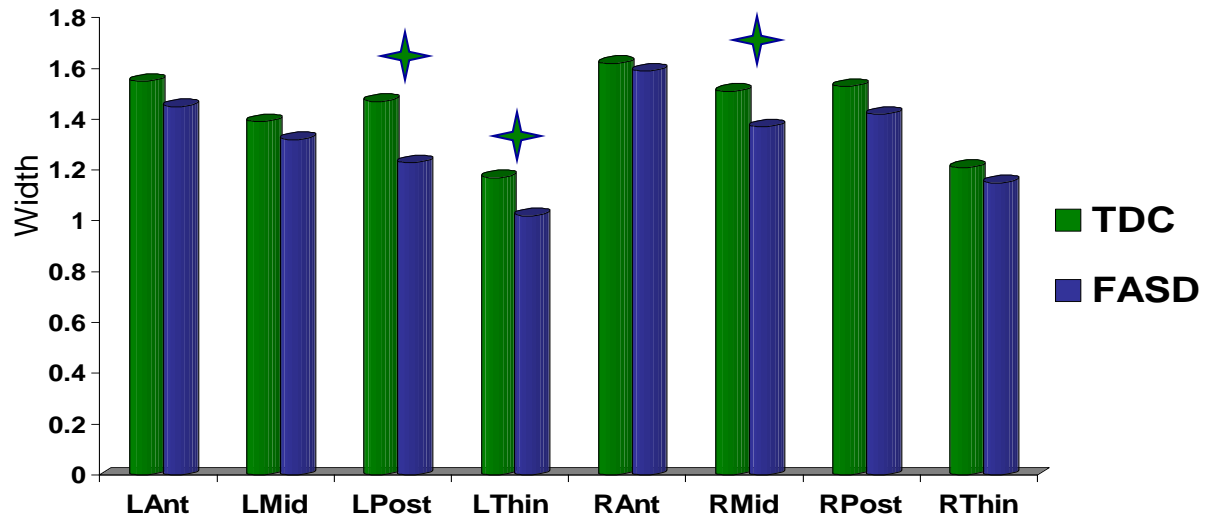
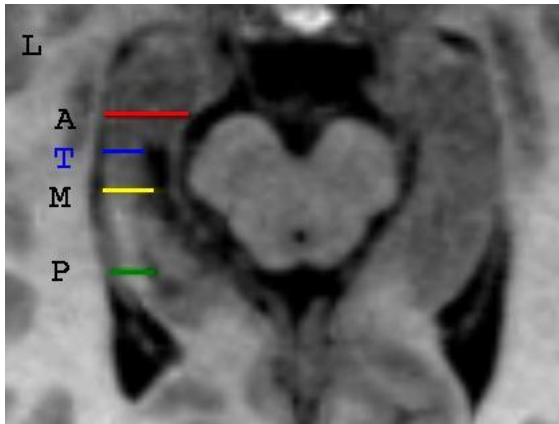
- The hippocampus plays a critical role in episodic memory



The Hippocampus in FASDs

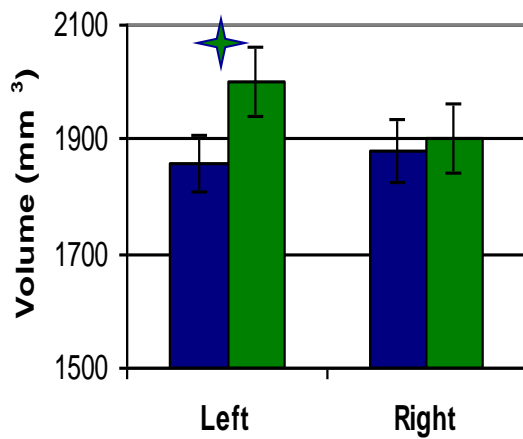
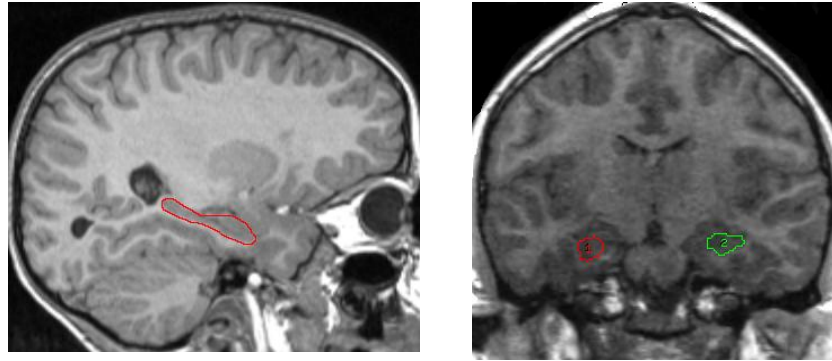
- We looked at multiple indices of hippocampal size and composition in children with FASDs (N=24, mean 12.8 yrs) compared to TDCs (N= 21, mean 12.4 yrs)

1. Hippocampal Width:

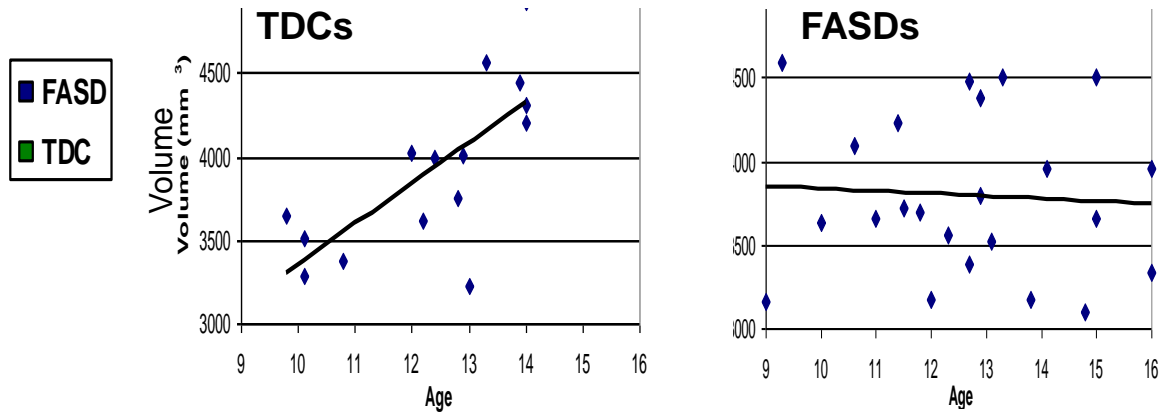


The Hippocampus in FASDs

2. Hippocampal Volume:



Hippocampal Volume X Age

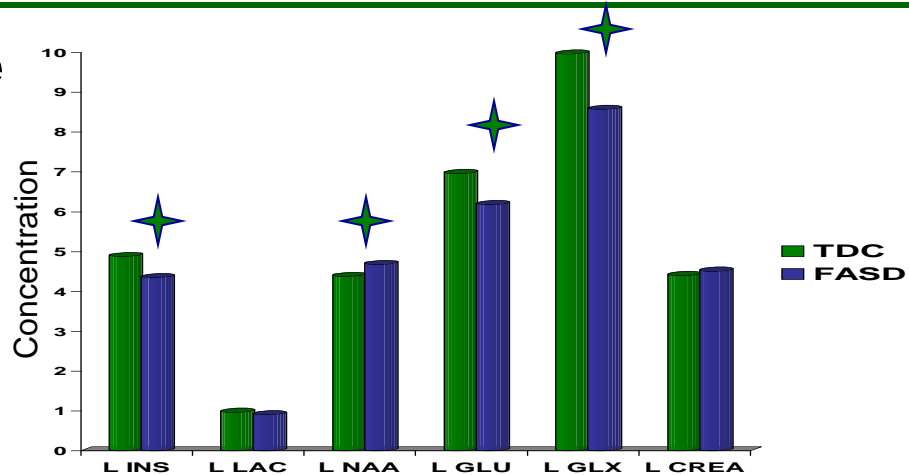


(Willoughby et al., JINS, 2008)

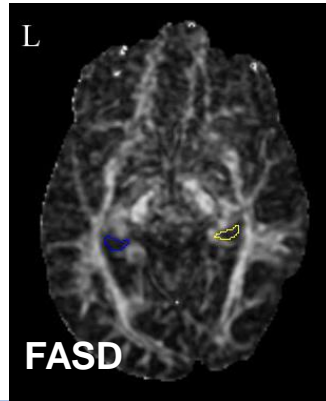
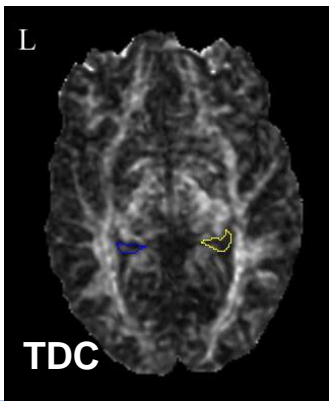


The Hippocampus in FASDs

3. Hippocampal Metabolite Concentrations:



4. Hippocampal Diffusion Properties:

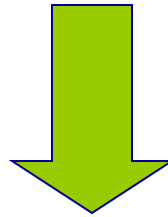


- Mean, axial, and radial diffusivity reduced in left MTL and radial diffusivity reduced in right MTL ($p < .05$)
- Altered tissue microstructure and architecture



Hippocampal Function in FASDs?

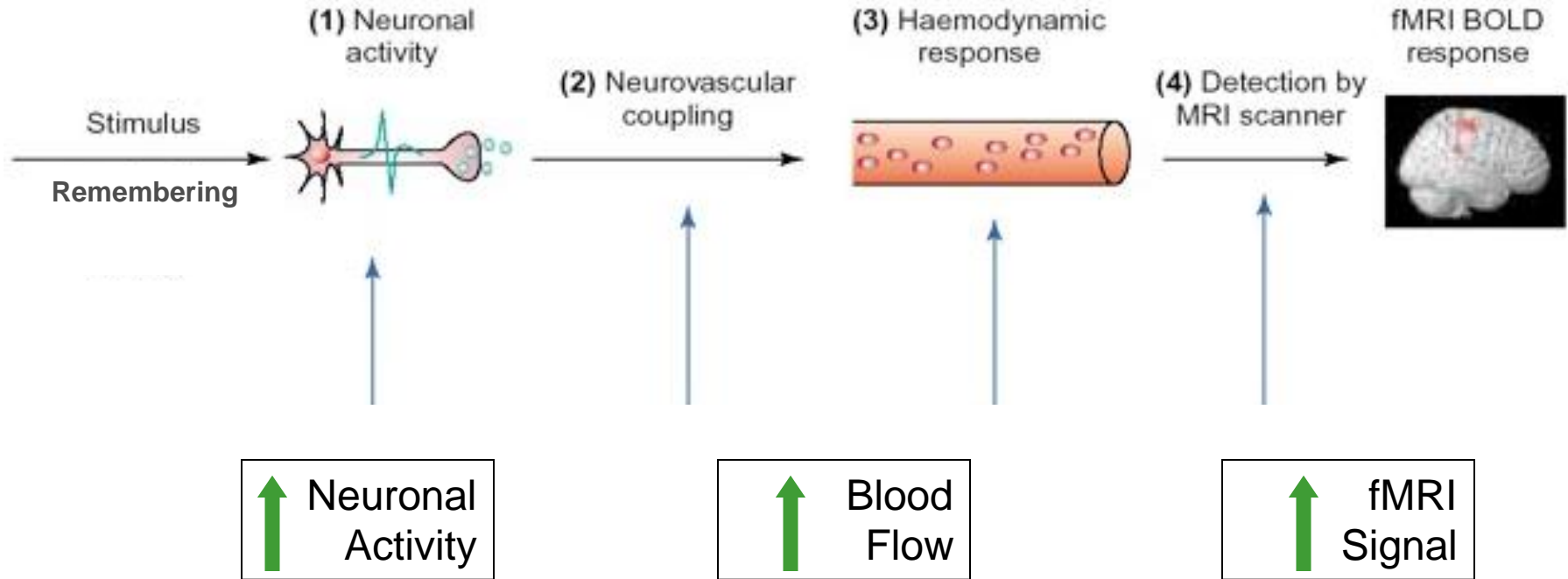
1. Individuals with FASDs show impairments on a wide range episodic memory tasks
2. Individuals with FASDs have hippocampal abnormalities



- **Aim:** Use fMRI to study hippocampal *function* in FASDs
- **Hypothesis:** Even when children with FASDs correctly remember, the magnitude and scope of hippocampal activation will differ from Typically Developing Controls (TDCs)



Investigating Hippocampal Function Using fMRI



Blood **O**xxygenation **L**evel **D**ependant (**BOLD**) signal

(Arthurs & Boniface, 2002)



Hippocampal Function in FASDs

- **Participants:** **21** TDCs and **19** with FASDs (mean 12.6 yrs and 12.6 yrs respectively, range 11-15 yrs)

- **Method:**
 - **Scanner:** 1.5T GE, sequence optimized for detecting hippocampal activation
 - **Memory Tasks**
 - Shown in adults to engage hippocampal processing
 - Designed to equate accuracy in FASDs and TDCs - only correct trials analyzed

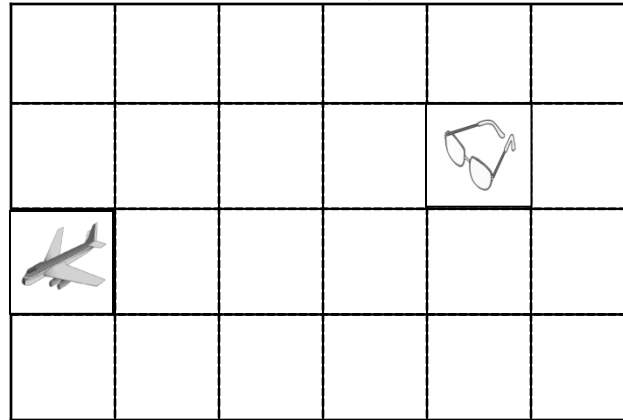
- 1. **Visuospatial Paired Associates Task**
(modified from Köhler et al. 2005, Hippocampus 15:763-774)

- 2. **Verbal Paired Associates Task**
(modified from Giovanello et al. 2004, Hippocampus 14:5-8)

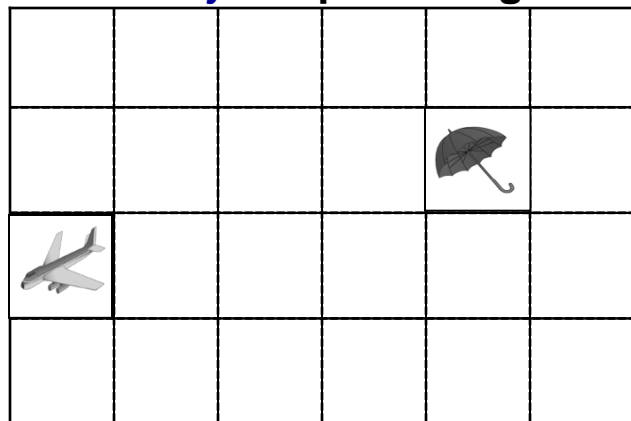


Visuospatial Paired Associates Task

Study

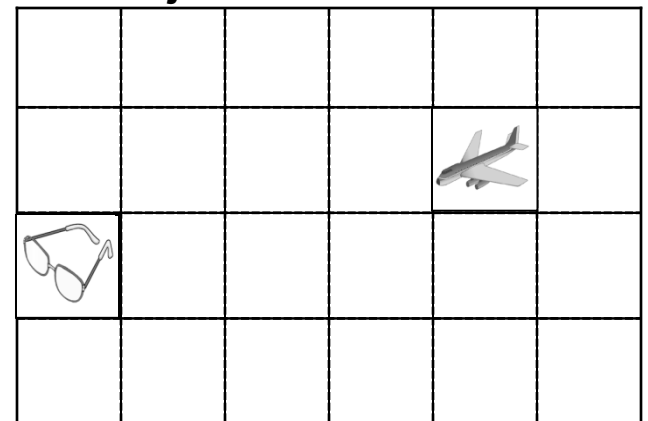


Were the *objects* paired together?



No

Are the objects in the same *location*?

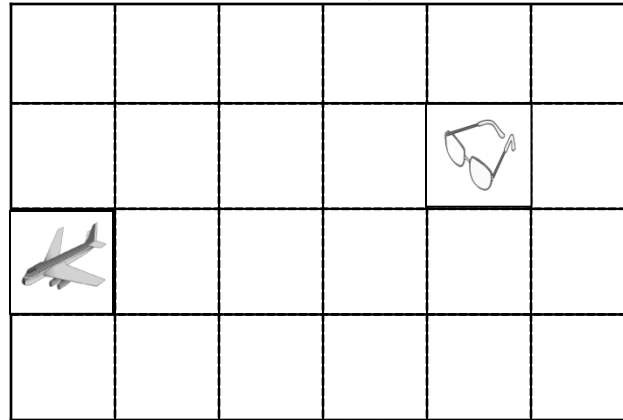


No

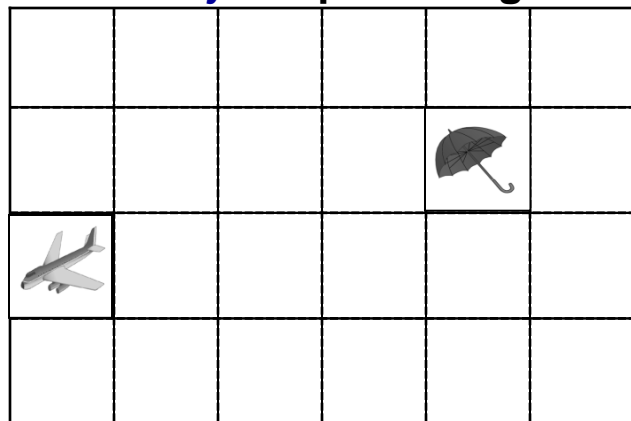


Visuospatial Paired Associates Task

Study



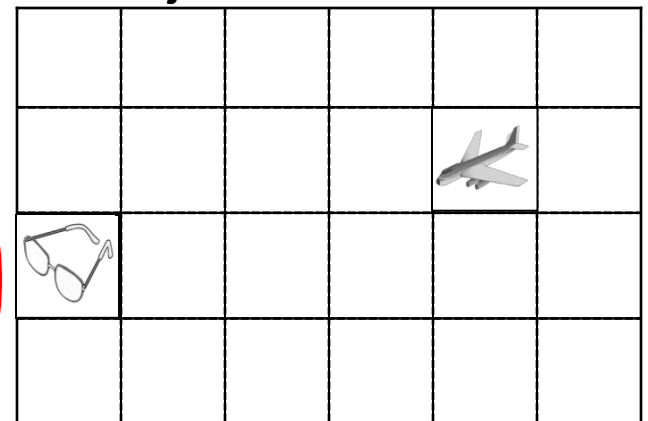
Were the *objects* paired together?



No

Yes

Are the objects in the same *location*?



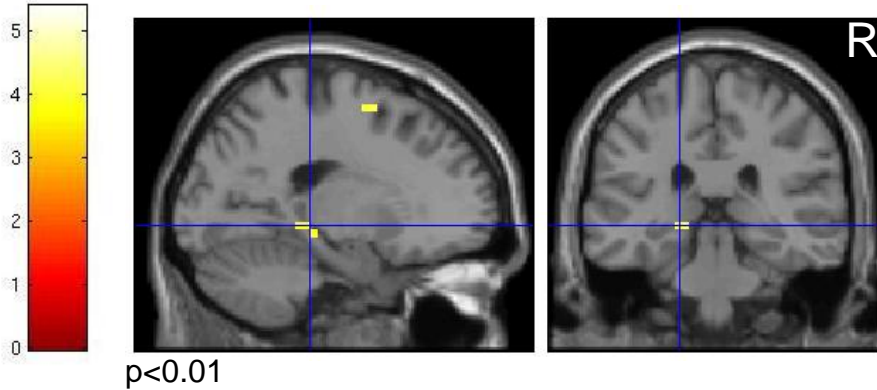
No

Yes

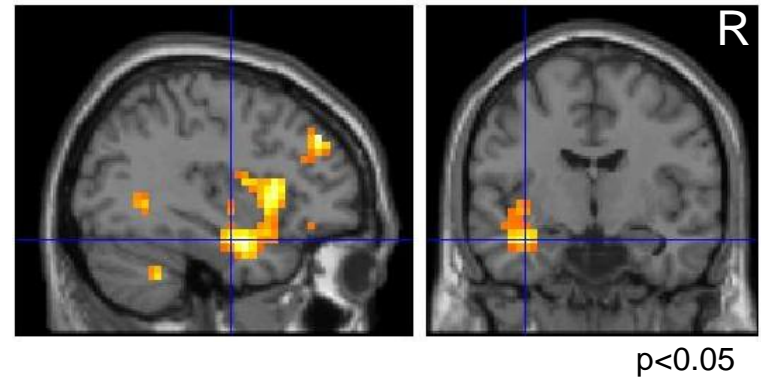


Visuospatial Paired Associates Task — Objects

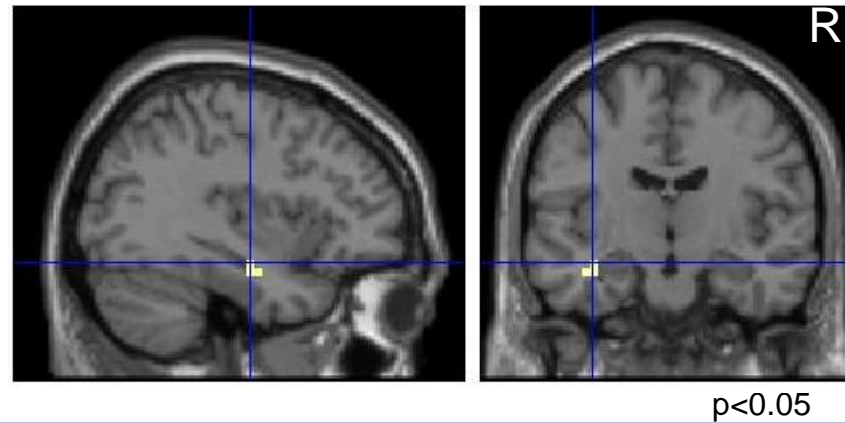
Control - left hippocampus



FASDs - left hippocampus



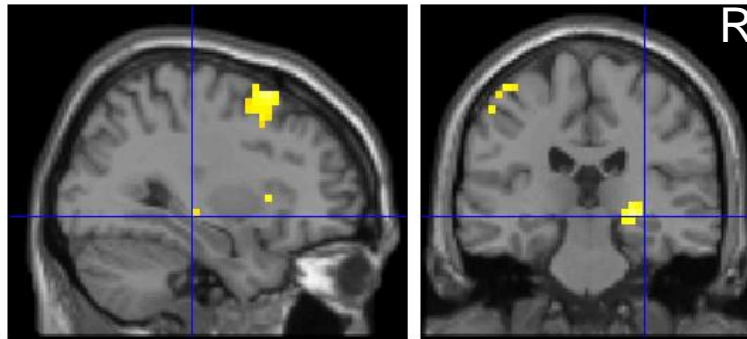
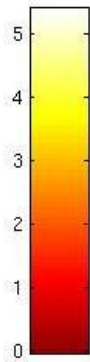
FASDs > Control - left hippocampus



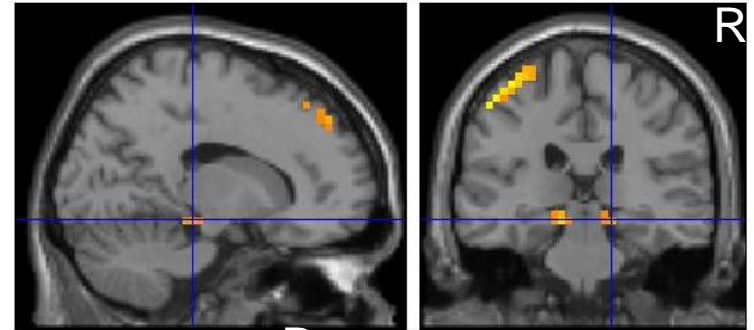
Visuospatial Paired Associates Task — Locations

Control - left and right hippocampus

FASDs - left and right hippocampus



$p < 0.005$

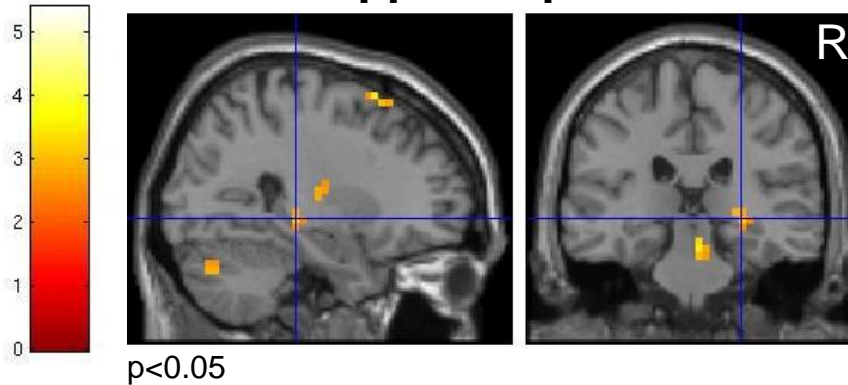


$p < 0.05$

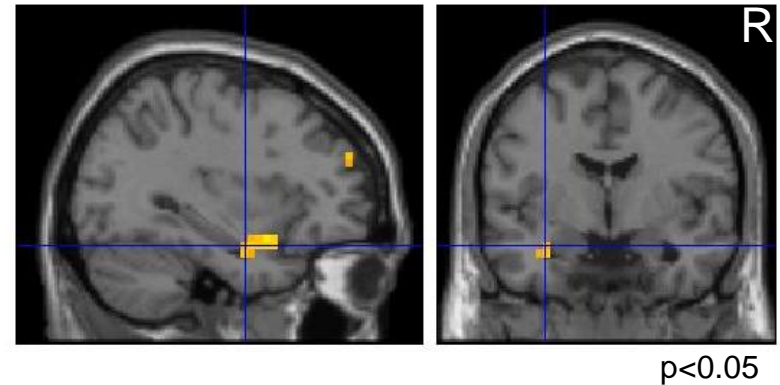


Visuospatial Paired Associates Task — Locations

Control > FASDs - left and right hippocampus



FASDs > Control - left hippocampus

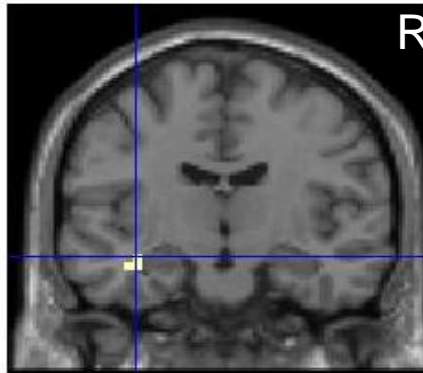


FASDs Recruit Different Neural Resources

- For Visuospatial task, FASDs:
 - Greater **hippocampal activation** for both novel object pairs and locations in **left** hippocampus
 - Different hippocampal activation for locations in **both left and right**

FASDs > Control

Objects



p<0.05

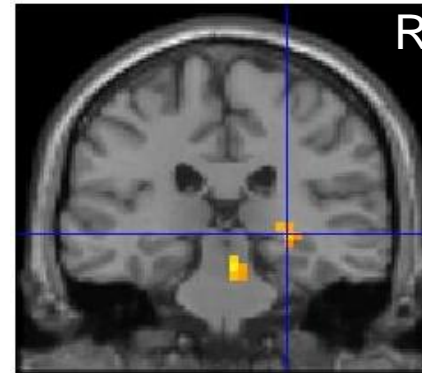
Locations



p<0.05

Control > FASDs

Locations



p<0.05



Verbal Paired Associates Task

Study

Bear – Penny

Knee – Truck

Desk – Horn

Associative: Together before?

Bear – Penny
(intact pair)

✓ (Old)

Knee – Horn
(rearranged pair)

X (New)

Tree – Bike
(new pair)

X (New)

Item: Seen before?

Bear – Truck
(rearranged pair)

✓ (Old)

Knee – Bottle
(old-new pair)

X (New)

Tree – Bike
(new pair)

X (New)



Verbal Paired Associates Task

Study

Bear – Penny
Knee – Truck
Desk – Horn

Associative: Together before?

Bear – Penny (intact pair)	✓ (Old)
Knee – Horn (rearranged pair)	X (New)
Tree – Bike (new pair)	X (New)

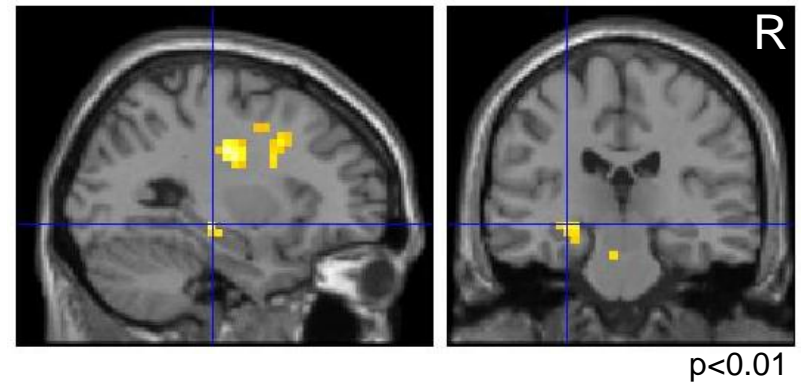
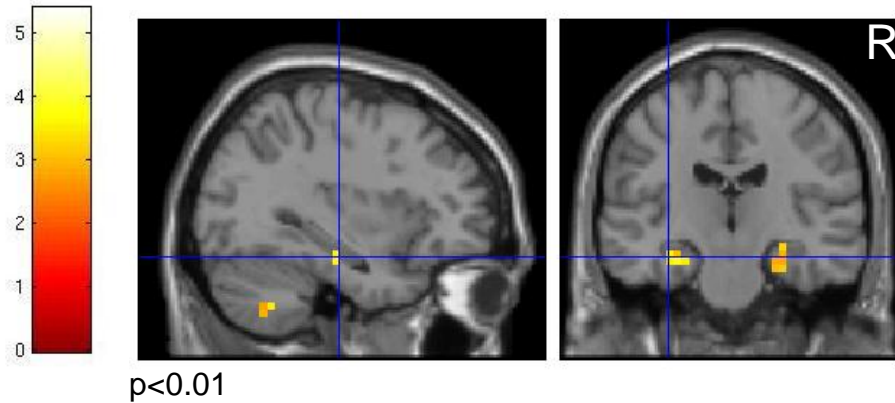
Item: Seen before?

Bear – Truck (rearranged pair)	✓ (Old)
Knee – Bottle (old-new pair)	X (New)
Tree – Bike (new pair)	X (New)



Verbal Paired Associates Task — Old Associations - Old Items

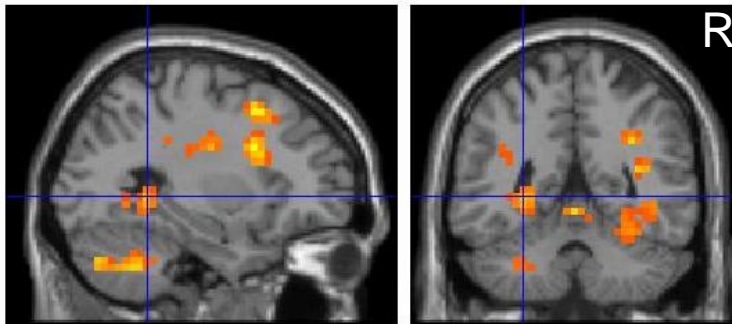
Control – left and right hippocampus FASDs – left and right hippocampus



Verbal Paired Associates Task — Old Associations - Old Items

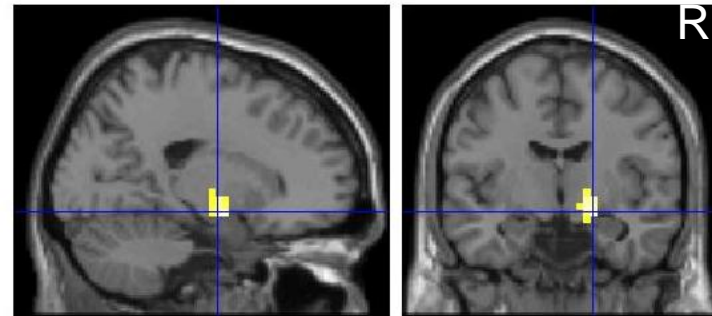
- Different hippocampal areas recruited to successfully remember verbal associations

Control > FASDs - left and right hippocampus



$p < 0.05$

FASDs > Control - right hippocampus



$p < 0.05$



Conclusions

- Even when children with FASDs correctly remember, the magnitude and extent of hippocampal activation differs from TDCs
 - **Visuospatial memory task:** *additional* and *different* hippocampal activation
 - **Verbal memory task:** *different* hippocampal activation
- Results suggest that adolescents with FASDs need to recruit additional and different neural resources to successfully remember
- Findings support the hypothesis that altered hippocampal function in FASDs underlies their episodic memory impairments



Implications

- Understanding the memory impairments and the underlying neural basis in FASDs will inform:

1. Diagnosis –

- Identifying the pattern of memory strengths and deficits for selection of neuropsychological measures

2. Intervention –

- Cognitive interventions may be constrained or guided by brain function
 - Effective interventions will build on strengths and emphasize alternatives to hippocampally-dependent learning and retrieval
- Potential to develop interventions that encourage neuroplasticity or neurogenesis in the hippocampus



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Motherisk

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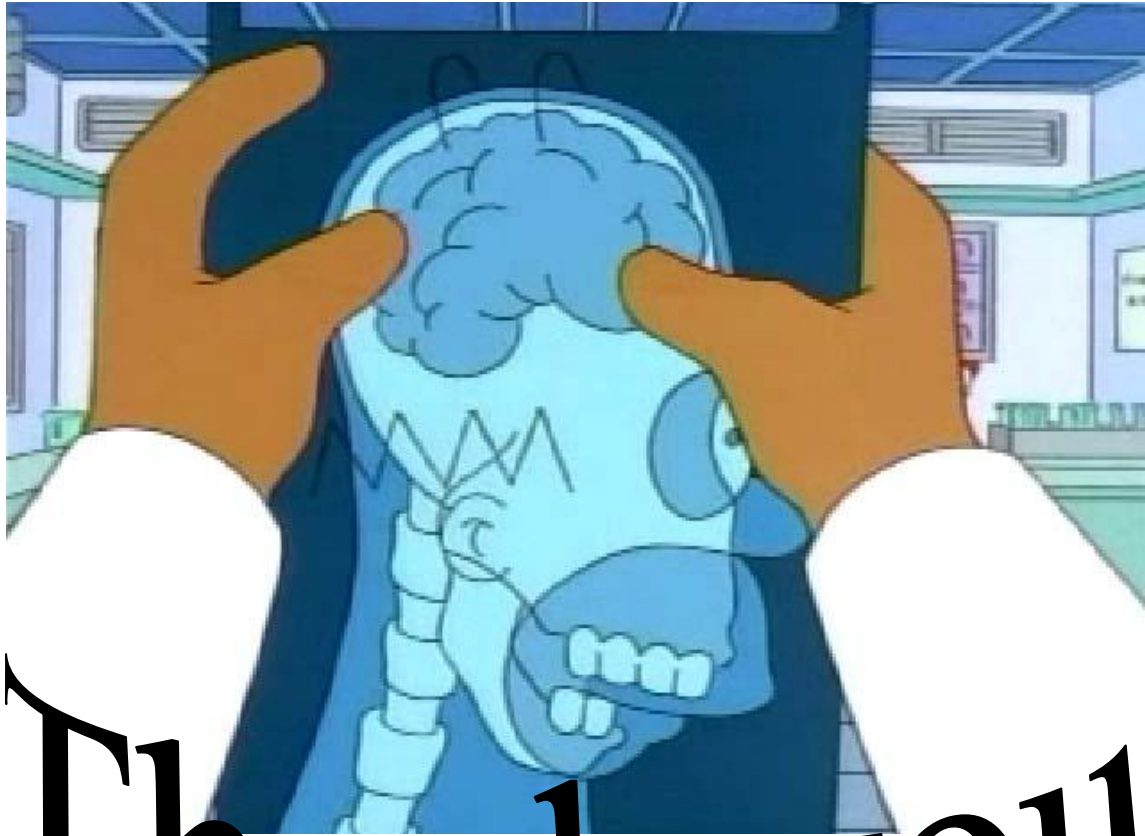


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Thank you

