Alterations in the autobiographical retrieval network associated with left mesial temporal dysfunction

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Introduction

- Recent neuroimaging studies of autobiographical memory (AM) retrieval have consistently reported the activation of an AM network that includes hippocampus, parahippocampus, posterior cingulate, precuneus, and medial frontal regions.[1,2]
- The preferential activation of the hippocampus (HC) during AM retrieval is consistent with evidence of AM impairment associated with HC damage.[3,4]
- We have found reduced activation in the entire AM network in patients with dysfunction in the left mesial temporal region associated with temporal lobe epilepsy (TLE).[5]
- The direct influence of medial temporal damage on network activation and interactions amongst nodes has only been characterized for only a single patients with mesial temporal damage.[6]
- Here we used univariate regression to identify regions in which activation correlated with structural integrity of the HC (measured as medial temporal width[7]) and structural equation modelling (SEM) to explore further the integrity of network connections in patients with left TLE.

Methods

Participants

- 14 controls (6 male)
- 11 left TLE (6 male)

Pre-Scan Interview

- Participants retrieved 20 AMs and devised AM "titles" to be used as cues during scanning.
- Each AM rated on a five – point scale for level of detail and personal significance

Scanning Protocol

- *AM task*
  - Retrieve AM in response to visually presented AM title (6 *s*)
  - Rate AM for either level of detail or personal significance (4 s)
  - Rest (6 s)
- *Control task: Sentence completion*
  - Complete a visually presented sentence (4 s)
  - Rate for task difficulty (4 s)
  - Rest (8 s)
- *Control task: Size discrimination*
  - Decide largest of two named objects (4 s)
  - Rate for task difficulty (4 s)
  - Rest (8 s)
- Ten of each task randomly presented during each run; participants completed two runs
- Post – scan interview to verify retrieval success

Medial Temporal Lobe (MTL) Width[6]

- Measure of hippocampal atrophy
- *3-step process using Analyze*
  - Reconstruct slices along long axis of HC
  - Use intercollicular sulcus as landmark for S-I measurement boundary and midbrain endpoints for A-P boundaries
  - Sum anterior, posterior, and middle widths

Analyses

Univariate Analyses

SPM2 random – effects analyses

1. AM – control tasks for each group
2. Group contrasts of AM – control tasks with AI internal detail as covariate.
3. Correlation of MTL width with AM activation in patient group

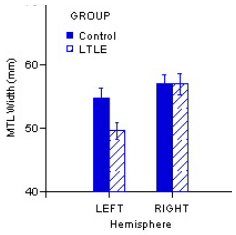
Effective Connectivity Analyses

- Nodes and connections selected based on prior connectivity analyses[1,2], regions observed in our univariate contrast (#2 above) and known neuroanatomy (variety of sources).
- Anatomical model consisted of 11 regions and 18 connections, following preliminary analyses to identify a stable omnibus model (stability indices < 1).
- Estimates of path coefficients calculated based upon correlations of beta values (from peak voxels for individuals) among the regions in the anatomical model.
- Use of stacked-model approach to evaluate whether model in which all connection weights are free to vary between groups) provides a better fit to the data than the null model.
- Stepwise assessment of specific connections undertaken to identify those that contribute significantly to discriminating between the null (no group difference) and alternate (group difference) models.

Results

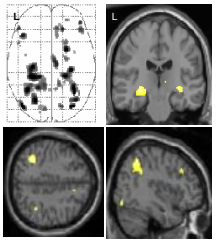
MTL Width

Significant atrophy in affected side for LTLE group (sum of anterior, middle and posterior measurements)



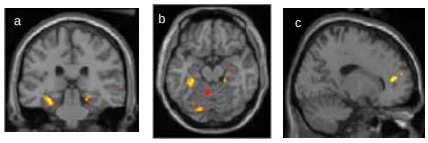
Controls vs. LTLE: AM retrieval – control tasks

- Controls show significantly more activity throughout the AM network, including bilateral HC ($p < .001$, uncorr)
- HC ROI analysis: LHC difference significant ($p < .05$, corr)



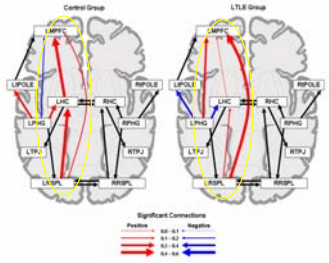
Atrophy and activation in LTLE

- MTL width is correlated to a modest degree with activation in particular regions of the AM network ($p < .01$, uncorr)
- Positive correlations include bilateral parahippocampal gyrus (PHG) and HC (a,b)
- Negative correlations include right medial prefrontal cortex (c)



Alterations in Network Connectivity

- Omnibus test indicates a difference between control and LTLE models [χ2diff(18) = 59.17, $p < .0001$].
- Main differences (p<.01) are influences involving the left HC, with patients showing:
  - reduced input from posterior regions, and
  - Greater direct influence of parahippocampal cortex (LPHG) and left retrosplenial cingulate (LRLSPL) on left medial prefrontal cortex (LMPFC).
- Nonetheless, several connections into and from the left HC, as well as all connections involving the right hemisphere, did not distinguish between the two groups (black arrows in figure below).
- Of interest, there was no indication of increased connectivity involving the unaffected (right) hemisphere in patients, even though the regions are known to be functionally connected during AM retrieval in controls.[2]



Conclusions

- These results indicate alterations in the neural network supporting AM retrieval in the context of unilateral HC damage.
- LTLE patients exhibited an overall decrease of activity across the AM network, including bilateral HC, in comparison to healthy controls.
- The magnitude of HC atrophy in patients was associated with reduced activity in related MTL regions (including bilateral PHG and HC); in contrast greater atrophy was related to increased activity in the medial frontal region.
- The pattern of regional interactions involving the HC also varied as a function of damage in this region, with a "bypass" of hippocampal influences in favour of stronger inputs into prefrontal cortex from other limbic regions.
- Contralateral MTL influences did not vary across groups, indicating that they do not appear to provide compensatory support.
- This altered connectivity may explain how AM retrieval is supported, albeit in a reduced behavioural capacity, in individuals with dysfunction in the 'hb' of the AM network.

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