Age at Hypoxia and the Pattern of Neuropathology in Children with Developmental Amnesia

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Introduction

Hypoxic events sustained perinatally and those sustained later in childhood can result in the same neuropsychological profile of marked impaired event memory and relatively preserved memory for facts (1). These events also appear to be associated with equivalent extents of hippocampal atrophy (measured volumetrically) regardless of when in childhood the hypoxic event occurs.

Morphometric analysis of structural MRI of the children who suffered hypoxic events perinatally has demonstrated bilateral reduction in grey matter density in the putamen, hippocampus and thalamus (2). The purpose of this study was to determine the differences and commonalities in the pattern of neuropathology between the group of children whose pathology was incurred early in life and the children whose pathology was incurred later in childhood.

Methods

The early group consisted of six children who suffered hypoxic episodes aged < 1 year. The late group consisted of four children who suffered hypoxic episodes between the ages of 6 and 14. Two control groups were chosen, age-matched to the early group and the late group respectively.

All subjects were scanned on a 1.5T Siemens Vision system, using a T1-weighted MPRAGE sequence. The 3D data sets were analysed in SPM99 (Wellcome Department of Cognitive Neurology, London, UK). Each scan was normalised and then segmented as described in Ashburner et al. (1997) (3). The images were smoothed with an isotropic Gaussian kernel. This renders the voxel values equal to the amount of grey matter per unit volume under the smoothing kernel.

Two smoothing kernels were used, 4mm and 8mm, in order to sensitise the analysis to the spatial scale of the expected neuropathology (hippocampus and putamen respectively).

The following statistical analyses were then carried out using SPM99. Four group-specific effects were modelled in the design matrix:
1: Early group
2: Early control group
3: Late group
4: Late control group

Adjustments for global grey matter differences were made in all analyses.

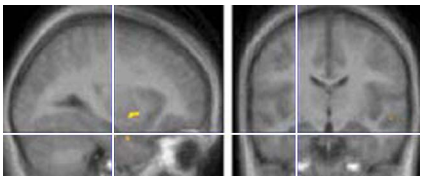
Interaction Analysis (Contrasts 1 -1 -1 1 and -1 1 1 -1)
This analysis searches for significant differences in the neuropathological pattern between the early and late groups when compared to their respective control groups.

Conjunction Analysis (Contrasts 1 -1 0 0; 0 0 1 -1 and -1 1 0 0; 0 0 -1 1)
This analysis searches for areas of abnormality common to both the early and late groups.

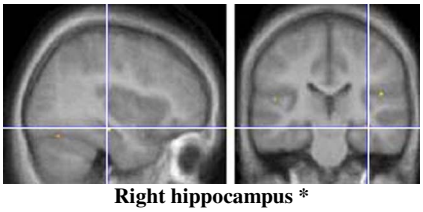
Results

There were no significant differences in the neuropathological pattern between the two patient groups.

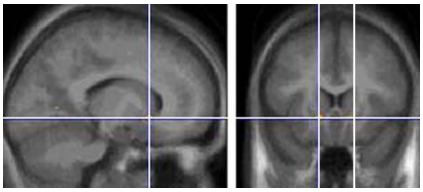
Both groups showed bilateral decreases in grey matter density in the hippocampus (HC), thalamus and putamen. In addition both groups showed abnormal decreases in grey matter density in the region of the right posterior cingulate gyrus (PCG). The positions of the hippocampus and putamen abnormalities are shown in the following figures.



Left hippocampus *



Right hippocampus *



Bilateral putamen *

* *Intersection of cross hairs indicate position of abnormality as detected by SPM*

Discussion

Both the early and late groups show the expected neuropathological pattern associated with hypoxic ischaemic episodes (bilateral hippocampus, thalamus and putamen abnormality).

In combination with the identical neuropsychological pattern that the two groups show, the evidence suggests that hypoxic episodes in childhood result in a predictable pattern of neuropathology and cognitive deficits regardless of when in childhood the injury occurs.

References

1 Vargha-Khadem et al., Science, 277, 376-380, 1997
2 Gadian et al, Brain, 123, 499-507, 2000
2 Ashburner et al., NeuroImage, 6, 209, 1997

Approximate Talairach coordinates and uncorrected p values for common areas of decreased grey matter density in both groups

	Uncorrect. p values	x	y	z
Left HC	<0.001	-30	-12	-22
Right HC	<0.001	37	-24	-15
Putamen	<0.001	±15	20	-8
Thalamus	<0.001	±8	-22	9
PCG	<0.001	12	-60	14