HIPPOCAMPAL ATROPHY IS THE CRITICAL BRAIN CHANGE IN PATIENTS WITH MEMORY DISORDER RESULTING FROM ANOXIC EPISODE

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Introduction: The more frequent cognitive and behavioral sequaelae of anoxic episode are memory deficit, visuo-spatial and visual recognition problems, reduced executive function, language, changes in personality and behaviour (Caine and Watson 2000). Even if anoxia is considered a good model to study amnesia, it is worthy of note that not all individuals who experience anoxic events develop memory problems(Caine and Watson 2000). The question whether in patients with amnesia and without significant other cognitive deficits the damage is limited to hippocampi is still unresolved (Zola-Morgan et al., 1986; Markowitsch et al., 1997). Here we investigated the brain damage in a selected sample of adults affected by exclusively amnesic syndrome after an anoxic episode, applying a quantitative MR technique, the Voxel Based Morphometry (Good et al., 2001).

Methods: we studied five anoxic patients and thirty-three sex- and age-matched healthy subjects. Four of patients had severe anterograde amnesia, one had moderate anterograde amnesia. Our aim was: a) to quantify regional grey and white matter changes associated with chronic anoxic damage compared to control subjects (Group Comparison analysis); b) to identify regions of common abnormality across all patients (Conjuction Analysis); c) to investigate whether measures of regional grey matter volume correlate with memory scores (Correlational Analysis).

Results: a) when we compared anoxic patients to healthy subjects, we found a significant reduction of gray matter volume in the hippocampus bilaterally (FWE p-corrected = 0.05) (see Figure 1). We also lowered the statistical threshold to check whether a more extensive pattern of atrophy is disclosed at reduced thresholds (p-uncorrected = 0.005). We found a larger areas of volume difference; however, these areas are centered around the peaks reported in our original analysis (see Figure 2); b) when we looked at the significant gray matter atrophy common to all patients, we found a gray matter reduction in the hippocampus bilaterally (see Figure 3); c) correlational analysis between memory scores and left and right hippocampal gray matter volume did not reach significance. Only the correlation between performance score on the Prose immediate free recall test and the left hippocampus gray matter volume showed a trend toward significance (Spearman's $\rho = 0.718$; p= 0.08, one tailed) (see Figure 4).

Discussion: Findings from the present study indicate that anoxic events can result in long-term brain damage, with the hippocampus being a region that is highly sensitive to anoxic damage. The hippocampus is the elective target of cerebral damage in adults with amnesia resulting from anoxia. Individual patients may present damage to other brain regions, but the results of the conjunction analysis point to the hippocampal atrophy as the critical damage for the rise of the memory disorder.

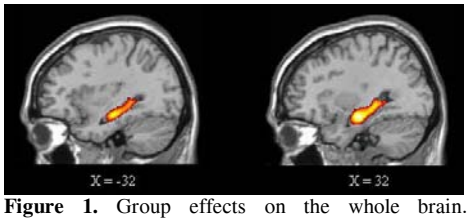

Figure 1. Group effects on the whole brain. Illustrated are regions of significant differences between anoxic patients and control subjects. The color bar encodes the p-value associated with the t-test analysis (FWE p_corrected = 0.05 corrected for multiple comparisons)

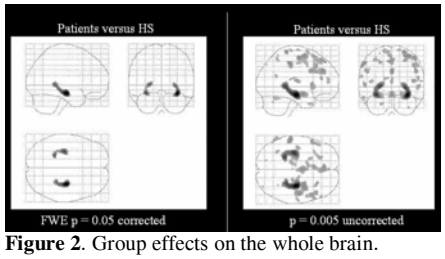

Figure 2. Group effects on the whole brain. Illustrated are regions of differences between anoxic patients and control subjects at the lower threshold (p_uncorrected = 0.05)

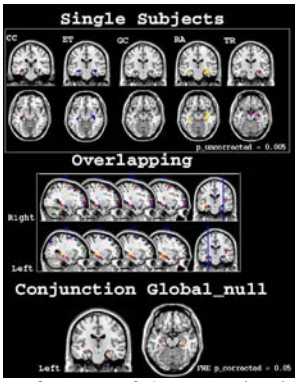

Figure 3. Areas of GM reduction in the patient group. Upper Panel: Area of GM reduction of each patients compared to control subject group (p= 0.005 uncorrected). Middle Panel: Results from each patient (showed in the above panel) overlaid on the single subject T1-weighted normalized brain of SPM5. Lower Panel: Conjuction analysis showing areas of common gray matter reduction across the patient group (p=0.05 corrected FWE). The color bar encodes the p-value associated with the conjuction analysis.

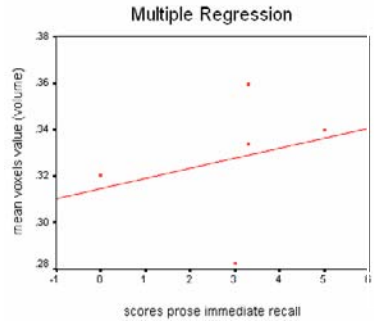

Figure 4. Plot showing the correlation between the Prose immediate free recall scores and the left hippocampus GM volume (Spearman's $\rho = 0.718$; p= 0.08, one tailed).