Institute for Ageing and Health

Newcastle University

An Examination of Cellular Morphology in the Hippocampal Formation in Late-Life Depression

Charlotte Rogers

Institute for Ageing and Health, Newcastle University, Newcastle-Upon-Tyne, NE4 5PL

c.b.t.rogers@newcastle.ac.uk

Introduction

Late-life depression is a major public health problem, with a prevalence of 12-15%[1] in the UK set to rise over the next few decades due to an ageing population. Whilst the precise neurobiology of late-life depression is not fully understood, significant vascular co-morbidities have been found[2] this has led to what is known as the 'vascular depression' hypothesis.[3] This implies that damage to the vasculature reaching the white matter circuitry involved in affective function may underlie the clinical manifestation in a proportion of late-life depressed patients.

The hippocampal formation plays a key role in mood regulation. Several imaging studies have reported smaller hippocampal volumes in patients with major depressive disorder and region-specific atrophy has been found in the cornu ammonis (CA) 1, 2 and 3, and subiculum regions of the hippocampus[4,5]

The study therefore examined neuronal morphology within the CA1 and subiculum of the hippocampus in late-life depressed patients compared with controls and disease control (Alzheimer's disease [AD]) patients.

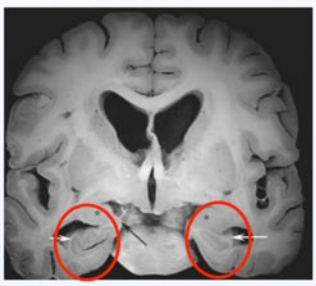


Figure 1: coronal MRI scan through the head of the hippocampus (circled). [4]

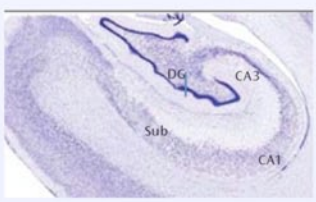


Figure 2: Nissl-stained coronal section of the human hippocampus. [5]

Methods

Post-mortem brain tissue was taken from the Newcastle Brain Tissue Resource, fixed in 10% phosphate buffered formalin before being embedded in paraffin blocks. 21 serial 30um/ 40um sections and 3 sections were sampled in a uniform, random manner. Nissl stain was used to identify neuronal populations.

A Zeiss AxioImager.Z1/ApoTome Microscope was used at x63 objective (using oil) with a AxioCam MRc Zeiss Digital Camera and integrated motorised stage was used. All analysis was conducted using Stereologer 2000 software. The reference area (subiculum and CA1) was defined at 2.5x and density and particle volume measurements taken at 63x magnification, using the optical disector and nucleator probes, respectively (Figure 3). All readings reached a satisfactory level of precision (coefficient of error [CE]<0.15).

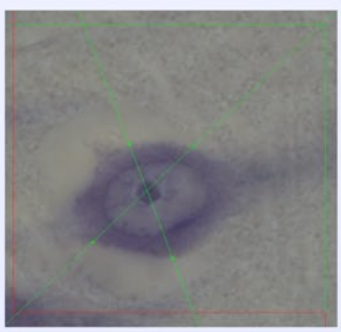
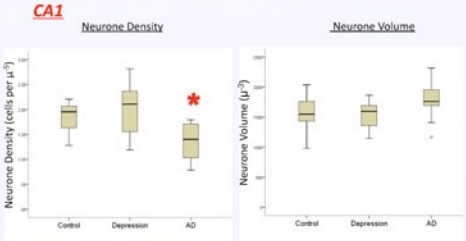


Figure 3: *pyramidal neurones were identified by their triangular soma and thick apical dendrite*. The green lines of the counting frame represent the acceptance region, the red lines the rejection region (prevents counting the same neurone twice).

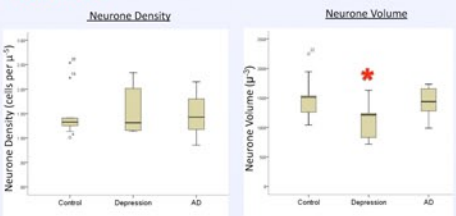
Results

CA1



There was a significant reduction in neuronal density for AD, but not in depressed, patients compared with controls in the CA1. No significant difference in volume was observed in any of the groups. (*P < 0.05)

Subiculum



There was a significant reduction in neuronal volume for the depressed (P=0.02), but no change in AD, patients against controls. There were no significant differences in neuronal density in depressed or AD groups. (*P < 0.05)

Discussion

We found a significant reduction in neuronal volume in the subiculum of the hippocampal formation in late-life depressed patients. However, no changes were found in neuronal density or volume in the CA1 region or in neuronal density in the subiculum. These findings therefore suggest evidence of region-specific neuronal atrophy within the hippocampus in late-life depression and are therefore in partial accordance with the 'vascular depression' hypothesis.

Future work should examine cellular morphology in CA2, CA3, CA4 and dentate gyrus regions of the hippocampus in late-life depressed patients.

References

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