Volume and cell number of the human hippocampus: a postmortem stereological study of hippocampus in depression, schizophrenia, and suicide.

Fenghua Chen[1,2], Raben Rosenberg[1], Jens R. Nyengaard[2,3], Karl-Anton Dorph-Petersen[1,3,4]

[1]Translational Neuropsychiatry Unit, [2]Stereology and Electron Microscopy Laboratory, Dept. of Clinical Medicine, Aarhus University, Denmark

[3]Centre for Stochastic Geometry and Advanced Bioimaging, Aarhus University, Denmark

[4]Translational Neuroscience Program, Dept. of Psychiatry, University of Pittsburgh, USA

Karl-Anton Dorph-Petersen: karl-anton@dorph-petersen.dk

Keywords

Hippocampus, stereology, depression, schizophrenia, suicide.

Introduction

The hippocampus is a cortical structure located bilaterally in the temporal lobes of the brain and plays an important role in the generation of emotions, spatial navigation, and formation of long term memory. Numerous *in vivo* imaging studies have reported that the volume of hippocampus may be reduced in depression. Also, substantial evidence suggests that structural plasticity in the hippocampus may play an important role in the pathophysiology of depression and its treatment. Furthermore, *in vivo* imaging studies indicate hippocampal changes including volume reduction in subjects with schizophrenia. In the present study we search for cellular correlates to these findings.

Materials and Methods

The current study is based upon postmortem brain samples from four groups of subjects: 8 subjects with major depression, 11 suicide victims with a history of depression, 10 subjects with schizophrenia, and 10 control subjects with no history of psychiatric or neurological diseases. The control and suicide subjects are selected from brains collected for previous studies at the Stereology and Electron Microscopy Laboratory. The schizophrenia and major depression subjects are carefully selected, excluding psychiatric comorbidities and suicide, from the large old Brain Collection at Aarhus University Hospital, Risskov which contains approximately 9500 brains from psychiatric patients.

We use a stereological approach based upon light microscopy to investigate if severe depression, suicide or schizophrenia is associated with volume changes of the hippocampal formation and/or changes in the numbers of neurons and/or glial cells in the different subregions of the hippocampus.

The microscopic analysis is based on state of the art stereological techniques based upon unbiased principles: the Cavalieri estimator (Gundersen & Jensen, 1987) is used to estimate the volume of hippocampus and its subregions, and the optical fractionator method (West et al., 1991) is used to estimate the total number of neurons and glial cells in the individual cell layers in four main regions of hippocampus: the granular cell layer, hilus, CA2/3, and CA1. In order to generate the needed systematic, uniformly random

histological sections from archival brain tissue, we use a technique of dissection, reassembling, and subsequent stereological precision slicing of the region of interest (Sweet et al., 2005; Dorph-Petersen et al., 2007)—see Fig. 1 for a reassembled hippocampus.

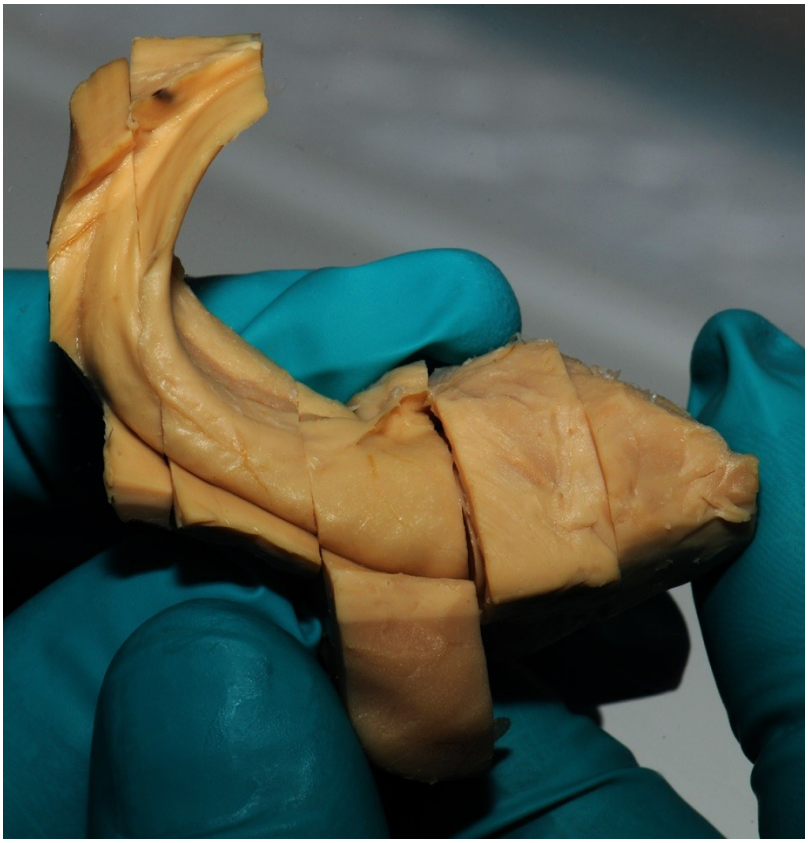

Figure 1. A reassembled human hippocampus

Results and Discussion

We found the volume and the number of neurons and glial cells substantially and significantly reduced in a similar way in depressed and schizophrenia subjects relative to control subjects across all hippocampal regions. Our detailed results will be presented at the 14th International Congress for Stereology and Image Analysis in Liège.

Conclusion

Our results elucidate some aspects of the pathological anatomy of depression and schizophrenia but also raise a number of new issues to be addressed in future studies.

References

Dorph-Petersen K-A, Pierri JN, Wu Q, Sampson AR & Lewis DA (2007) 'Primary visual cortex volume and total neuron number are reduced in schizophrenia.' *J Comp Neurol*, 501, 290-301.

Gundersen HJG, Jensen EB (1987) 'The efficiency of systematic sampling in stereology and its prediction.' *J Microsc*, 147, 229–263.

Sweet RA, Dorph-Petersen K-A & Lewis DA (2005) 'Mapping auditory core, lateral belt, and parabelt cortices in the human superior temporal gyrus.' *J Comp Neurol*, 491, 270-289.

West MJ, Slomianka L, Gundersen HJG (1991) ‘Unbiased stereological estimation of the total number of neurons in the subdivisions of the rat hippocampus using the optical fractionator.’ *Anat Rec*, 231, 482–497.