Imaging the Functions of Human Hippocampus

Bryan A. Strange

Ph. D. Thesis

Wellcome Department of Cognitive Neurology,
Institute of Neurology,

University College London

“*Memory frees us from the tyranny of the genes*.”

Malcolm Brown. Neuroanatomy lecture, Bristol Medical School, 1995.

I thank Ray Dolan and Karl Friston for their enthusiastic supervision, Rik Henson, Paul Fletcher, Leun Otten and Mick Rugg for their help and advice, and my family and friends for their support and encouragement.

Since the 1950s it has been known that damage to the hippocampus impairs conscious long-term memory for events and episodes. However, the precise functional role of the hippocampus in episodic memory remains controversial. Hippocampal damage impairs the acquisition of novel episodic memories, which may suggest a role in processing novel stimuli. In this thesis, a series of functional magnetic resonance imaging (fMRI) experiments were conducted to characterise the human hippocampal response to novelty. The results from four experiments suggest a functional dissociation between anterior and posterior hippocampal regions with respect to the relative familiarity of study items. Responses in anterior hippocampus index novelty whereas posterior hippocampal responses index familiarity. Anterior hippocampal responses showed adaptation with repeated presentations of a given stimulus, indicating this region is sensitive to the recency of prior occurrence. Anterior hippocampus was also engaged by stimuli that violated expectation, suggesting that the anterior hippocampal role is processing recency of prior occurrence reflects a more general role in detecting mismatches between expectation and experience. This anterior hippocampal mismatch response may represent an important component of episodic memory encoding. The posterior hippocampal familiarity response may reflect retrieval of familiar stimuli. This functional segregation, within human hippocampus for the processing of relative familiarity, may provide a basis for understanding the memory deficits that arise from damage to different regions of the hippocampus.

Table of Contents

Chapter 1 Introduction

Chapter 2 Materials and Methods

Part I Functional Magnetic Resonance Imaging

Part II Statistical Analysis of Functional MRI Time Series

Chapter 3 Functional Segregation within Human Hippocampus for Relative Familiarity

Chapter 4 Neuroanatomical Correlates of Rule Learning

Chapter 5 Detection of Perceptual, Semantic and Emotional Deviance

Part I Non-Adapting Responses

Part II Adapting Anterior Hippocampal Responses

Chapter 6 Human Medial Temporal Activity Predicts Subsequent Memory: Dissociable Perirhinal, Hippocampal and Parahippocampal Roles in Verbal Encoding

Chapter 7 Anatomical and Neuromodulatory Bases for Functional Segregation within the Hippocampus

Chapter 8 General Discussion

References

Table of Figures

Chapter 7