Available online at www.sciencedirect.com
ScienceDirect
Behavioural Brain Research 174 (2006) 304–312
BEHAVIOURAL BRAIN RESEARCH
www.elsevier.com/locate/bbr

Research report

Controlling hippocampal output: The central role of subiculum in hippocampal information processing

Shane O'Mara *

Trinity College Institute of Neuroscience, Trinity College, Dublin 2, Ireland

Received 26 July 2006; accepted 4 August 2006
Available online 10 October 2006

Abstract

The subiculum has a central position between the hippocampus proper and entorhinal and other cortices, as well as a range of subcortical structures. The functional role of subiculum within the hippocampal formation circuit remains largely unexplored and a theoretical and experimental consensus on its functions has yet to emerge. Presented here is a simple and speculative model of the functions of the subiculum, based partly on anatomical, behavioural and neurophysiological considerations. The model suggests, firstly, that the subiculum acts to amplify hippocampal output, given the prominent bursting behaviour of its neurons and, secondly, that there is a dorso-ventral segregation of function within the subiculum. The dorsal component appears principally concerned with the processing of information about space, movement and memory, whereas the ventral component appears to play a major regulatory role in the inhibition of the HPA axis.

Keywords: Subiculum; Synaptic plasticity; Hippocampal formation; Stress; Hypothalamus; Prefrontal cortex

1. Introduction

Traditional theoretical views of the neuroanatomy of the mammalian hippocampal formation have revolved around the tri-synaptic circuit: a set of forward-projecting processing pathways consisting of projections to the dentate gyrus (DG) from entorhinal cortex (EC) and thence to the hippocampus proper (consisting of areas CA3 and CA1) and a return projection to EC. Adjacent this circuit is another set of areas, sometimes named the 'subicular complex', consisting of several cortical fields located between area CA1 of the hippocampus proper and the EC ventrally, and CA1 and the retrosplenial cortex, dorsally [1]. The 'subicular complex' was usually divided into the subiculum proper, the presubiculum and the parasubiculum [35]. It is now clear [2], however, that the major output of the hippocampus proper – area CA1 – is actually to subiculum, which in turn sends its major projection to EC (Figs. 1 and 2 [1,2,22,23,32]), in addition to many cortical and subcortical targets. If the EC is the major input structure of the hippocampus proper, and the subiculum is the major output structure of the hippocampus proper, then where do the presubiculum and parasubiculum fit anatomically and functionally in this circuit [1,22,23]? Both presubiculum and parasubiculum receive inputs from subiculum, but these are not robust and neither area receives much input from the main hippocampal fields. This is in contrast to the subiculum itself, which receives a large and robust projection from CA1. Here, we treat the subiculum as properly part of the hippocampal formation itself; we suggest, given the major anatomical differences in terms of intrinsic and extrinsic properties that the term 'subicular complex' does not denote a useful anatomical and, by extension, functional grouping of structures, and should be discarded, with subiculum assuming its proper role as part of the hippocampal formation. Thus, the hippocampal formation circuit consists of EC, DG, CA3, CA1 and subiculum, with a forward projection from subiculum to EC completing the circuit.

The subiculum is under-investigated, by comparison, say, with hippocampal area CA1, a mere synapse behind; it is not surprising, therefore, that consensus on its neuroanatomical description and definition has only emerged over the past 20 years [1,2,22,35]. It is also safe to say that little is still known regarding the physiology of the mammalian subiculum and there is little theoretical consensus on the functions of the subiculum. In this paper, we summarise some of the conclusions from recent neuroanatomical, lesion and neurophysiological investigations

* Tel.: +353 1 896 8447.
E-mail address: shane.omara@tcd.ie.

0166-4328/$ – see front matter
doi:10.1016/j.bbr.2006.08.018

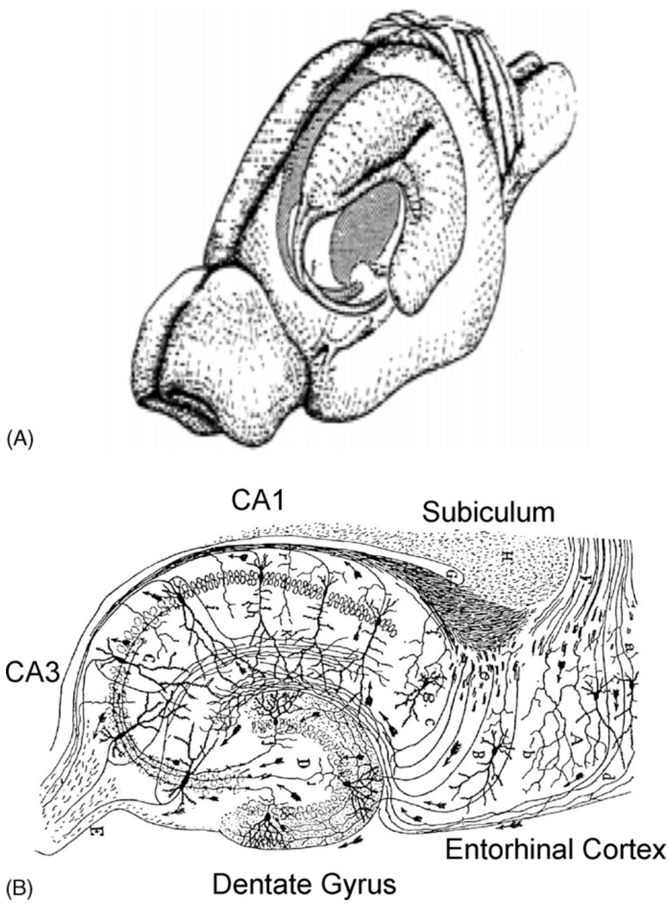

Fig. 1. The hippocampal formation (A) and location of subiculum (B), indicated as 's' in a section through the hippocampal formation.

of subiculum, and provide a simple framework for hypotheses regarding subicular function, emphasising the possibility that a dorso-ventral segregation of function exists across the longitudinal axis of the subiculum [22].

2. General anatomical description of subiculum

The subiculum has three principal layers: a molecular layer, continuous with strata lacunosum-moleculare and radiatum of the adjacent hippocampal area CA1 field; an enlarged pyramidal cell layer containing the soma of principal neurons and a polymorphic layer. Cell packing in the pyramidal layer of the subiculum is looser than hippocampal area CA1. The principal cell layer of the subiculum is populated with large pyramidal neurons; among the pyramidal cells are many smaller neurons which are considered as subicular interneurons [1,30]. Hippocampal area CA1 sends its primary projection to all regions of the subiculum, which in turn projects to many cortical and subcortical targets (Figs. 2 and 4), so subiculum is the major output structure of the hippocampus [1,2,23,35]. The CA1-subiculum projection is organised in a simple pattern, with all portions of CA1 projecting to the subiculum, and all regions of subiculum receiving CA1 projections [2]. Here, following Amaral et al. [2], we will use the term 'proximal CA1' to refer to the area bordering CA3 and 'distal CA1' for the area bordering the subiculum. The subiculum is similarly defined, with proximal subiculum bordering CA1 and distal subiculum bordering the presubiculum. To summarise these projections (Amaral et al. [2]; Fig. 3a); cells in proximal CA1 project to distal subiculum, cells in mid-CA1 project to mid-subiculum and cells in distal CA1 project across the CA1-subiculum border into proximal subiculum. Combined single unit and morphological studies suggest that the CA1-subicular pathway is a monosynaptic projection ([13]; Fig. 3b), and that it returns a minor oligosynaptic projection to CA1 ([9]; Fig. 3c). Finally, subiculum receives cortical inputs from the entorhinal, perirhinal and prefrontal cortices, to which it returns important and prominent projections; it also receives inputs from and distributes to some other secondary and tertiary cortices.

There are extensive reciprocal connections between the subiculum and many subcortical structures (and particularly to various hypothalamic nuclei; Fig. 4). Subcortical structures projecting to the subiculum include the ventral premammillary nucleus (to ventral subiculum); the medial septum/nucleus of the diagonal band and all areas of the anteroventral (AV) and anteromedial (AM) nuclei of the thalamus (see [6,16,26]). Ventral subiculum projects to the hypothalamus via the post-commissural fornix, the medial corticohypothalamic tract and via the amygdala; these projections innervate the medial preoptic area, the ventromedial and dorsomedial nuclei, and ventral premammillary and medial mammillary nuclei. Lowry [17] summarises this extensive projection system as follows: "The ventral subiculum projection system projects to a distributed forebrain limbic system associated with inhibitory input to the hypothalamic-pituitary-adrenal (HPA) axis and the hypothalamic-spinal-adrenal (HSA). Inhibition of the HPA axis is thought to be mediated transynaptically via GABAergic neurones that project directly to the paraventricular nucleus or hypothalamic autonomic control systems. Neurones within the median raphe nucleus project extensively and selectively to the ventral subiculum projection system, including the medial hypothalamic defensive system associated with active emotional coping responses". Thus, at least one major function of vSUB is terminating or limiting the response of the HPA axis to stress, in addition to other possible roles (see below).

3. Recordings of subicular neurons in the freely moving, behaving animal

Understanding the neurocognitive functions of subiculum involves understanding the information represented by subicular neurons. Standardised methods have evolved for studying the discharge correlates of single neurons and neuronal ensembles [21,25]. Briefly, these require a freely moving rat to traverse mazes or open fields (often in search of food), neuronal activity is recorded and correlated with the moment-to-moment position of the rat. These correlations are used to generate colour-coded contour maps representing the density of spike firing at all points occupied by the rat. Under these conditions, many hippocampal formation neurons (particular in area CA1) fire in a locally defined area of the maze (usually no more than a few percent of the total maze area) and remain silent or fire at low rates (<1 Hz)