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BRAIN RESEARCH

Research Report

# Dentate granule cells form hilar basal dendrites in a rat model of hypoxia–ischemia

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ABSTRACT

Hilar basal dendrites form on dentate granule cells following seizures. To determine whether other brain insults cause the formation of hilar basal dendrites, a model of global cerebral hypoxia/ischemia was used. Rats underwent a transient induction of ischemia by occlusion of both common carotid arteries followed by reperfusion. Hippocampal slices were prepared from these animals 1 month after the ischemic insult, and granule cells were labeled with a retrograde tracing technique after biocytin injections into stratum lucidum of CA3b. Ischemic rats had numerous biocytin-labeled granule cells with hilar basal dendrites located at the hilar border of the granule cell layer. Quantitative analysis of ischemic rats compared to controls showed a significant increase in the percentage of biocytin-labeled granule cells with hilar basal dendrites. These data demonstrate that other brain insults in addition to epilepsy may result in the formation of hilar basal dendrites on granule cells.



## 1. Introduction

Granule cells in the rodent dentate gyrus are organized in a densely packed cell layer with their apical dendrites extending into the molecular layer and their axons arising from the opposite pole of the soma and projecting into the hilus (Lorente de Nó, 1934). Although most granule cells have this regular appearance, other granule cells may have an apical dendrite arising from the base of their cell body or an axon originating from either the apical pole of the soma or an apical dendrite (Ribak et al., 2000; Yan et al., 2001; Dashtipour et al., 2002). These morphological findings suggest that granule cells are more heterogeneous than previously indicated. In addition, granule cells respond to seizures with two different neuroplastic changes, mossy fiber sprouting (Tauck and Nadler, 1985; Sutula et al., 1989) and the formation of hilar basal dendrites (Spigelman et al., 1998; Buckmaster and Dudek, 1999). These studies show that the granule cells of the dentate gyrus can have both their dendritic and axonal morphology modified to form increased recurrent excitatory circuitry (Okazaki et al., 1995; Sutula et al., 1998; Zhang and Houser, 1999; Ribak et al., 2000; Shapiro et al., 2008; Thind et al., 2008).

Rats subjected to global ischemia are similar to those undergoing recurrent seizures in that both groups show a similar pattern of hilar cell death, comparable increases in

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neurotrophic factors and in high affinity receptors in granule cells (Lindvall et al., 1994). However, current evidence suggests that global ischemia does not lead to behaviorally observed status epilepticus or recurrent spontaneous limbic seizures (Epsztein et al., 2006), but EEG observed seizure activity was reported in vivo after global ischemia and during the reperfusion phase (Caruana et al., 2008). In contrast, unilateral hypoxia–ischemia does lead to mossy fiber sprouting and the development of spontaneous recurrent seizures in a small (15%) proportion of animals 6–12 months after the ischemic insult (Williams and Dudek, 2007).

The present study was undertaken to determine whether hilar cell death without status epilepticus is a necessary and sufficient stimulus to induce the formation of hilar basal dendrites on dentate granule cells. We examined biocytin-labeled granule cells using a retrograde labeling approach at the light microscopic level to determine whether bilateral hypoxia–ischemia induces the formation of hilar basal dendrites on granule cells.

## 2. Results

The appearance of granule cell bodies and the arborization pattern of their apical dendrites within the molecular layer of the dentate gyrus in ischemic rats were similar to those of the control group (Spigelman et al., 1998; Yan et al., 2001). However, biocytin-labeled granule cells were identified with thick and long basal dendrites in ischemic rats, as shown in Fig. 1. Furthermore, the axons of these granule cells arose from their hilar pole and entered the hilus (Fig. 2). These basal dendrites most frequently arose from the hilar pole of the granule cell bodies, and were easily distinguished from the axons of these cells (Figs. 1 and 2). Basal dendrites were less

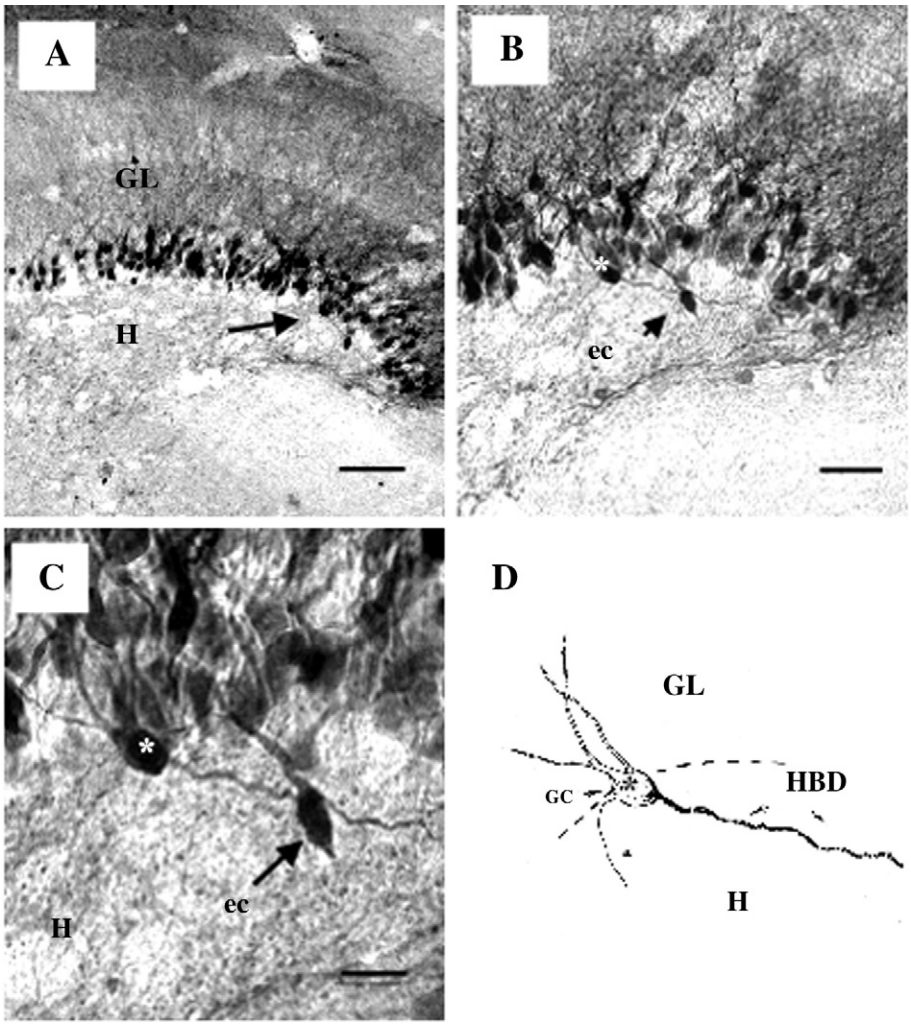


**Fig. 1 – Biocytin-labeled granule cells (GC) from ischemic rats. A is a low magnification of the dentate gyrus that shows the granule cell layer (GL) and hilus (H) with many labeled granule cells and their dendrites. The area indicated by the arrow in A is enlarged in B and in C to show a granule cell with a hilar basal dendrite (white asterisk) and an ectopic (ec) granule cell (arrow) in the subgranular zone. In D, a camera lucida drawing of the granule cell GC (*) with the long and thick hilar basal dendrite (HBD) extending into the hilus (H). The thinner process arising from this granule cell is its axon (a). Scale bars: in A = 40 μm; B = 25 μm and C = 10 μm.**