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Research article

Neurogenesis and precursor cell differences in the dorsal and ventral adult canine hippocampus

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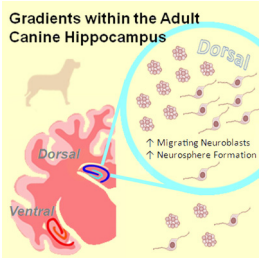
HIGHLIGHTS

- Adult canine hippocampal neurogenesis is dependent on dorsal–ventral location.
- Canine dorsal dentate gyrus has markedly higher rate of neurogenesis than ventral.
- Precursors from *post mortem* hippocampus differentiate into neurons & glia.

GRAPHICAL ABSTRACT



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ABSTRACT

During evolution a unique anterior–posterior flexure posited the canine dentate gyrus in two distinct dorsal and ventral positions. We therefore sought to explore neurogenesis and neurogenic cell-related difference along the canine hippocampal dorsal–ventral axis. *Post mortem* histological analysis revealed 49.1% greater doublecortin (DCX)-positive cells and a 158.5% greater percentage of double labeled DCX-positive/neuronal nuclei (NeuN) positive cells in the dorsal subgranular zone compared to the ventral. We then show neural precursor cells isolated from fresh hippocampal tissue are capable of proliferating long term, and after differentiation, express neuronal and glial markers. Dorsal hippocampal isolates produced a 120.0% higher frequency of sphere-forming neural precursor cells compared to ventral hippocampal tissue. Histological DCX and neurosphere assay results were highly correlated. Overall, we provide the first evidence that the dorsal canine hippocampus has a markedly higher rate of adult neurogenesis than the ventral hippocampus, possibly related to a greater frequency of contributory neural precursor cells.

1. Introduction

Neurogenesis occurs in the adult canine hippocampus (*Canis familiaris*) [1] as in many other canid mammals [2,3], but well described dorsal–ventral distinctions in rodents [4] are yet to be studied in dogs. This is particularly interesting because of the unique anatomy of the canine hippocampus that recalls features of both humans and rodents [5].

During evolution, the septal pole of the rodent hippocampus that was located dorsally (*i.e.*, superior to the lateral ventricles (Fig. 1A) migrated to lie much flatter near the base of the brain in humans (Fig. 1C) [6]. The hippocampus of the dog was arrested in the middle of this evolutionary transit, undergoing a

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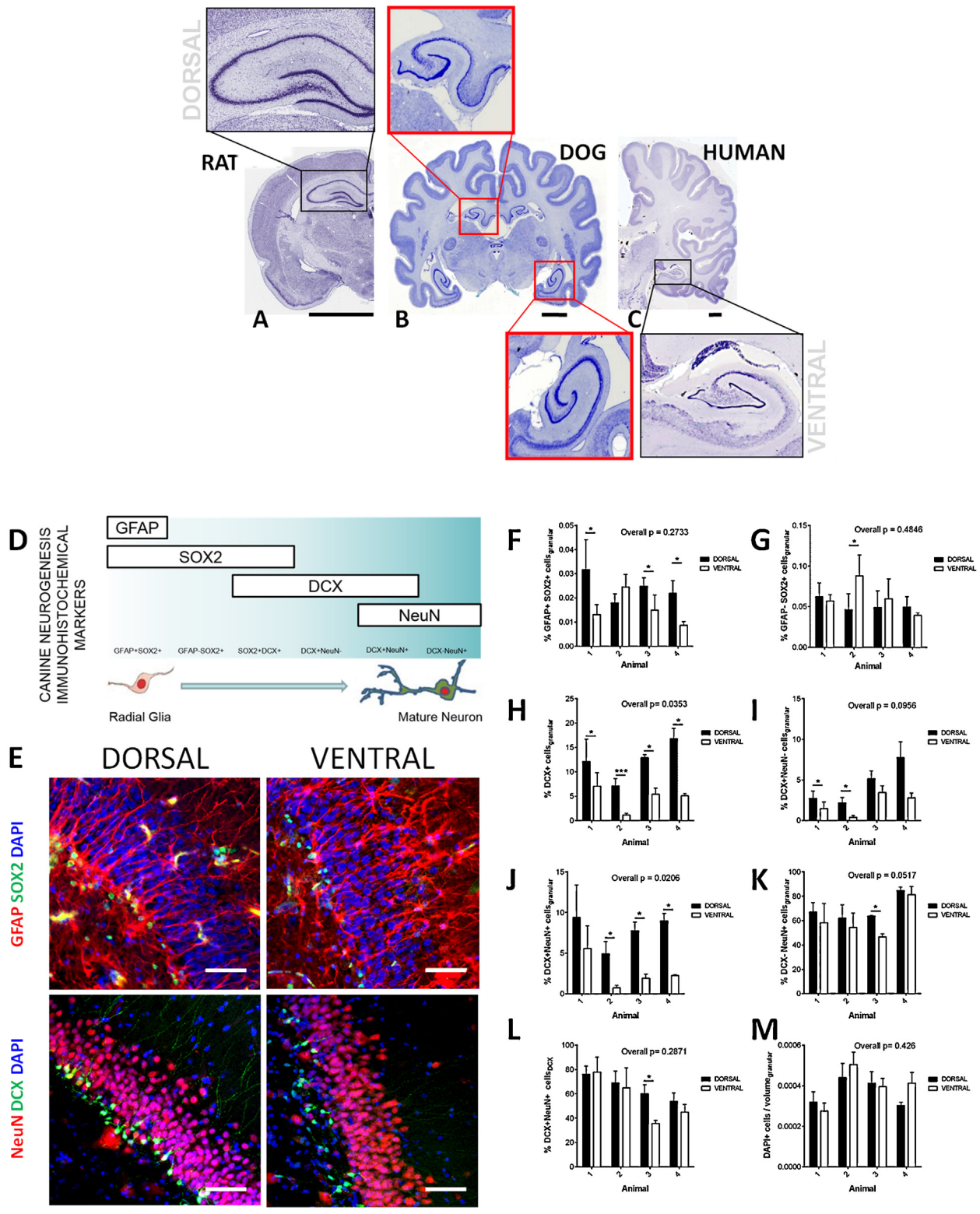

Fig. 1. Comparative anatomy of hippocampus and dentate gyrus in (A) rodents, (B) canines and (C) humans. All coronal sections Nissl stained. Rat Nissl image obtained from brainmaps.org [38]. Canine image reproduced from 'The Beagle Brain in Stereotaxic Coordinates' with written permission from author Xavier Palazzi [39]. Human hemisphere, obtained from the 'Zoomable brain atlas' and reproduced with written permission from author Georg Striedter [40]. Scale bar 1 cm. (D) Immunohistochemical Markers of Neurogenesis. (E) Co-expression of Glial Fibrillary Acidic Protein (GFAP, Red) and Sex determining region Y-box 2 (SOX2, Green) (top). Co-expression of Doublecortin (DCX, Green) and Neuronal Nuclei (NeuN, Red) (bottom) in the subgranular zone of the dorsal and ventral adult canine hippocampus. No significant differences in the percentage of F) GFAP + SOX2+, G) GFAP-SOX2+ cells. (H) Significantly greater dorsal than ventral DCX density was found in all dogs (* $p < 0.05$). Overall significant regional effects for DCX ($p = 0.035$). (I) No difference between DCX+NeuN- percentages. (J) Significant differences in DCX+NeuN+ ($p = 0.02$) expression between the dorsal and ventral subgranular zones. No overall significant effects in (K) percentage of DCX–NeuN+ or (L) percentage of DCX+ cells coexpressing DCX+NeuN+ or (M) the number of DAPI positive cells in the granular zone. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)