

Adult neurogenesis in the giant otter shrew (*Potamogale velox*)

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Introduction

Adult neurogenesis is present throughout vertebrate species. In mammals, the generation of new neurons is for the most part restricted to the subgranular zone of the hippocampal dentate gyrus and the subventricular zone, from where cells migrate along the rostral migratory stream (RMS) to the olfactory bulb. Most of the studies on adult neurogenesis to date have been undertaken on laboratory animals, but it is very important to analyse neurogenesis in wild living species to determine if the patterns observed are consistent through phylogeny. In the present study we investigated adult neurogenesis in the brain of the giant otter shrew (*Potamogale velox*), a central African rainforest mammal of the family Tenrecidae, belonging to the superorder Afrotheria.

We examined neurogenesis immunohistochemically, using the endogenous marker doublecortin (DCX), which is expressed in neuronal precursor cells and immature neurons.

Methods

Following an overdose of sodium pentobarbitone, the animals were perfused through the left ventricle with 0.9% saline, followed by 4% paraformaldehyde in a 0.1 M phosphate-buffered solution (PB, 4°C, pH 7.4), within 4 hours of being captured in the rainforest. The brains were cryosectioned into 50 µm coronal sections and an immunohistochemical detection of DCX (anti-DCX, 1/300, C-18, polyclonal goat IgG, Santa Cruz) was performed to label neuronal precursor cells and immature neurons. One corresponding serial set of sections was stained for Nissl and one for myelin, to visualize the neural architecture.



Conclusions

- The giant otter shrew reveals similar patterns of adult neurogenesis as seen in previous studies of laboratory mammals. We found neuronal precursor cells in the DG of the Hippocampus and SVZ, from where the newly generated neurons migrated along the RMS to the GCL and the GL of the olfactory bulb.
- Newly generated neurons were also found in the piriform cortex and the olfactory tubercle. DCX positive processes were observed in the amygdala and the hypothalamus. These regions were previously demonstrated to be potentially neurogenic; however the data available to date is inconsistent and not widely accepted.
- In this study, we demonstrated for the first time the appearance of neuronal precursor cells in the anterior commissure, migrating to the contralateral hemisphere. This is a unique finding and possibly a derived feature of the Tenrecidae family, as a previous study showed the presence of DCX fibers in the anterior commissure of the hedgehog and mole.

Supported by the ISN SSAJRP Funding to A.O.I.

Results

Hippocampus

DCX positive cells were identified in the subgranular (SGL) and granular cell layers (GCL) of the dentate gyrus and labelled DCX positive processes, presumably axons of the newly generated granular cells, were observed in the hilus and the CA3 regions of the hippocampus.

Amygdala

DCX positive processes were found in the presumed intercalated amygdaloid nucleus (I).

Anterior commissure

DCX positive cells and fibres were observed in the anterior commissure (AC).

These DCX positive cells and fibres were presumably present in the lateral portion of the anterior commissure.

It appears that from the RMS an additional stream of neuronal precursor cells splits off. These cells then migrate further towards the anterior commissure via which they cross to the contralateral hemisphere.

In addition, a second stream seems to diverge from the RMS, from where newly generated neurons migrate towards the olfactory tubercle (Tu).

Olfactory bulb

Densely packed DCX positive cells migrated from the SVZ along the RMS to the olfactory bulb.

In the olfactory bulb, DCX expressing cells were primarily present in the granular cell layer (GCL) with tangentially orientated dendrites and in the glomerular layer (GL) representing periglomerular cells, however, a few migrating neuronal precursor cells were also observed in all olfactory bulb layers.

Piriform Cortex

DCX positive cells were found in layer II of the piriform cortex (Pi).

Neuronal precursor cells seem to migrate to the piriform cortex from the ventral tip of the lateral ventricle via the ventrobasal stream.

Hypothalamus

DCX positive processes were found in the presumed ventromedial hypothalamic nucleus (VMH).

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Introduction

Wernicke-Korsakoff syndrome is an amnesic disorder which arises from thiamine deficiency and is most commonly observed in chronic alcoholics. Pyridoxamine-induced thiamine deficiency (PTD) is an animal model that recapitulates both neuroanatomy and cognitive deficits observed in human WKS. Interestingly, there appears to be cortical functional damage in both WKS and PTD. Treatment depends primarily on access to the disaccharide, inulin and mannuronic bodies. Research from our laboratory has revealed there is limited AChE efflux in the medial frontal (MFC) and retrosplenial (RSC) cortex during behavioral testing. Thiamine studies have shown that voluntary exercise (VE) has beneficial effects on the CNS, and more importantly, it has been shown that VE is able to attenuate hippocampal behavior deficits observed in the PTD model. It has also been suggested that VE has the potential to modulate cytoskeletal changes through its effects on neurotrophic factors, including brain derived neurotrophic factor (BDNF), neural growth factor (NGF) and vascular endothelial growth factor (VEGF). However, it remains uncertain whether the therapeutic potential of VE has the capacity to ameliorate the cortical deficits observed in the FC and RSC. Thus, FC and RSC BDNF cell survival was assessed as a function of VE and PTD treatment and cellular phenotypes were obtained. Furthermore, behavioral performance was assessed in addition to changes in BDNF, NGF, and VEGF neurotrophic levels.

Methods

Subjects - 32 male Long-Evans (LE) 12-13 months old PTD (PTD) (n=16), Pyridoxamine (PM) (n=16), and thiamine (TH) (n=16) were used for this study. All subjects were housed in a temperature controlled environment (22°C) and given access to food and water ad libitum.

Behavior - Subjects were tested 3 weeks later on a 4-arm radial maze task for 20-25 days.

These preparations (PM, TH) were collected and processed for BDNF, NGF, and VEGF levels of surviving cells.

Statistical Analysis - Student's t-test was used to compare the mean values of the PM, TH, and PTD groups.

Statistical Significance - Data is presented as mean ± SEM. *p < 0.05, **p < 0.01, ***p < 0.001.

Conclusions

1. VE treatment significantly increased BDNF levels in the FC and RSC.

2. VE treatment significantly increased NGF levels in the FC and RSC.

3. VE treatment significantly increased VEGF levels in the FC and RSC.

4. VE treatment significantly improved behavioral performance in the FC and RSC.

