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PROCEEDING BOOK

Basic Molecular Biology Course on

AGING AND REGENERATIVE MEDICINE:

Is It Possible to Reach Healthy Aging?

2019

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TABLE OF CONTENTS

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New Neurons : The Future of Regenerative Brain Therapy

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Abstract

The world's future will be an aging society because enormous 'baby boom' generation will reach retirement age over the next decade with 'aging brain' as a related problem. Aging brain is common and is not a sign of a serious neurological disorder, but it can be a frustrating and cause reduction of productivity, a burden to community and nation. Adult neural stem cell and neurogenesis confer a unique mode of neuroplasticity in the brain, creates a glimmer of hope in the development of future therapies to 'prevent' aging brain, and more specifically, treat some untreatable diseases. A lot of research is being done on this topic and some of them have opened a new perspective for the identification and development of new therapeutic approaches to enhance neurogenesis and produce new neurons for neurodegenerative disorders.

Keywords: Aging brain, neurological disorder, adult neural stem cell, neurogenesis, neuroplasticity, therapy

Introduction

The world's future will be an aging society because enormous 'baby boom' generation will reach retirement age over the next decade (8). A significant proportion of those older than 65 years will be a problem related with 'aging brain'. Aging brain is common and is not a sign of a serious neurological disorder, but it can be a frustrating and cause reduction of productivity, a burden to community and nation. Nowadays, a lot of theory and research on the brain and adult neurogenesis theory broke the previous concept that the brain can not regenerate. New neuron cells can appear to replace damaged or

old cells. Of course this is a breakthrough in the future to overcome the aging brain and other neurological disorders.

Adult Neurogenesis

The central nervous system (CNS) is one of the most complex and intriguing organs in human, and its development, function and pathology has attracted the attention of many neuroscientist throughout centuries (1). One of the amazing phenomena that occur in the CNS is the process of new neuron generation or neurogenesis (1).

Two neurogenic niches in the adult mammalian brain have been identified : the subventricular zone (SVZ) of the lateral ventricle, and the subgranular zone (SGZ) of the hippocampal dentate gyrus (12). New neurons are continuously integrated into existing neural circuits in adult dentate gyrus of the mammalian brain (3). These new neurons are involved in learning and memory (6, 7).

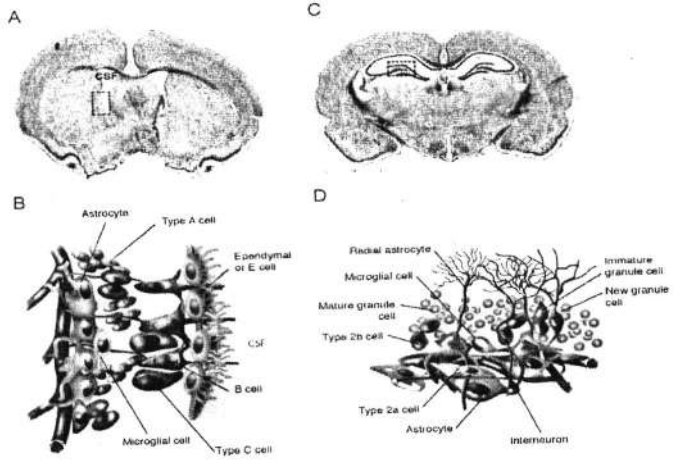

Figure 1. Adult neural stem cell: A. Subventricular zone (SVZ) and B. Subgranular zone (SGZ). (Lin R, Iacovitti L. Brain Res, 2015).

Studies have demonstrated that many kinds of injury, including traumatic brain injury, hypoxia-ischemia, and stroke trigger neurogenesis in the injured brain (5, 9). Following brain insult, both traumatic or ischemic, neural stem cells in different brain regions are

activated, increase their proliferation rate and migrate to the injury site (2, 5).

Enhancing neurogenesis for neurorestoration in aging brain or after brain injury remains a compelling and viable means for improving outcome in many neurological diseases. Pharmacological modulation of neurogenesis can be a useful tool to design a therapeutic strategy against brain insult and neuronal loss (10). Different strategies are under investigation, including the infusion of growth factors, neurotrophins, chemokins, hormones, anti-inflammatory drugs and other neuroprotective agent (10).

Cellular Therapy

The nervous system, unlike many other tissues, has a limited capacity for self-repair, mature nerve cells lack the ability to regenerate, and neural stem cells, although they exist in the adult brain, still have a limited ability to generate new functional neurons in respons to injury (11).

Transplantation of stem cells into the injured or aging area of the brain are to rebuild circuitry is another potential approach for cell repair or recovery (13). Various kind of stem cells have been tested in a variety of animal models and human clinical trial (4). Several studies have shown improvement in neurological status after transplantation, although through different mechanism (12). Stem cell-based therapy therapies could potentially beneficial by acting through several mechanism : (1) cell replacement, where transplants of cells are given to directly replace those that are lost or damage, (2) paracrine effect, where the cells are used to promote survival of affected neurons and endogenous repair of the diseased brain areas, (3) modulation of inflammation, which may be involved in the disease process (11).

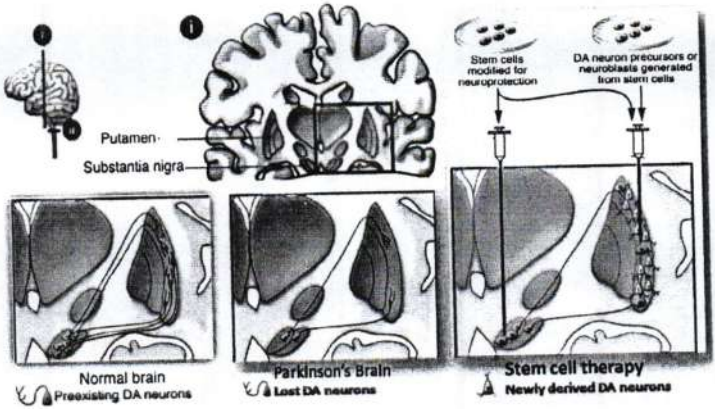

Figure 2. Pathology of Parkinson's disease and Neural Stem Cells based approach for cellular therapy. (Vishwakarma SK, Bardia A, Tiwari SK, Paspala SAB, Khan AA. Adv. Res, 2014).

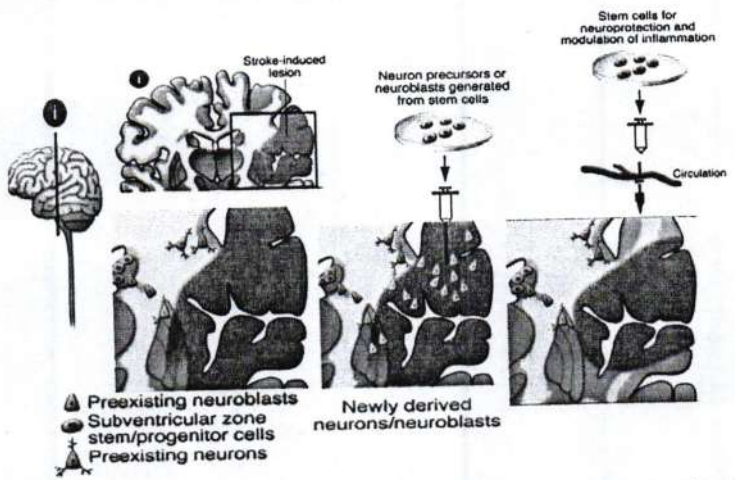

Figure 3. Pathology of stroke in brain and Neural Stem Cells based cellular therapy. (Vishwakarma SK, Bardia A, Tiwari SK, Paspala SAB, Khan AA. Adv. Res, 2014).

In the prospect of stem cell therapy, the implanted cell must be able to survive and generate new neurons of the appropriate types that functionally integrate into the damage host brain circuitry (11).

Future Perspective

Adult neural stem cell and neurogenesis confer a unique mode of neuroplasticity in the brain. This situation creates a glimmer of hope in the development of future therapies to 'prevent' aging brain, and more specifically, treat some untreatable diseases, such as stroke, multiple sclerosis, brain injury, alzheimer's, parkinson's etc. A lot of research is being done on this topic, the development of pharmacotherapy to stimulate neurogenesis, physiotherapy and exercise methods to improve endogenous stimulation in neural stem cells and cellular therapy (stem cell) to replace or stimulate neurogenesis. Increase in basic knowledge will open new perspective for the identification and development of new therapeutic approaches to enhance neurogenesis and produce new neurons for neurodegenerative disorders.

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