شبكة المعلومات الجامعية

بسم الله الرحمن الرحيم

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأفلام قد أعدت دون أية تغيرات

يجب أن

تحفظ هذه الأفلام بعيدا عن الغبار

في درجة حرارة من ١٥-٢٥ مئوية ورطوبة نسبية من ٢٠-٤٠%

To be Kept away from Dust in Dry Cool place of 15-25- c and relative humidity 20-40%

بعض الوثائـــــــق الاصليـــــة تالفـــة

بالرسالة صفحات لم ترد بالاصل

THE EFFECT OF AGE ON PERIPHERAL NERVE REGENERATION AFTER PERIPHERAL NERVE CRUSH IN ALBINO RATS

THESIS

SUBMITTED FOR PARTIAL FULFILMENT OF M.SC. DEGREE IN BASIC MEDICAL SCIENCE (Anatomy)

Presented By

Girgis saad Kamel

(MB.BCH.)

Faculty Of Medicine – Minia University

Supervised By

Prof. Dr. Mohamed Ahmed Desouky

Prof. And Head Of anatomy Department- Faculty Of Medicine- Minia University

Prof. Dr. Mohamed Moustafa

Prof. of Anatomy and Vice Dean of Student Affair - Faculty Of Medicine- Minia University

Assit. Prof. Nabil Abd Elkader Hassan

Assistant Prof. Of Anatomy- Faculty Of Medicine- Minia University

Minia University-Faculty of Medicine

2005

ACKNOWLEDGEMENT

First of all thanks to **God**, the most grateful and merciful whose guidance help and grace was instrumental in making this work a reality.

I would like to express my deepest thanks and gratitude to **Prof. Mohamed Ahmed Desouky**, professor and head of Anatomy department Minia University, who gave me much of his effort and close supervision throughout the work. His patients and continuous guidance

I am internally grateful to **Prof. Mohamed Moustafa Ahmed** Professor of Anatomy and vice dean of student affair, Faculty Of Medicine- Minia University from whom I received faithful supervision, sincere direction and continuous guidance throughout this work.

Also I would thank **Dr Nabil Abdel-Kader**, assistant professor of anatomy Minia faculty of medicine who has learned me the preparatory techniques of my research and has helped me revision of these thesis

I extend my thanks to all members of Anatomy department for their help and cooperation.

Introduction

Introduction

The nerve fiber is the functional component of the peripheral nerve responsible for transmitting stimuli. The nerve fiber is composed of an axon, Schwann cell, and myelin sheath in myelinated nerve fibers **(Schwartz, 1999).**

When peripheral nerves are subjected to a crush injury, axons and their myelin sheaths degenerate distally in the presence of macrophages, a process called **Wallerian degeneration**. Proximal to the crush, axons begin regeneration, cross the injury zone and associate with columns of Schwann cells in the distal stump. These Schwann cells ensheath bundles of regenerating axons and then develop a one to one relationship with those destined to become myelinated. New myelin sheaths appear and become thicker and longer as axonal regeneration progress **(Kaoru et al., 1992).**

Axotomy of peripheral nerve fibers triggers a variety of responses in the neuronal perikarya and in the axons proximal to the site of injury, with secondary effect on myelination. In the perikarya a sequence of changes occurs, collectively referred to as central chromatolysis or axon. These include peripheral migration of the nuclei and dispersion of the ribosomes associated with the rough endoplasmic reticulum of Nissl bodies. The chromatolytic reaction varies with the age of the animal, proximity of the lesion to the cell body and neuronal type. **(Andres, 1961; Watson, 1968; Liberman, 1971; Price and Porter, 1972; Torvik, 1976).**

The process of nerve injury and regeneration involves many interactions between cellular elements and between these and the extra cellular matrix. Immediately after axotomy, the proximal and distal nerve stump retract, axoplasm leaks out and damaged membranes collapse.

Macrophages are recruited to the site of the lesion during the first week post injury **(Perry et al., 1987)**, contributing to lysis and phagocytosis of myelin and subsequent Schwann cell proliferation **(Beuche and Friede, 1984)**. Both Schwann cells and macrophages secrete mitogens and growth factors, which play a role in regeneration and remyelination **(DeVaries, 1993; Reynolds and Woolf, 1993)**.

In the distal stump, Wallerian degeneration takes place during the first few days post injury. The axons degenerate, their myelin sheathes degrades and the degradation products together with macrophage secretion stimulate the Schwann cells within the distal stump to proliferate within their basal lamina tubes **(Salzer and Bunge, 1980; Salzer et al., 1980 and De Varies, 1993)**, forming the band of Bungner **(Bunge, 1980)**. This proliferation continues for approximately 2 weeks, with the Schwann cells forming a conduit that guides the regenerating axons to their targets **(Son and Thompson, 1995)**.

Schwann cells are vital for the process of axonal regeneration **(Hall, 1986 and 1997)**, and one of their roles is as a source of neurotrophic factors **(Heumann et al., 1987; Acheson et al., 1991; Sendtner et al., 1992)**. These diffuse from the distal stump across the injury area to exert a trophic effect on the axons regenerating from proximal stump that

stimulate a second phase of Schwann cells proliferation **(Reynolds and Woolf, 1993)**.

However, if axonal regeneration is delayed Schwann cells decrease progressively in number and become less responsive to axonal regeneration **(Li et al., 1997; Terenghi et al., 1998)**.

In the proximal stump, the axon degenerate retrogradely as far as to the first node of Ranvier, creating a small area of wallerian degeneration. Within a few hours, the injured axons give rise to several neuronal sprouts **(Wong and Mattox, 1991)**, whose number in excess of the number of axons originally in nerve fascicles. Some of these sprouts will die back through axonal pruning because of insufficient survival signal from the target organ, most probably in the form of growth factors **(Brushart, 1993)**.

The growth cone responds to contact guidance and actively searches for suitable matrix and environment to support axonal growth **(Bixby et al., 1988; Rutishauser, 1993)**. Schwann cells are the most effective substrate to produce direct regeneration **(Bixby et al., 1988)**.

It is well known that the degree of functional recovery after wallerian degeneration of damaged peripheral nerve fibers depends upon whether the connective tissue sheaths (endoneurium and/or perineurim) have been disrupted at time of the injury **(Sunderland, 1978)**. Where the endoneurial sheaths are not damaged called second-degree nerve injury **(Sunderland, 1951)**.

It is generally agreed that the recovery is nearly perfect because the regrowing nerve fibers are constrained to run along inside the old basal lamina sheaths which make up the inner layer of endoneurium and are thus led automatically back to the appropriate place **(Thomas, 1974)**.

Most studies of age-related changes during nerve regeneration concern responses of neurons, their axons and their endings.

In older animals subjected to axotomy, axonal sprouting is reduced and the chromatolytic response of neurons is altered **(Moyer et al., 1960; Pestronk et al., 1980; Vaughan, 1990)**.

Slower axonal transport is associated with less rapid elongation of axons **(Black and Lasek 1979; Pestronk et al., 1980; Alberghina et al., 1983; Mcmartin, 1983)**. There are also changes in distribution of axonal microtubules and filaments **(Vaughan, 1992)** and the reinnervation of endings **(Hopkins et al., 1986; Jacob and Robbins, 1990)**.

Aim of the work

Aim of the work

The peripheral nervous system as well as the central nervous system is subjected to many age dependent disorders. Functional deficits may be the consequence of structural and biochemical changes that result in slowly progressive loss of neurons and nerve fibers. This loss is not compensated because of the decreased regenerative and reinnervating capabilities of nerve fibers in aged subjects. Previous reviews have offered different opinions on the influence of age on peripheral nerve regeneration **(Verdu` and Navarro, 1995; Kerezoudi and Thomas, 1999).**

Clinical reviews have suggested that functional recovery from nerve injury occurs faster and more efficiently in children than in adults **(Tajima and Imai, 1989; Glickman and Mackinon, 1990; Barrios and Paplos, 1991; Burton et al., 1994).** However, experimental studies have demonstrated greater nerve cell death after nerve injury in newly born rats than mature rats. So the purpose of this study is to review the effect of age on peripheral nerve regeneration after sciatic nerve crushing.

Review of literature