EFFECT OF EXOGENOUS MELATONIN ADMINISTRATION ON TRANSIENT GLOBAL CEREBRAL ISCHEMIA AND ADULT NEUROGENESIS

Dr. Moyosore Salihu Ajao

A thesis submitted to the Faculty of Science, University of the Witwatersrand, Johannesburg, in fulfilment of the requirements for the degree of Doctor of Philosophy.

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Declaration

I, SALIHU MOYOSORE AJAO, declare that this thesis is my own, unaided work. It is being submitted for the Degree of Doctor of Philosophy in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination in any University.

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(Signature of candidate)

……day of …….....20.....

Dedication

This thesis is dedicated to my Late Mother **ASMAWU ASINMI AJOKE AJAO** whose death stimulated me into working on this topic and to all victims of stroke.

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Abstract

This study investigated the effect of exogenous melatonin administration on transient global cerebral ischemia and adult neurogenesis in adult male Sprague-Dawley rats. It also determined serum melatonin concentrations in all the experimental groups and established any effect of melatonin on estimated total granule cell numbers. Adult male Sprague-Dawley rats were divided into eight groups with each group consisting of 6 rats (n = 6). Post-induction time durations of 72 hours and 7 days was used. Single dose of 5 mg/kg exogenous melatonin was administered at each phases of 30 minutes before and after a 10 minutes transient bilateral occlusion of the common carotid arteries in the different groups, followed by reperfusion. Rats were anesthetized with 20 mg/kg of ketamine and 2.5 mls of blood was collected via cardiac puncture for estimation of serum melatonin concentration using commercially prepared radioimmunoassay ELISA kit. Free floating brain sections cut at 50 μm were immunostained for Ki-67, marker for proliferating cells. The total granule cell number in the dentate gyrus was estimated using the optical fractionator method on plastic embedded brain sections. Mean melatonin concentration (pg/mol) was 268.54 ± 28.73 (72 hours) and 277.83 ± 28.73 (7 days) compared to the sham control; 266.94 ± 37.6 and non surgical 262.96 ± 23.85 respectively. Differences in the concentration were not statistically significant ($P<0.05$). Histological finding indicated neuropil disruption with potentiation of restoration as the post ischemia days progressed in the melatonin administered groups. The estimated total granule cell number in the dentate gyrus of the hippocampus was not affected by exogenous melatonin administration. However, there was potentiation in proliferations of the

neurogenic niche in the dentate gyrus of the hippocampus demonstrating a very strong indications that melatonin enhanced the generations of proliferating cells in adult male Sprague-Dawley rats.