

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

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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.

.....

(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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## Table of Content

Title page	i
Declaration	ii
Dedication	iii
Acknowledgements	iv
Table of content	vii
List of Figures	xii
List of Tables	xv
Abstract	xvi
<b>Chapter One</b>	
1.0: General Introduction and Literature Review	1
1.1 Introduction	1
1.2 Epidemiology of stroke	3
1.2.1 Types of stroke	4
1.2.2 Pathophysiology of ischemia/Reperfusion injury	5
1.3 Current Advances in Neuronal Repair	8
1.4 Predisposing/ aetiological factors to ischemic stroke	11
1.5 Melatonin	12

1.6 Neuroprotective Role of Melatonin in ischemia	13
1.7 Adult Neurogenesis: Mechanisms and Potential Role in Stroke	17
1.8 Main objective of the study	21
1.8. 1 Specific Objectives	21
1.9 Rationale for the study	21
1.10: Limitations of the study	22
<b>Chapter Two</b>	
2.0 Materials and Methodology	23
2.1 Pilot study to create an ischemic model	23
2.2 Experimental animals use in second study	24
2.3 Pre and Post Melatonin administration	26
2.4 Surgical preparations and procedure	26
2.5 Collection of blood samples	28
2.6 Perfusion fixation and removal of the brains	29
2.7 Assay of melatonin concentration in the serum	29
2.8 Sectioning	30
2.9 Haematoxylin and Eosin staining	31
2.10 Ki-67 Immunohistochemistry	31



2.11 Plastic Embedding technique	32
2.12 Giemsa staining	34
2.13 Light microscopy analysis	35
2.14 Total Ki-67 positive cell count	35
2.15 Total pyknotic cell count	35
2.16 Total granule cell count	36
2.17 Statistical analysis	36
<b>Chapter Three</b>	
3.0 Results	38
3.1 Pilot study Result	38
3.2 General Observations after surgery	45
3.3 Histology findings in the brains	45
3.4 Immunohistochemical staining of Ki-67	55
3.5 Quantitative Results	60
3.6 Total proliferating cell Number	60
3.7 Identification of pyknotic cells	67
3.8 Total pyknotic cell Number	70
3.9 Total granule cell Number	74

3.10 Relationship between proliferating cells and pyknotic cells numbers	79
3.11 Ratio of proliferating per pyknotic cells number in the dentate gyrus	85
3.12 Regression of coefficient of pyknotic and proliferating cell number	87
3. 13 Estimated melatonin concentration	89
3.14 Correlation between melatonin concentration and total proliferating cell number	95
3.15 Correlation between melatonin concentration and estimated total granule cell number	98
3.16 Correlation between melatonin concentration and pyknotic cell number	101
<b>Chapter Four</b>	
4.0 Discussion	104
4.1 Creating the ischemia animal model in Sprague-Dawley rats	104
4.2 Dosage and estimation of melatonin concentration	109
4.3 The role of melatonin in ischemia	110
4.4 The role of melatonin in adult neurogenesis	113
<b>Chapter Five</b>	
5.0 Conclusion	120
5.1 Further study	122
Conferences attended and Paper presented	123

Communications and publications	124
<b>References</b>	<b>125</b>

## List of figures

3.1.1 Photomicrographs of the cerebral cortex of pilot study	40
3.1.2 Photomicrographs of the dentate gyrus of pilot study	42
3.1.3 Photomicrographs of the cerebellum of pilot study	44
3. 3. 1 Photomicrographs of the dentate gyrus with ischemia	48
3. 3. 2 Photomicrographs of the dentate gyrus with restoration	50
3. 3. 3 Photomicrographs of the cerebral cortex with ischemia	52
3. 4. 4 Photomicrographs of the cerebral cortex with treatment	54
3. 4. 1 Photomicrographs of Ki-67 cells in pre-ischemic melatonin	57
3. 4. 2 Photomicrographs of Ki-67 cells in post-ischemic melatonin	59
3. 6. 1 Comparison of total proliferating cell number (pre-melatonin)	62
3.6.2 Comparison of total proliferating cell number (post-melatonin)	63
3. 6. 3 Cell proliferation and pyknotic cell in pre-melatonin (72 hours)	65
3.6.4 Cell proliferation and pyknotic cell in pre-melatonin (7 days)	66
3. 7. 1 Giemsa staining of pyknotic cells	69
3.8. 1 Graph of pyknotic cells number in pre-ischemic melatonin	71
3.8.2 Graph of pyknotic cells number in post-ischemic melatonin	73
3. 9. 1 Estimated mean total granule cell number (Pre-ischemic)	77

3. 9. 2 Estimated mean total granule cell number (Post-ischemic)	78
3. 10.1 Correlation of total pyknotic cell number and total proliferating cell number in 72 hours pre-ischemic melatonin group	80
3.10.2 Correlation of total pyknotic cell number and total proliferating cell number in 7 days pre-ischemic melatonin group	81
3.10.3 Correlation of total pyknotic cell number and total proliferating cell number in 72 hours post-ischemic melatonin group	83
3.10.4 Correlation of total pyknotic cell number and total proliferating cell number in 7 days post-ischemic melatonin group	84
3. 11.1 Graph of ratio of proliferation per pyknotic cell number	86
3. 12.1 Scattered diagram showing the regression line	88
3.13.1 Graph of the estimated serum melatonin concentration in pre-ischemic melatonin group	91
3.13.2 Graph of the estimated serum melatonin concentration in post-ischemic melatonin group	94
3.14.1 Correlation of melatonin concentration and total proliferating cell number after 72 hours post ischemia	96
3.14.2 Correlation of melatonin concentration and total proliferating cell number after 7 days hours post ischemia	97

3.15.1 Correlation of melatonin concentration and estimated total granule cell number after 72 hours post ischemia	99
3.15.2 Correlation of melatonin concentration and estimated total granule cell number after 7 days post ischemia	100
3.16.1 Correlation of melatonin concentration and total pyknotic cell number after 72 hours post ischemia	102
3.16.1 Correlation of melatonin concentration and total pyknotic cell number after 7 days post ischemia	103

## **List of tables**

2.2. 1 Animal groups with experimental description of the procedure	25
3. 6. 1 Mean total proliferating and pyknotic cells count	61
3. 9. 1 Stereological parameter of optical fractionators	75
3. 9. 2 Mean estimated total granule cell counts	76
3. 13. 1 Estimated melatonin concentration in 72 hours group	90
3. 13. 2 Estimated melatonin concentration in 7 days group	93

## 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  $\mu\text{m}$  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  $268.54 \pm 28.73$  (72 hours) and  $277.83 \pm 28.73$  (7 days) compared to the sham control;  $266.94 \pm 37.6$  and non surgical  $262.96 \pm 23.85$  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.