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

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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.

September, 2011
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.
Acknowledgements

I am sincerely grateful to Almighty Allah (SWT) for His infinite mercies upon me and for giving me the strength and wisdom required for the completion of this project. I will always be faithful to you. My sincere thanks to Professor Amadi Ogonda Ihunwo and Professor Paul R. Manger for their belief in me and accepting to provide the necessary supervision and guidance required in the course of this work. Your kind but firm and useful criticisms in every role are highly appreciated. You have indeed touched me and I have grown. I acknowledge with special thanks; Mrs H Ali and Mrs S Rogers of School of Anatomical Sciences, WITS for all the assistance I received during my laboratory procedures. I am very grateful to Professor Hans-Peter Lipp, Dr Imgard Amrien and Dr Lutz Slomianka of Institute of Anatomy, University of Zurich, Switzerland for all your assistance and support with my stereological analysis while I was there. I appreciate the effort of Dr Virginia Mesekancite for her guidance in every immunohistochemical techniques.

My sincere gratitude goes to my immediate family: Adenike, Olawunmi, Kareemah, Ridwan, Aminat, Zainab and Badru Bamidele for their patience, prayers and continuous support throughout the period of my study. To my father; Alhaji Badru Ajao, my elder brother; Babatunde Yusuf Ajape and my younger brother and sister; Sulyman Ajao and Mrs Khadijat Sulyman for their constant support and encouragement in all my academic pursuit. I appreciate the love, prayers and support of: Mufutau Bolaji Ayoku, Waheed Shola Yusuf, Dr Saka Abdulkareem, Dr Abubakar Kasum, Dr Rasaq Atata, Alhaji Hamsat
Balogun, Alhaji Munir Ibrahim, Dr Taofiq Ige, Rev Segun Egunjobi and his wife, Dr (Mrs) Uchenna B Amadi-Ihunwo, Alhaji Saka Issau (SAN), Chief and Chief (Mrs) M. B. Abolarinwa, Olamide Sulyman, Rashidat Olaitan and Dr Ayokunle Olawepo. You have all left your feet in the sand of time in my entire life.

To all my friends: Dr Ajape Wahab, Dr Rabiu Jimoh, Dr Luqman Olayaki, Dr Idowu Abioye, Ahmed Jamiu, Dr Kamaldeen Baba, Hajji Wasiu Azeez, Tajudeen Lawal, Dr Ekpo Okobi, Sikiru Jimoh, Dr Rosie Mcneil, Prof Rasaq Akande, Dr Toyin Yakubu, Saliu Saad, Mr and Mrs Omiwole, Aliu Lanre, and the entire Muslim Jamaa of South Africa for their supports, prayers and encouragement during the period of the course.

My appreciations also go to my colleagues and friends in the Department of Anatomy, Faculty of Basic Medical Sciences, College of Health Sciences, University of Ilorin and the administration of University of Ilorin for granting the opportunity that enable me to undertake the course.

Three organization also deserve my appreciation: The International Society for Neurochemistry (ISN) for providing travel grant in 2009 with subsistence allowance from the Switzerland – South Africa Joint Research Project (SSAJRP) held by Prof. A. O Ihunwo, which contributed to my research stay in Zurich, Switzerland; the International Brain Research Organization (IBRO) which travel grants in 2008 enable me to attend an international conference in Cuba and the University of the Witwatersrand, Johannesburg, South Africa for their various grants and awards that contributed towards my subsistence in
South Africa. SSAJRP for funding to SONA conference in Egypt December, 2009.

Finally, I am grateful to the entire staff of the Central Animal Service (CAS) for their assistance during the surgical procedure and the excellent ways at which they looked after the animals post operatively. I appreciate the entire staff of School of Anatomical Sciences, Faculty of Health Sciences, University of the Witwatersrand for their cooperation, tolerance and understanding during my stay.
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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.