EFFECTS OF *TRYPANOSOMA BRUCEI BRUCEI* INFECTION ON THE HISTOLOGY AND FUNCTIONING OF THE HYPOTHALAMO-THALAMUS-PINEAL GLAND AXIS IN MALE ALBINO RATS (*Rattus novergicus)*

BY

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DECLARATION

Declaration by the Candidate

This thesis is my original work and has not been presented for a degree in any other University. No part of this thesis may be reproduced without the prior written permission of the author and/or University of Eldoret.

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DEDICATION

This thesis is dedicated to my late father Maina Kahwaga and mother Jane Muthoni. The latter saw me begin my doctorate degree but did not live long enough to see its completion. May the Almighty God rest their souls in eternal peace.

To my dear wife Grace Nyawira, and sons Kevin Maina, Keith Kiune, and Geoffrey Kahwaga, for their endless love, prayers and encouragement.

ABSTRACT

Trypanosomosis is a major health problem threatening the lives of over 60 million people in 37 countries in sub-Saharan Africa. It is caused by *Trypanosoma* parasites which are transmitted through a bite of an infected tsetse fly of the genus *Glossina*. The disease is characterized by sleep/wake disturbances, and disruptions in other circadian rhythm activities like body temperature and hormone secretion. Since histopathological studies on brain regions involved in the control of circadian rhythms are scanty, this study investigated the effects of *T.b. brucei* infection on the hypothalamic suprachiasmatic and paraventricular nuclei, thalamic lateral geniculate nucleus, anterior pituitary and pineal glands in albino rats. It also investigated the effects of *T.b. brucei* infection on plasma concentration of melatonin and adrenocorticotropic hormone (ACTH). Twelve control and twelve experimental male albino rats, aged 3-3½ months, were used in this study. Body weight and temperature of each rat was measured four days in a week. The experimental rats were injected intraperitoneally with 0.2ml of infected blood containing 1 x 10^4 live *T.b. brucei* parasites. Once a week, 1ml of blood was obtained from the tail of each rat and the concentration of melatonin and ACTH in the plasma determined using an automated immunoanalyzer. The infected animals were allowed to go through the full course of infection, without treatment, and sacrificed when they were *in extremis*. For every experimental rat sacrificed, a control rat was sacrificed. Each rat was anaesthetized, decapitated, and the brain immediately extracted from the skull. The brain was fixed in neutral buffered formalin for at least 48 hours. The anterior pituitary and pineal glands were later extracted from the brain and a coronal section of the brain made. These tissues were processed histologically and stained using the haematoxylin and eosin method. The stained slides were examined under a microscope and photomicrographs taken. Parasites were detected in the blood of experimental rats 5-8 days post-infection. Significant differences in body weight ($p = 0.0114$), temperature ($p = 0.0113$), and plasma concentration of melatonin ($p = 0.0382$) and ACTH ($p = 0.0190$), were recorded between the control and experimental rats. Histopathological changes, including tissue degeneration and infiltration and proliferation of glial cells, were observed in the suprachiasmatic nucleus, paraventricular nucleus, lateral geniculate nucleus, anterior pituitary gland, and pineal gland of infected rats. These findings provide a basis for understanding the physiological and behavioural changes that characterize trypanosomosis.

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LIST OF ABBREVIATIONS, ACRONYMS AND SYMBOLS

ACTH	adrenocorticotropic hormone
BBB	blood-brain barrier
b/v	blood vessel
CC	corpus callosum
CDC	Centres for Disease Control and Prevention
CG	ciliary ganglion
CLIP	corticotropin-like intermediate peptide
CNS	central nervous system
CRH	corticotropin-releasing hormone
CSF	cerebrospinal fluid
DNA	deoxyribonucleic acid
EDTA	ethylene diamine tetra acetate
EEG	electroencephalograph
EW	Edinger-Westphal
FAO	Food and Agriculture Organization
GHT	geniculohypothalamic tract
Hc	hippocampus
HPA	Hypothalamic-pituitary-adrenal
IFN	interferon
IGL	intergeniculate leaflet
IL	interleukine
ILRAD	International Laboratory for Research on Animal Diseases
ILRI	International Livestock Research Institute
IML	intermediolateral

ipRGCs	intrinsically photosensitive retinal ganglion cells
LGN	lateral geniculate nucleus
LV	lateral ventricle
Mg	magnification
MHC	major histocompatibility complex
micro-CATT	micro-card agglutination test for trypanosomosis
ml	milliliter
mm	millimeter
MSH	melanocyte stimulating hormone
NK	natural killer
NO	nitric oxide
NPY	neuropeptide Y
NRC	National Research Council
OC	optic chiasma
OIE	Office International des Epizooties
OPN	olivary pretectal nucleus
PATTEC	Pan African Tsetse and Trypanosomosis Eradication Campaign
p.i.	post-infection
PBS	phosphate buffered saline
POMC	pro-opiomelanocortin
PTRE	post-treatment reactive encephalopathy
PVN	paraventricular nucleus
QBC	quantitative buffy coat
REM	rapid eye movement
RHT	retinohypothalamic tract

RNA	ribonucleic acid
SCG	superior cervical ganglion
SCN	suprachiasmatic nucleus
SO	supraoptic nucleus
STDM	standard trypanosome detection methods
SWS	slow wave sleep
T.b.	*Trypanosoma brucei*
Tltf	trypanosome-derived lymphocyte triggering factor
TNF	tumor necrosis factor
US/USA	United States of America
VATs	variant antigenic types
VIP	vasoactive intestinal polypeptide
VSG	variable surface glycoprotein
wb-CATT	whole blood- card agglutination test for trypanosomosis
wb-LATEX	whole blood latex agglutination test
WHO	World Health Organization
ZT	*zeitgeber*
α	alpha
β	beta
γ	gamma
£	dollar

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