

Postnatal Development of the Hippocampus in Male Albino Rats: A Histomorphometric Study

Thesis

Submitted for partial fulfillment of Master's Degree in
Anatomy

Presented by

Aya Abdrabo Ali Baraka

M.B.B.Ch. Faculty of Medicine – Ain shams University

Supervised by

Prof. Dr. Kawther Ahmed Hafez

Professor of Anatomy and Embryology
Faculty of Medicine –Ain shams University
Department: Anatomy and Embryology

Dr. Asmaa Ibrahim Ahmed Othman

Assistant professor of Anatomy and Embryology
Faculty of Medicine –Ain shams University
Department: Anatomy and Embryology

Dr. Ashraf Mohammed Mostafa Sadek

Lecturer of Anatomy and Embryology
Faculty of Medicine –Ain shams University
Department: Anatomy and Embryology

**Faculty of Medicine
Ain shams University**

-2019-



Acknowledgement

First of all, all gratitude is due to Allah almighty for granting me the strength and the faith and blessing this work, until it has reached its end, as a part of his generous help

*Really I can hardly find the words to express my gratitude to **Prof. Dr. Kawther Ahmed Hafez**, Professor of Anatomy and Embryology Department, Faculty of Medicine –Ain shams University for her supervision, continuous help, encouragement throughout this work and tremendous effort she has done in the meticulous revision of the whole work. It is a great honor to work under her guidance and supervision.*

*I would like also to express my sincere appreciation and gratitude to **Dr. Asmaa Ibrahim Ahmed Othman**, Assistant professor of Anatomy and Embryology Department, Faculty of Medicine –Ain shams University for her invaluable efforts, tireless guidance and for her patience and support to get this work into light.*

*I cannot forget the great help of **Dr. Ashraf Mohammed Mostafa Sadek**, Lecturer of Anatomy and Embryology Department, Faculty of Medicine –Ain shams University for his continuous directions and support throughout the whole work,*

Also, I would like to extend my thanks to **Prof. Dr. Shahira Youssef Mikhail** Head of Anatomy and Embryology Department, Faculty of Medicine, Ain Shams University, for her continuous care, support and encouragement to me and my colleagues to do researches using new research tools.

Special thanks to **Dr. Ahmed Farid**, Lecturer of Anatomy and Embryology Department, Faculty of Medicine –Ain shams University for his efforts and great contribution throughout the work.

Lastly and not least, I would like to send my deepest love and gratitude to **my family , friends and my colleagues** for their love and support. I appreciate all those who have supported me to bear the hardships I have endured and to overcome difficulties and make me stronger than I was.

I dedicate this work to **my parents and my little angel “my son Moaz”** whom without their sincere emotional support, pushing me forward this work would not have ever been completed.



Aya Abdrabo Ali Baraka

List of Contents

	Page
Acknowledgment	--
List of Abbreviations	i
List of Tables	ii
List of charts	v
Introduction	1
Aim of the Work	3
Review of Literature	4
• Functional anatomy of the hippocampus.....	4
• Anatomical divisions of the human hippocampus.....	6
• Anatomy of the rat hippocampus.....	7
• Histology of the rat hippocampus.....	9
• Neurogenesis of the hippocampus.....	13
• The trilaminar structure of the DG.....	16
• Synaptogenesis of the hippocampus	21
• Development of the hippocampus	23
• Development of the central nervous:.....	23
• Development of human hippocampus	25
• Development of rat hippocampus.....	27
• Correlation between weaning and maternal separation and the postnatal hippocampal development.....	31
Materials and Methods	34
Results	40
Histological results.....	40
Statistical Results	91
Discussion	101
Summary and Conclusion	117
Appendix	123
References	128
Arabic Summary	--

List of Abbreviations

1ry	: Primary
2ry	: Secondary
3ry	: Tertiary
A	: Alveus
ABR	: Avidin Biotin Reagent
ADHD	: Attention Deficit Hyperactivity Disorder
BDNF	: Brain-Derived Neurotrophic Factor
CA	: Cornu Ammonis
CARE	: Committee of Animal Research Ethics
CH	: Cortical Hem
CNS	: Central Nervous System
D	: Dorsal
DAB	: Di AminoBenzidine
DG	: Dentate Gyrus
DNE	: Dentate NeuroEpithelium
EC	: Entorhinal Cortex
ERK	: Extracellular signal-Regulated Kinase
F	: Fimbria
GABA	: Gamma-AminoButyric Acid
GD	: Gestational Day
GFAP	: Glial Fibrillary Acid Protein

GL	: Granule cell Layer
H	: Hilus
HNE	: Hippocampal NeuroEpithelium
HPF	: High Power Field
HP	: Hippocampus Proper
HPA	: Hypothalamic Pituitary adrenal Axis
Hx &E	: Hematoxylin and Eosin
IGF-1	: Insulin-like Growth Factor-1

List of Abbreviations (Cont.)

L	: Lateral
LL	: Lower Limb
LV	: Lateral ventricle
M	: Medial
mGluR5	: Metabotropic Glutamate Receptor
ML	: Molecular Layer
MRC	: Medical Research Center
MRI	: Magnetic Resonance Imaging
NADPH	: Nicotinamide Adenine Dinucleotide Phosphate
NGS	: Normal Goat Serum
NPCs	: NeuroProgenitor Cells
OL	: Polymorphic Layer
PBS	: Phosphate Buffered Saline
PL	: Pyramidal Layer

PND	: Post Natal Day
PTSD	: Post-Traumatic Stress Disorder
RES	: Reticulo Endothelial System
ROS	: Reactive Oxygen Species
S	: Subiculum
SD	: Standard Deviation
SGZ	: Sub Granular Zone
SHRP	: Stress Hypo Responsive Period
SLS	: Sever Life Stress
SPSS	: Statistical Package for the Social Sciences
SVZ	: Sub Ventricular Zone
TLE	: Temporal Lobe Epilepsy
UL	: Upper Limb
V	: Ventral
VEGF	: Vascular Endothelial Growth Factor
VZ	: Ventricular Zone

List of Tables

Table	Title	Page
1	Means \pm SD of the thickness of the polymorphic layer of the CA in um/ HPF in the groups.	91
2	Means \pm SD of the thickness of the pyramidal layer of the CA in um/ HPF in all groups.	92
3	Means \pm SD of the thickness of the molecular layer of the CA in um/ HPF in all groups.	93
4	Means \pm SD of the thickness of the molecular layer of the dentate gyrus in um/ HPF in all groups.	94
5	Means \pm SD of the thickness of the granule cell layer of the dentate gyrus in um/ HPF in all groups.	95
6	Means \pm SD of the thickness of the polymorphic layer of the dentate gyrus in um/ HPF in all groups.	96
7	Means \pm SD of the number of pyramidal cells in CA1/HPF in all groups.	97
8	Means \pm SD of the pyramidal cell count in CA3/HPF in all groups	98

Table	Title	Page
9	Means \pm SD of the granule cell count of the dentate gyrus (DG) /HPF in all groups.	99
10	Means \pm SD of the astrocytes count (GFAP technique) /HPF in all groups.	100

List of Charts

Charts	Title	Page
1	Means of the thickness of the polymorphic layer of the CA in um/ HPF in all groups.	91
2	Means of the thickness of the pyramidal layer of the CA in um/ HPF in all groups.	92
3	Means of the thickness of the molecular layer of the CA in um/ HPF in all groups.	93
4	Means of the thickness of the molecular layer of the dentate gyrus in um/ HPF in all groups.	94
5	Means of the thickness of the granule cell layer of the dentate gyrus in um/ HPF in all groups.	95
6	Means of the thickness of the polymorphic layer of the dentate gyrus in um/ HPF in all groups.	96
7	Means of the number of pyramidal cells in CA1/HPF in all groups.	97
8	Means of the number of pyramidal cells in cornu amnion3 (CA3)/HPF in all groups.	98
9	Means of the number of granule cells of the	99

Charts	Title	Page
	dentate gyrus (DG) /HPF in all groups.	
10	Means of the number of astrocytes (GFAP technique) /HPF in all groups.	100

Introduction

The hippocampus has an important role in the process of learning and memory. It also functions as a part of the limbic system in the regulation of sexual and emotional behaviors. Damage to hippocampus leads to memory loss. So, it is difficult to imagine life without intimate memories with family and close friends (**Moser et al., 2014**).

The hippocampus is generally assumed to play a key role in the consolidation of memory i.e., the integration of relevant new information and its transfer from short-term to long-term memory especially spatial memory and learning (**Markovitch, 2000**).

Many diseases of the central nervous system accompanied by neuron damage of the hippocampus. Neurodegenerative diseases such as Alzheimer's disease, Schizophrenia and Parkinson's disease are examples of neuronal damage in the hippocampus (**Lee et al., 2013**).

The hippocampus is a curved elevation of grey matter that extends throughout the entire length of the floor of the inferior horn of the lateral ventricle. Its anterior end is expanded to form the pes hippocampus. It is named hippocampus because it resembles a sea horse in coronal section (**Snell, 2010**).

The hippocampal formation is composed of the hippocampus proper, the dentate gyrus and the subiculum. The hippocampus proper is the largest part and is subdivided into fields designated as Cornu Ammonis (CA) or Ammon's horn from CA1 to CA4. Ammon's horn is continuous with the subiculum, which acts as the main output source of the hippocampal formation. The subiculum connects with the parahippocampal gyrus, a region of the cerebral cortex that surrounds the hippocampus. The parahippocampal gyrus is involved in memory storage and recall (**El Falougy et al., 2008**).

The hippocampus proper is a three-layered archicortex formed of; polymorphic (OL), pyramidal (PL), and molecular (ML) layers. The dentate gyrus is also a three -layered archicortex formed of; molecular (ML), granule cell (GL) and polymorphic layers (OL) (**Abdelrahim and Eltony, 2011**).

In most regions of the brain, neurons are generated at specific periods of early development, and not born in adulthood. In contrast, hippocampal neurons are generated throughout development and adult life (**Kier et al., 1997; Insausti et al., 2010**).

The hippocampal dentate gyrus was reported to be one of the few regions of the mammalian brain where neurogenesis continue to occur throughout adulthood. The neurogenesis in the dentate gyrus was thought to play an important role in hippocampus-dependent learning and memory (**Gao et al., 2007; Li et al., 2008**)