DRUGS & CHEMICALS-INDUCED DEMENTIA

THESIS

Submitted for partial fulfilment of Master Degree

in Neuropsychiatry

By

Mohamed zaki Mustafa

M. B. B. Ch.

Supervisors

Prof. Dr. Yousif Ali Abu Zeid

Professor of Neurology

Faculty of Medicine

Ain Shams University

Dr. Amira Ahmed Zaki

Assistant Professor of Neurology & Psychiatry

Faculty of Medicine

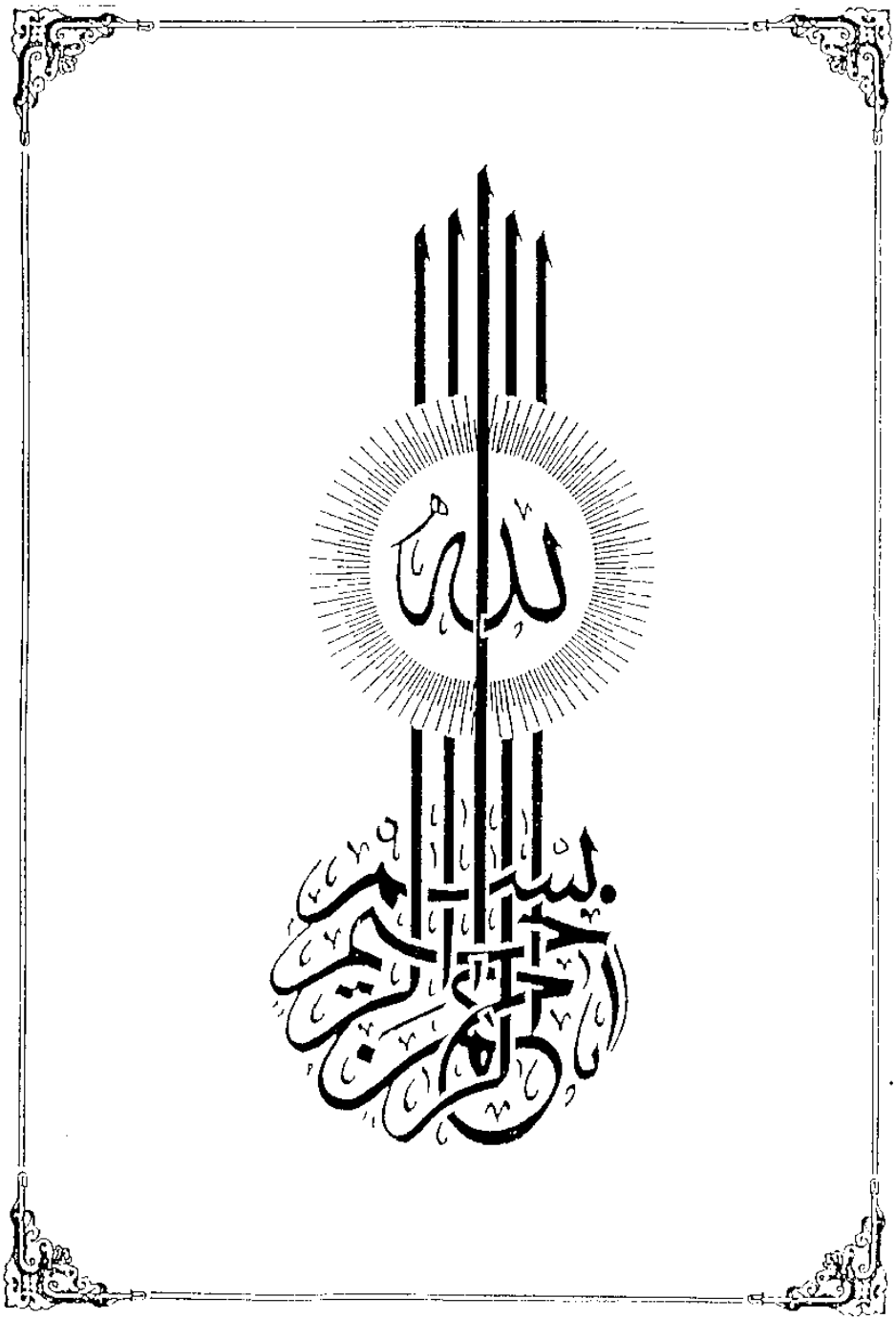
Ain Shams University

Faculty of Medicine

Ain Shams University

1989

CONTENT



Page

ACKNOWLEDGMENT

It has been my great fortune to carry out this work under the supervision of Professor Dr. YOUSIF ALI ABU ZIED, professor of Neurology, Ein Shams University, to whom I owe a debt of gratitude for his constant guidance, encouragement, and constructive suggestions without which this work would not have appeared in its present form.

I am also deeply grateful to Dr. AMIRA AHMED ZAKI, assistant professor of Neurology and Psychiatry, Ein Shams university, for her courtesy, generous supply of references, and fruitful discussions.

INTRODUCTION

AND

AIM OF THE WORK

INTRODUCTION

Untill recently it was believed in the definition of dementia that it is an irreversible deterioration of memory and intellectual abilities but now by knowing the different causes , the conclusion now becomes that dementia can be revesibale and treatable by knowing of its causes.

From the important causes of reversible dementia are drugs and chemicals.

The rapid rate of technology progression allover the world and in different fields of life, also the increase use of chemicals and its exposure in different fields of daily life and also the increase in using and taking drugs specially that which are not prescribed or even directed by doctors. These things led to increase in the rate of various type of diseases which will endanger the human health. specially his psychological and mental health. Example of these diseases are dementia together with other neuropsychiatric disorders.

AIM OF THE WORK

It seems necessary to study and review the literature concerning this subject to direct further beam of light and to give more attention about the dangerous role of chemicals and drugs in inducing dementia.

THE NERVOUS TISSUE

THE NERVOUS TISSUE

The brain consists of only a few cell types predominantly about 10^{10} neurons and glial cells, in which, moreover, each neuron may be connected by synapses to several hundred even thousand, of other neurons. **White, et al, 1978.**

At a given moment each neurones may either signal or not signal, based on integration of its inhibitory and excitatory stimuli. The primary biochemical questions are:

What is the nature of the excitatory process?

What is the mechanism of oxonal conduction?

What is the muscluar basis of the synaptic transmission?

How are all these events made possible by the chemical composition and organization of nervous tissue?

Understanding the synaps is the key to understanding brain function, for it is through neuronal interaction that the brain processes the complex inputs recieved from its enviroment.

Neural Function:

The nervous system, then, is a network of living fibers that interconnect with each other and with other cell types.

A small gap visualized by electron microscopy is always present between theses not quite connected cells.

Communication between them consists of "signaling" from one cell to the next (transmission).

If a given cell is to serve as a bridge between two nerve cells or between a nerve cell and, say, a muscle cell this signal must, travel the full length of the intervening axon.

Such signaling can be detected by electrical means. Between cells the signal is communicated by release and flow across the synapse of an organic compound, that binds to a receptor on the other side.

This binding constitutes receipt of the signal and initiates the next event. The signal must be communicated along the axon-sometimes a meter or many meters - before it can be transmitted at the next junction.

The response of the nerve cell to a few molecules of an arriving stimulatory synaptic transmitters an

initiation of process by which the nerve cell, by its own mechanism, "conducts" a signal to its other end where, again, a transmitter is released. Particularly in the central nervous system, a given nerve cell may synapse with a very large number of other nerve cells.

When one or more of the latter transmit an excitatory signal of sufficient magnitude, the recipient cell is prompted of "fire". However, other neurons that synapses with the same cell may transmit inhibitor substances across those synapses.

In no case is the mechanism of inhibition completely clear, but the decision to fire or not to fire is some how an itegeration of the sum of such events.

The nerve cell cannot deliver a weaker or partial signal.

For a given nerve cell, the size of each impulse is the same; as many as 500 impulses/s may be transmitted.

Such impulses may be conducted in medullated nerve at a speed of 100m/s, almost one-third the speed of sound in air.

Conduction of the Nervous Impulse:

Nerve axons are cyclindrical fibers cabatle when stimulated, of propagating electrical impulses along their entire length, thus making it possible to conduct signals rapidly between remote points.

This process, "conduction" reliese on the structure of the nonconducting plasma membrane about 6nm thick.

At rest there is a potential difference across the membrance of about 75 mv, inside negative. This arises primarily from the following facts:
(1) Although the membrane is rather permeable to K^+, the concentration of the latter is 20 to 50 times greater inside than outsie the axon; (2) The principal anions inside the cell, such as proteins and nucleic acids are not free to leave and cl^-, abundant outside, crosses only slowly and (3) permeability to Na^+ is only about one-twentieth that for K^+.

The potential exists because the K^+ tends to leave the cell in the direction that would equilibrate its concentration.

However, this leaves behind an excess of anions so that a negative electrical charge builds up, restraining any further tendency toward concentration quilibration.

CL^+ behaves in reciprocol fashion; it must remain out side to balance the poorly permeable Na^+ electrically but tends to move inward along its concentration gradient.

The Action Potential:

Stimuli to the nerves are phenomena that cause a local depalarization of the membrane, i.e., a decrease in the magnitude of the transmembrane potential, most frequently by entry of some Na^+.

When of a small patch of membrane is lowered to its threshold, about - 50mv, the conduction (permeability) of the membrane to Na^+ rapidly increase by as much as hundredfold; N^+ rushed across the membrane, in accord with the $[Na^+]$ gradient and attracted by the negative charge.

This usually results in an overshoot, and may go from -75 to +30 mv.

This positive charge repels further Na^+ entry; conductance to Na^+ declines, and the Na^+ pump restores the original conduction.

This set of events, complete in about 1ms, is the action potential. All the events associated with rising phase of the action potential occur spontaneously, once

initiated; metabolic energy is expended only during the decreasing phase, when ATP is employed to restore the resting distribution of ions.

Neurohumoral Transmission:

Trevor and Paul Turner, 1982. said that the effect of drugs on mood, perception and consciousness can best be understood in terms of their action on the underlying chemical mechanisms responsible for normal function of the central nervous system.

The contacts between one nerve cell and another within the central nervous system as well as in the peripheral autonomic ganglia are called "synpases"

This term was first introduced by sherrington in 1897 and is derived from the Greek Word synopsis, meaning "clasp".

It reflects the intimate nature of the contact between cells which scherrington, like others before him, recognised to be present.

The mechanism by which nerve impulses are propagated from one cell across the synapse to the other was a matter of considerable contraversy until the middle of this century. According to one school of thought, synaptic transmission could be explained solely in terms of electrical events, whereas a second shcool of thought maintained that nerve impulses were

transmitted by chemical substance released from the nerve endings. This idea was strengthened at the turn of the century by the observation that injection of extract from adrenal glands produced similar effect in experimental animals to stimulation of sympathetic nerves.

Elliott, in 1904, suggested that sympathetic nerve impulses released minute amounts of an adrenaline-like substance in close contact with the effector cells. In 1907, **Dixon** drew attention to the close similarity between the effects of the alkoloid muscarine and responses to vagal stimulation and put forward the hypothesis that such stimulation and liberated a muscarine-like substance which acted as a chemical transmitter of the impulses to the effector cell. It was not until 1921, however, that **Loewi** demonstrated that stimulation of the vagus nerve of one frog heart released a substance into the perfusion fluid which slowed the rate of a second heart when the perfusion fluid flowed through it. **Loewi and Navratil, 1921** went on to show that this substance was acetylcholine. It is now generally agreed that transmission at most, if not all synapses in the mammalian central nervous system is mediated by chemical agents.