NEUROBIOLOGY OF PANIC DISORDER

Thesis

SUBMITTED FOR PARTIAL FULFILLMENT OF
MASTER DEGREE IN NEUROPSYCHIATRY

BY

Hany Mahmoud Zaki-El-Dine
M.B.,B.CH

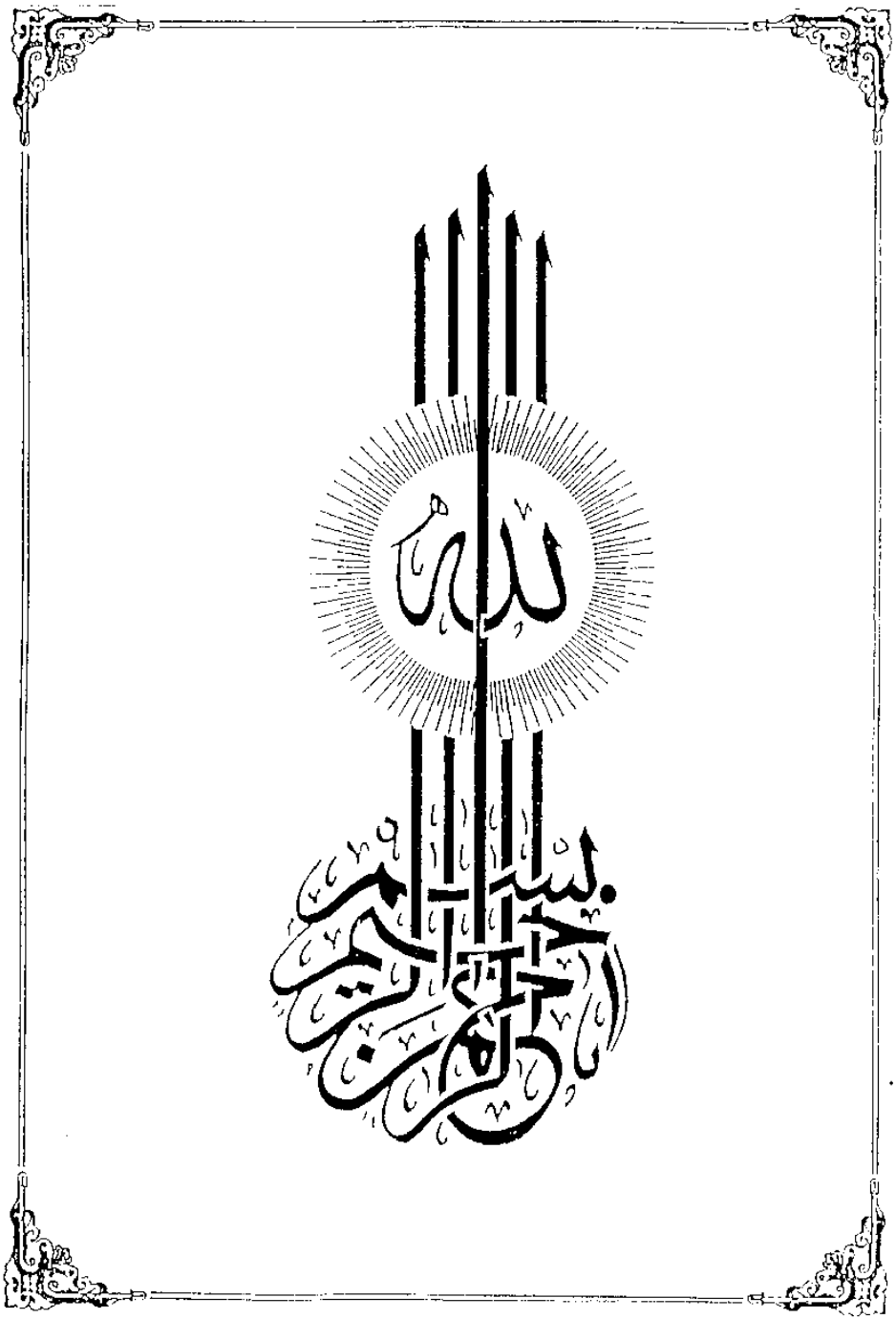
UNDER SUPERVISION OF

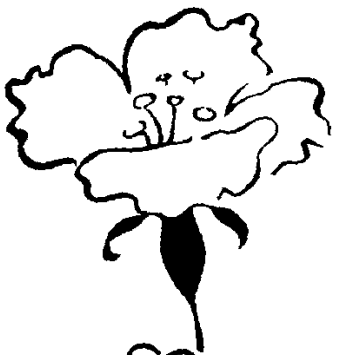
PROF.MOSTAFA KAMEL ISMAIL
Professor and Chairman Of the
Neuropsychiatry Department
Faculty of Medicine
Ain Shams University

PROF.ABD EL-MONEM MAHMOUD ASHOUR
Professor of Neuropsychiatry
Faculty of Medicine
Ain Shams University

DR.MOHAMED YASSER METWALLY
Assistant prof. of Neurology
Faculty of Medicine
Ain Shams University

1997





بسم الله الرحمن الرحيم

TO MY FAMILY

ACKNOWLEDGMENT

First, and foremost, I feel always indebted to **Allah.** The most kind and the most merciful.

Thanks to **Allah** who have lightened my path to become a humble student of a noble profession and granted me the ability to accomplish this work.

Words can never express my heartly thanks and indebtedness to **prof. Dr.Moustafa Kamel Ismail** for selecting this interesting topic and for his continuous support, advice and fatherly guidance.

I am profoundly grateful to **Prof. Dr Abd-El-Monem Mahmoud Ashour-** for his continuous support, help and critical comments without which this work would have lost much of its value.

Thanks also goes to **Dr Mohamed Yasser Metwally Lecturer of Neurology** -for his meticulous revision of the manuscript of this work, his valuable comments and brotherly attitude.

The help of **Prof. Dr Ahmed Okasha** and **Prof. Dr Anwar Etribi** and **Prof. Dr Afaf H. Khalil** whose continuous supply of recent literatures not available elsewhere,markedly enriched this work and made it more valuable.

I'am also very grateful to **prof. Dr Adel Sadek , Prof. Dr Zeinab Bishry, Prof.Dr. Farouk Lotaief, Prof.Dr. Amira Zaki**, for their continuous guidance and support.

I would like to cease this apportunity to thank all my colleagues at the neuropsychiatry department for their support, particularly **Dr. Mona I., Hanan H., Amira N and Ahmed S.**

Lastly, but not least, I would like to thank my family whose continuous encouragement, support and love made this work easier to accomplish

CONTENTS

List of Figures

INTRODUCTION

Panic disorder is a common; chronic disorder associated with considerable morbidity and social cost*(Fyer,Mannuzza and Coplan,1995).*

Its central features are recurrent unexpected panic attacks that are not associated with a specific situation or object nor are associated with marked exertion or exposure to dangerous or life threatening situation. These attacks often occur spontaneously (ie unpredictable) and are characterized by an abrupt onset of intense fear or discomfort which reaches a maximum within few minutes and lasts at least some minutes. They are associated with autonomic arousal, respiratory and abdominal symptoms. These episodes should not be due to a physical disorder nor an organic mental disorder nor other mental disorder as schizophrenia, mood disorder or somatoform disorder*(International classification of diseases; ICD -10;WHO 1990).*

Although panic symptoms have been well described for over a century only in the past decade has panic been widely recognized as a distinct psychiatric illness. Since then several epidemiological studies have been performed and have shown that the life prevalence of panic disorder range from 1.6-3.5% *(Eaton et al., 1994).*

History of Panic Disorder:

(A)Origin of the word Panic :

The word derives from the Greek word" panikon deimo", that is, fear caused by the action of the God Pan. Pan is the Greek God of flocks, hills, pastures and wild life. The phenomenon was described in relation to an army fleeting in a wild, uncoordinated panic which is very closely linked to noise and is described quite clearly before a special word for panic existed in the Israelite army under Gideon, C.1130 BC. Thus from early times, panic referred both to a group occurrence of a disoriented army, and to the state of fear induced in an individual. There are two distinctive elements of panic, first, it implies sudden onset; second, it implies a state of being; of terror or fear. It differ, however, from terror or fear by implying action *(Baker, 1989)*.

(B)The Psychiatric Origins Of Panic Disorder:

Clinical descriptions of the condition that we today consider panic disorder were frequent in the 19th century. For example, the German psychiatrist Westphal (1872) published his observations on four patients with agoraphobia that we now recognize as a description of the classic symptoms of the syndrome. At about the same time, Dr Jacob .Dacosta (1871) vividly described panic attacks on the basis of his observations of soldiers in the American civil war *(Klerman et al., 1993)*.

A turning point in the descriptive nosolgy of panic disorder came in 1894 with Freud's use of the term "anxiety neurosis" for the first time

and his proposal of the separation of anxiety neurosis from neurasthenia. Freud also provided a clinical description of two types of anxiety, that today would be labelled panic attacks and generalized anxiety Freud also noted the comorbidity of panic disorder with depression and the high degree of associated avoidance behaviour and social disability *(Klerman et al., 1993)*.

The literature on anxiety grew gradually between word wars I and II."Cardiac neuroses" and "Soldiers heart" figured prominently on world war I military psychiatry. PD has also been named irritable heart syndrome "effort syndrome". One important group of early studies was conducted by cardiologists at the Massachusetts General Hospital under the leadership of Paul Dudley white. They collected data on patients referred to them for diagnostic evaluation and identified a group of patients who did not have organic heart disease but did have a functional disorder that they diagnosed as "neurocirulatory asthenia". Also, in Great Britain, Roth (1960) described phobic depersonalization; a syndrome similar to panic disorder*(Klerman et al., 1993)*.

In the 1950s and 1960s, extensive clinical investigations were conducted on a variety of psychopharmacological treatments for panic disorder, including barbiturates, phenosthiazines, meprobamate, B-adrenergic blocking agents and several nonbarbiturate sedatives. Those treatments were almost uniformly found to be ineffective. In the 1960s, two parallel discoveries in psychopharmacology laid the groundwork for effective treatment of patients with panic disorder. (1) the demonstration of

efficacy of MAOIs for atypical depression and phobic anxiety, first described in Great Britain (Sargant and Dally, 1962) and (2)The demonstration of the efficacy of TCAs, which was first reported in the USA (Klein and Fink, 1962). Klien reversed the logic of Freud by proposing that "Panic attacks" appear spontaneously, out of the blue. It is only after a series of such extremely unpleasant experiences that the person develops "A secondary anticipatory anxiety" between panic attacks *(Baker, 1989)*.

Thus anticipatory anxiety followed, not preceded, panic attacks. Klein also proposed a much closer and clearer link than Freud had between panic attacks and phobias. Klien considered phobic avoidance to be a tertiary development. As the person anxiously anticipates further panic attacks, he or she avoids situations where the attacks are likely to occur. It is also Klein and Fink who described anxiety attacks as "panic attacks". They pointed out that the common term "anxiety" as used in anxiety attacks" and "expectant anxiety" obscures an important underlying difference; the use of the term " panic attacks" reinforce the difference *(Baker, 1989)*.

The emphasis on panic attacks was made more prominent by the work of Pitts and McClure (1967). They demonstrated that "anxiety attacks" could be generated in patients with a history of anxiety neurosis by I.V sodium lactate, further strengthening the idea of a biological substrate for panic attacks*(Baker, 1989)*.