STUDY OF SOME HORMONAL CHANGES IN MAJOR DEPRESSION

THESIS

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to

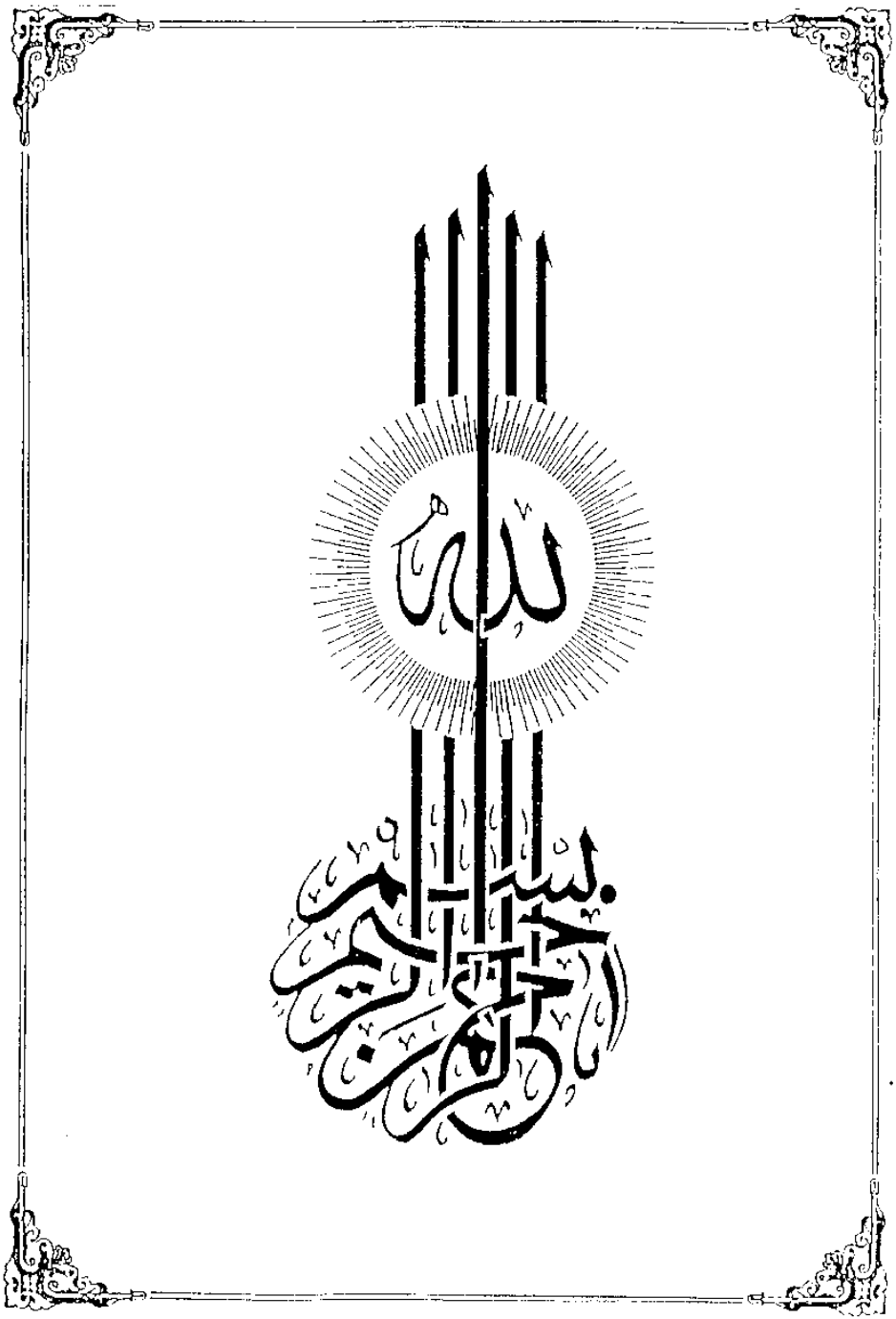
بسم الله الرحمن الرحيم

قالوا سبحانك لا علم لنا إلا ما علمتنا إنك أنت العليم الحكيم

سورة البقرة

In The Name Of ALLAH, The Beneficent The Merciful

They said "Be glorified we have no knowledge except that which you have tought us indeed you are the knower, the wise"



TO MY BELOVED PARENTS FOR
THEIR GREAT DEVOTION
SACRIFICE AND SELF-DENIAL

Karim

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Karim Yehia

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INTRODUCTION AND AIM OF THE WORK

oduction:

to Major depression is one of the most important and prevalent syndromes
ong the major affective disorders. The latter are classified into primary affective
sorders including unipolar depression (major depressive episodes only) and
ipolar disorders (manic and major depressive episodes) ***(Kaplan and Sadock, 1988)***.

The concept of endocrinological psychiatry has recently been introduced. In this respect, several studies have been done on the endocrinal and biochemical variations occurring in case of depression. Among these are the variations in thyroid hormones mainly T3, T4 and TSH. Studies on the hypothalamic-pituitary-elevation of T3 and T4 during the depressive phases with normalization of the hormone level following treatment with electroconvulsive therapy ***(Kirkegaard and Faber, 1981)***.

Meanwhile, other studies have demonstrated a decrease in thyroid hormone levels in cases of depression ***(Shoda et al., 1991)***.

The relation between major depression and melatonin has also been subject of interest during the past few years. Melatonin (N-acetyl-5 methoxy tryptamine) is

ompound which is derived from serotonin. It is secreted from the pineal glands to ammals and other vertebrates.

Melatonin is secreted at night under the influence of noradrenergic fibers rom the superior cervical ganglion. These are under control of the supra chiasmatic nuclei of the hypothalamus. Hence, any abnormality of melatonin might be taken as a support for a noradrenergic defect or a hypothalamic abnormality ***Thompson et al., 1988)***. Reduction in melatonin secretion has been reported in cases of depression ***(Wetterberg et al., 1979; Claustrat et al., 1984 and Brown et al., 1985)***. Meanwhile, other investigators found no considerable variation in melatonin level.

Aim of the work:

The aim of the present work is to study the variation in thyroid gland hormones namely T3, T4 and TSH and in melatonin secretion in Egyptian patients with bipolar affective disorders during the depressive episodes.

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REVIEW OF LITERATURE

1. MAJOR DEPRESSION

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ntroduction to Major Depression:

Major depression is a heritable, recurrent, syndromal illness. The negative charge it lends to mood and thought, which dampens hope and impoverishes self-respect, is the best-recognized symptom. However, equally important components of the syndrome include physiologic changes that suggest on involvement of the brain areas influencing arousal, food intake, reproduction, circadian rhythms, and pituitary regulation ***(Gold et al., 1988)***.

Major depression is a common and serious mood disorder. Studies show that 18% to 23% of women and 8% to 11% of men have an episode of major depression at some time in their life ***(American psychiatric Association, 1980)***. The episode is severe enough to require hospitalization in 6% of women and 3% of men. Bipolar disorders, which involve episodes of both depression and mania, occur in 0.4% to 1.2% of adults, equally in men and women ***(American Psychiatric Association, 1980)***. Not only are the symptoms painful and disabling but 15% of persons with serious episodes die by suicide ***(Guze and Rubins, 1970)***.

Clinical Diagnosis of Major Depression:

to

Although neurobiology came to dominate efforts to understand psychiatric ess, no definitive biologic marker for major depression has yet been identified.

Consequently, attempts to distinguish major depression as a discrete illness from the various depressive symptoms that are an inescapable part of living must ely on diagnostic parameters based on empirical clinical observations ***(Gold et al., 1988)***.

In the United states, the diagnostic and statistical manual of mental disorders (third edition, revised) (DSM 111-R) represents the most widely used system of psychiatry diagnosis ***(Gold et al., 1988)***. The manual's criteria reflect the contemporary view that major depression is a syndromal illness with both psychological and biologic components e.g., depressed mood, withdrawal of interest, feelings of worthlessness, anorexia or hyperphagia, and insomnia or hypersomnia (Table 1). Though the DSM 111-R specifies that a major depressive episode must last for at least two weeks, it has been criticized for over inclusiveness because it fails to require a periodic or recurrent course as essential for diagnosis. Accordingly, it has been customary to subdivide patients with major affective disorders on the basis of a pattern of recurrence, with the bipolar pattern

ecting recurrent depression and mania, and the unipolar pattern reflecting
rrent depression alone *(Perris, 1962)*.
to

ble (1):

Symptoms of major depression *(American Psychiatric Association, 1987)*:

1) Depressed mood (or irritable mood in children and adolescents) most of the day, nearly every day.
2) Markedly diminished interest or pleasure in all, or almost all activities most of the day, nearly every day.
3) Significant weight loss or weight gain when not dieting or decrease or increase in appetite nearly every day.
4) Insomnia or hypersomnia nearly every day.
5) Psychomotor agitation or retardation nearly every day.
6) Fatigue or loss of energy nearly every day.
7) Feelings of worthlessness or excessive or inappropriate guilt nearly every day.
8) Diminished ability to think or concentrate, or indecisiveness nearly every day.
9) Recurrent thoughts of death, recurrent suicidal ideation with out a specific plan, or a suicide attempt or a specific plan for committing suicide.

C. Theories of Depression:

1. Psychodynamic and cognitive theory:

From a psychodynamic point of view, chronic childhood exposure to a hypercritical exploitative, or emotionally unresponsive environment complicates the

ks of maintaining self-esteem and responding effectively to inevitable life sses. Accordingly, such childhood experiences produce a burden of painfully to rged, poorly integrated feelings that can emerge reflexively in adult life when er there is a particularly painful disappointment or loss. Because the adult strongly desires to avoid re-experiencing such intensely painful emotions, rigid defenses often emerge to protect against loss. Paradoxically, these expose the person even more to potentially damaging stress ***(Gold et al., 1988)***.

Although many consider negative and distorted thinking as a consequence rather than a cause of major depression, cognitive therapists view such thinking as the psychological precursor of depression. The distorted perceptions may be enhanced by the persistence into adult hood of rigid all or none rules of conduct or the maintenance of inflexible and unattainable goals ***(Beck, 1976)***.

2. Neurotransmitter Hypothesis:

The first major hypothesis to address the biologic basis of major affective disorder emerged from the observation that depressive symptoms developed in approximately 15 percent of the patients who were treated for hypertension with the biogenic amine-depleting agent reserpine ***(Schild kraut, 1965)***. Subsequently, the mono amine oxidase inhibitors were found to be effective as antidepressant

nts, presumably because of their interference with the enzymatic degradation to ne biogenic amines, similarly, tricyclic anti depressant agents were found to ck the synaptic reuptake of amines into presynaptic neurones ***(Bunney and avis, 1965)***.

These observations gave rise to the original catecholamine (norepinephrine) hypothesis of major depression, which stated that this disorder resulted from a 'functional deficit of norepinephrine at critical effector sites in the central nervous system ***(Bunney and Davis, 1965)***.

The location and functional effects of norepinephrine were appropriate for a neurotransmitter thought to be involved in a syndromal illness like major depression. One of its principal sites of synthesis, the locus ceruleus in the mid - pons, sends a dense network of fibers to terminal fields in such disparate areas as the hypothalamus and hippocampus, and throughout the cerebral cortex ***(Moore and Bloom, 1979)***.

Early measurements by flurometric assay of the norepinephrine metabolite 3-methoxy 4-hydroxy phenylglycol (MHPG) showed generally decreased levels in the cerebrospinal fluid, plasma, and urine of patients with major depression ***(Schild kraut, 1978)***. These studies were interpreted as supporting the original