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بقسم التوثيق الإلكتروني بمركز الشبكات وتكثولوجيا المطومات دون أدنى مسنولية عن محتوى هذه الرسالة.

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بمكات وتكنولوجبارته

# Ghrelin Serum Level in a Sample of Egyptian Major Depressive Disorder Patients

#### Thesis

Submitted for Partial Fulfilment of Master Degree in Neuropsychiatry

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### Tist of Abbreviations

Abb.	Full term
5-HT	5 hydroxytryptamine
AG	· · · · · · · · · · · · · · · · · · ·
AGRP	Agouti-related protein
<i>AMPA</i>	a-amino-3-hydroxy-5-methyl-4-isoxazole- propionic acid
ARC	Arcuate nucleus
BDI	Beck depression inventory
<i>BDNF</i>	Brain derived neurotrophic factor
<i>BLA</i>	Basolateral complex of the amygdala
BMI	Body mass index
<i>CA</i>	Cornu ammonis
CDK2	Cyclin dependent kinase 2
CNS	Central nervous system
<i>DAG</i>	Des-acyl ghrelin
DSM-IV	Diagnostic and statistical manual of mental disorders
E2F1	E2F transcription factor
ELISA	Enzyme-linked immunoassay
<i>GH</i>	Growth hormone
GHQ-28	General health questionnaire-28
GHSR1a	Growth hormone secretagogue receptor 1a
GHSR1b	Growth hormone secretagogue receptor 1b
GOAT	Ghrelin O-acyltransferse
GRs	$ Glucocorticoid\ receptors$
HAM-D	Hamilton depression scale
HPA	Hypothalamic pituitary axis
<i>IDO</i>	Indoleamine 2, 3 dioxygenase
<i>IL-12</i>	Interleukin 12
<i>IL-13</i>	Interleukin 13

### Tist of Abbreviations (Cont...)

Abb.	Full term
IL-18	.Interleukin 18
<i>IL-1RA</i>	.Interleukin 1 receptor antagonist
<i>IL-6</i>	.Interleukin 6
<i>IQR</i>	.Interquartile range
<i>KYN</i>	.Kynurenine
<i>MAPK</i>	.Mitogen-activated protein kinase
<i>MDD</i>	.Major depressive disorder
miRNA	.Microribonucleic acid
MRs	.Mineralocorticoid receptors
<i>NAC</i>	.Nucleus accumbens
<i>NMDA</i>	. N-methyl- $D$ -aspartate
<i>NPY</i>	.Neuropeptide y
<i>NREM</i>	Non rapid eye movement
<i>NSC</i>	.Neural stem cells
<i>PC</i>	.Personal computer
<i>PFC</i>	.Prefrontal cortex
PI3K/Akt	.Phosphatidylinositol 3-kinase/Ak strain
	transforming
<i>POMC</i>	. Proopio me la no cortin
<i>PTSD</i>	.Post-traumatic stress disorder
<i>REM</i>	.Rapid eye movement
<i>RNS</i>	.Reactive nitrogen species
<i>ROS</i>	.Reactive oxygen species
SCID-I	. Structured clinical interview for the DSM-IV
	axis I disorders
	.Standard deviation
	.Statistical package for Social Science
	.Selective serotonin reuptake inhibitors
sTNFR2	. Soluble tumour necrosis factor receptor 2

### Tist of Abbreviations (Cont...)

Abb.	Full term	
SUD	Substance use disorder	
<i>TDO</i>	Tryptophan dioxygenase	
TNFa	Tumour necrosis factor alpha	
<i>VAS</i>	Visual analogue scale for hunger	
VTA	Ventral tegmental area	
<i>WHO</i>	World health organisation	
<i>YLD</i>	Years lived with disability	

#### Introduction

epression is a common mental disorder with an estimated lifetime prevalence of 13-18% (*de Graaf et al.*, 2012).

Major depressive disorder (MDD); is a leading psychiatric illness across the world, severely affecting quality of life and causing an increased incidence of suicide, although it is underlying pathophysiology is still unclear and recently multiple studies were concerned with the relation between serum Ghrelin level and MDD (*Ting et al.*, 2020).

Moreover, different parts of the brain are involved in the regulation of mood and the expression of emotions, where neuroimaging and neuropathological studies supported that the medial prefrontal cortex, the caudolateral orbital cortex, the amygdala, the hippocampus and the ventromedial parts of the basal ganglia are networks which modulate emotional behavior and so there is evidence that the function of these structures is altered in patients with MDD (*Drevets et al.*, 2008).

The areas of the brain mentioned above are not only associated to MDD but they also have an important role in feeding behavior and nutrition hormones as Ghrelin and Leptin (*Gibson*, 2006).

Ghrelin is a 28 amino acid peptide, secreted from stomach and functions as an orexigenic hormone, which

increases before meals and decreases after meals (Druce et al., 2005, Kojima, 2010, Toska et al., 2013). It is acylated [acyl ghrelin (AG)] by ghrelin-O-acyl transferase in the stomach and 10%20% of circulating ghrelin exists in this form (Kojima, *2010*).

Although ghrelin is present in the stomach other peripheral tissues like the pancreas, it is also found in smalls amounts in the hypothalamus, therefore ghrelin affects the CNS and does not act only as a hunger signal but it is also involved in reward, motivation and signaling pathways, and is in this way linked with stress, anxiety disorders and depression (Schellekens et al., 2012, Zarouna et al., 2015).

The relation between Ghrelin and MDD is controversial, as different studies in animals yielded contrasting findings, where some showed that ghrelin could be an anxiogenic hormone whereas others revealed that it can have anxiolytic and antidepressant effect. A few human studies were performed about ghrelin levels in patients with depression and the findings were inconsistent. A study reported low ghrelin levels in depressive patients. However, many others suggested no difference in ghrelin levels between depressive patients and healthy controls. Nevertheless, some studies found high serum ghrelin levels in patients with major depression (Ozosy et al., 2014, Zarouna et al., 2015).