A Study of Serotonin Transporter Gene Polymorphisms with Obstructive Sleep Apnea Syndrome

Thesis

Submitted for partial fulfillment of the master degree of ***Chest Disease***

By:

Fatma Salim Ali Elgohary
Mahalla Chest Hospital

Supervised by

Prof. Mohamad Awad Tag Eldin
Professor of Chest Medicine
Faculty of Medicine, Ain Shams University

Prof. Aya M. M.Abdel Dayem
Professor of Chest Medicine
Faculty of Medicine, Ain Shams University

Dr. Omayma Mohamed Hassanin
Associated Consultant of Clinical Pathology
Faculty of Medicine, Ain shams University

Faculty of Medicine
Ain Shams University
2014

سورة البقرة الآية: ٣٢

Acknowledgement

Thanks first and last to ***Allah*** *as we own him for his great care, support and guidance in every step in our life.*

My deepest appreciation and infinite gratitude to ***Prof. Mohamad Awad Tag Eldin****, Professor of chest diseases, Faculty of medicine, Ain Shams University, for his continuous encouragement and kind supervision .*

I wish to express my sincere feelings of gratitude to ***Prof. Aya M.M.Abd El Dayem,*** *professor of chest diseases, Faculty of medicine, Ain Shams University , for her support, supervision, continuous encouragement.*

I would like to express my honest feeling to ***Dr . Omayma Mohamad Hassanin,*** *Associated consultant of clinical pathology , Faculty of medicine Ain Shams University Hospitals, for her unlimited help, continuous encouragement and kind supervision .*

Finally I would like to thank my family whose continuous encouragement and support have made this work easier to accomplish, specially my mother God bless her.

Fatma Salim Ali Elgohary

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Arabic Summary ..... --

List of Abbreviations

AHI	:	Apnea-hypopnea index
AI	:	Arousal index
ASDA	:	American sleep disorders associates
ASUH	:	Ain shams university hospital
BIPAP	:	Bilevel positive airway pressure
BMI	:	Body mass index
CNS	:	Central nervous system
CPAP	:	Continuous positive airway pressure
CSAS	:	Central sleep apnea syndrome
DI	:	Desaturation index
ECG	:	Electroencephalogram
EMG	:	Electromyogram
EOG	:	Electro-occulogram
FEV1	:	Forced expiratory volume1
FVC	:	Forced vital capacity
h	:	Hour
min	:	Minute
NP	:	Nasal prong
NPSG	:	Noctornalpolysomnography
NREM	:	Non-rapid eye movement
OSA	:	Obstructive sleep apnea
OSAS	:	Obstructive sleep apnea syndrome
PCO2	:	Partial pressure of carbon dioxide
PLMS	:	Periodic leg movement during sleep
PO2	:	Partial pressure of oxygen
REM	:	Rapid eye movement
Sao2	:	Oxygen saturation
SCN	:	Suprachiasmatic nuclei
Sec	:	Second
SI	:	Snoring index
STG	:	Serotonin transporter gene polymorphism
TA	:	Total apnea
TDI	:	Total desaturation index

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Introduction

Obstructive sleep apnea syndrome is one of the most complex disorders of sleep. it involves several genetic factors that contribute to phenotype serotonin [5-HT] regulate avarity of visceral and physiological functions including sleep. Gene 5-HTR2A polymorphisms may change the transcription of several receptors in the serotoninergic system contributing to OSAS (***Bayazit et al ., 2006).***

Obstructive sleep apnea syndrome [OSAS] has been to aggregate significantly within families ***(Pilla and Larvie,1995)***. Family studies have suggested that the risk of OSAS may be from 2to 4 fold as great in relatives of patients with OSAS than in controls and that nearly 40 %of the variance in the apnea hypopnea index [AHI] of patients with OSAS may be explained by genetic Factors ***(Redline et al.,1995).***

Since the serotonin [5-HT] is associated with circadian rhythm and breathing regulation, the serotonin transporter [5-HTT] which plays an important role in serotoninergic transmission, might be a strong candidate gene in the pathogenesis of obstructive sleep apnea syndrome [OSAS].

Several lines of pharmacological ,neurobehavioral, and therapeutic evidence have implicated that serotonin [5-HT] is involved in the pathogenesis of OSAS ***(Carly et al., 2007)***. By regulating the magnitude and duration of serotonergic receptors, the serotonin transporter [5-HTT] is central to the fine tuning of brain serotonergic neurotransmission and of the peripheral actions of serotonin (5-HT).

The serotonin transporter (5-HTT) protein is encoded by a single gene , which locates on chromosome 17q11,1-17q12 ***(Lesch et al.,1994)***.

Two common polymorphisms have been described in the gene ,5-HTT gene linked polymorphic region(5-HTTLPR) and a variable number of tandem repeats at intron 2 (STin2.VNTR)***(Battersby et al.,1996)***. These polymorphisms make the 5-HTT a strong candidate gene for study in obstructive sleep apnea disorders (Battersby et al.,1996).

Aim of the work

The aim of this work was to investigate the association of serotonin trasporter gene polymorphisms with obstructive sleep apnea syndrome and clinical characteristics.

Sleep physiology:

Sleep is a state of reduced awareness and responsiveness. In humans, sleep is also associated with reduced movement.

Sleep consists of two different phases:

- Rapid eye movement (REM) sleep; and
- Non-REM sleep or slow wave sleep.

(Iber et al., 2007)

REM sleep

REM sleep is characterised by the presence of rapid eye movements during sleep. This type of sleep is less restful than slow-wave sleep and is associated with dreaming and bodily muscle movements. During REM sleep a person's threshold to be aroused by external stimuli is higher than during slow-wave sleep. Heart rate and breathing become irregular during REM sleep, a feature of the dream state. The brain is extremely active during REM sleep. The electroencephalogram shows patterns of brain wave activity similar to those that occur during the waking hours. Due to this feature of REM sleep, it is often also referred to as paradoxical sleep as it is a paradox that one can be asleep and yet the brain is incredibly active ***(Epstein et al.,2009).***

Non-REM sleep

In contrast, non-REM sleep is characterised by deep sleep. The duration of REM sleep episodes is longer earlier in the night when one is most tired. As one becomes more rested during the night, the duration of REM sleep episodes decreases. During non-REM sleep the blood pressure, breathing and metabolic rate are all depressed significantly. Bodily movements do not occur during non-REM sleep. Non-REM sleep is also referred to as slow wave sleep as during this