NEUROLOGICAL SOFT SIGNS AND COGNITIVE IMPAIRMENT IN OBSESSIVE COMPULSIVE DISORDER PATIENTS AND THEIR FIRST DEGREE RELATIVES

Thesis

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List Of Abbreviations

ACC : Anterior cingulate cortex

ASP : Antisocial Personality

CBI : Cambridge Neurological Inventory

DSM-IV : Diagnostic and Statistical Manual of Mental Disorders- Forth Edition- Text Revision

DZ: Dizygotic twins

EF : Executive Function

FPPC: Fronto-Polar Prefrontal Cortex

GHQ : General Health Questionair

GM : Gray Matter

LOD : Log Of The Odds

MRI : Magnetic Resonance Imaging

MZ: Monozygotic twins

NSSs: Neurological soft signs

OCD : Obsessive compulsive disorder

OFC : Orbitofrontal cortex

PANDAS : Pediatric Autoimmune Neuropsychiatric Disorders Associated with streptococcal infection

PET : Positron Emission Tomography

ROI : Region of Interest

SCID I: Structured Clinical Interview for DSM-IV Axis I Disorders

SPECT : Single Photon Emission Computed Tomography

SSRIS : Selective Serotonin Reuptake Inhibitors

WCST: Wisconsin Card Sorting Test

WMS-III_ Abbreviated : The Wechsler Memory Scale®—Third Edition—Abbreviated

Y_BOCS: Yale-Brown Obsessive Compulsive Scale

INTRODUCTION

Obsessive-Compulsive Disorder (OCD) is characterized by the presence of either obsessions or compulsions that cause significant distress to afflicted individuals. OCD is a relatively frequent psychiatric disorder with the 12-month prevalence in adults ranging from 0.6% to 1.0% for DSM-IV OCD and an estimated lifetime of 1.6%. Estimates of prevalence vary slightly across countries and depending on different methodology *(Wahl et al., 2011)*.

The World Health Organization places OCD among the 10 most disabling medical conditions worldwide, and the National Comorbidity Survey Replication indicates that OCD is the anxiety disorder with the highest percentage (50.6%) of serious cases *(Wahl et al., 2011).*

Although the pathophysiology of OCD remains controversial, there is substantial evidence suggesting that disturbances in the frontal-striatal-thalamic circuits may be implicated. Previous functional neuroimaging studies have shown functional abnormality in the orbitofrontal cortex (OFC), the anterior cingulate cortex (ACC), the caudate nucleus, and the thalamus.

Dysfunction in these circuits may be associated with implicit processing deficits and intrusive symptoms *(Togao et al., 2010).*

Neurological soft signs (NSSs) are minor neurological abnormalities that are thought to be secondary to a neurodevelopmental abnormality, and they cannot be localized by brain screening tests. These signs may reflect brain dysfunctions in psychiatric disorders. NSSs can be generally grouped as sensory integration, motor coordination, sequencing of complex motor acts and others *(Tumkaya et al., 2011).*

Although contradictory results have been reported in studies evaluating NSSs in OCD patients, graphesthesia disorder, among the sensory integration subgroup of NSSs, is consistently found to be more common in OCD patients; in studies comparing NSS subscale scores separately. On the other hand, we can find only one study in the literature, comparing OCD and schizophrenia patients in terms of NSSs. Schizophrenia patients performed worse than OCD patients in all NSS subgroups except sensory integration in the above-mentioned study *(Tumkaya et al., 2011).*

Besides their documented presence in adult psychiatric conditions, neurological soft signs may play an indicative role in the neurodevelopment of the

brain, as early soft signs have been shown to precede adult-onset schizophrenia and anxiety disorders *(Shaffer et al., 2009)*.

A recent area of research has been the characterization of neuropsychological deficits in patients with OCD. This has contributed to the understanding of biological underpinnings of the illness. Cognitive deficits could be functioning as an intermediate variable between neurobiological abnormalities and OCD symptoms. Reductions in social competence and the capacity for independent living and vocational success may be the result of neurocognitive compromise *(Rampacher et al., 2010).*

A large number of previous neuroimaging studies using positron emission tomography (PET), single photon emission computed tomography (SPECT), or functional MRI have identified abnormally high activities throughout the frontal cortex and subcortical structures in patients with OCD. Several neuroimaging studies reported activation of areas such as the orbitofrontal cortex (OFC), caudate nucleus, thalamus, and anterior cingulate cortex (ACC) during provocation of obsessive-compulsive symptoms *(Yoshiura et al., 2011).*

In the context of OCD, deficits in non-verbal memory and certain executive functions (set shifting ability, response inhibition, and decision making) have been widely reported *(Viswanath et al., 2010).*

Two recent studies have demonstrated the presence of such deficits in remitted patients also *(Bannon et al., 2006; Rao et al., 2008)*. There have been only two studies in this regard that revealed deficits in planning *(Delorme et al., 2007)* and, in response inhibition and set shifting *(Chamberlain et al., 2007)* in relatives of index probands. However, these studies chose more than one type of unaffected first-degree relative; samples combining more than one generation of relatives may be biased due to the differing neurodevelopment stages of subjects *(Viswanath et al., 2010).*

Rationale of the study

Studies have placed the estimated lifetime prevalence of 2-3% for OCD, more than twice that of schizophrenia, so that in Egypt there will be approximately 250000 OCD patients *(The statistical Year Book, 2004).* Most of the patients are ranging between 20-40yrs old. This constitutes an economic burden on the families and the country as a whole, as

this is expected to be the age of active productivity and participation in the national development.

Our study will throw some light on the presence of the neuorological soft signs and cognitive impairment in OCD patients to offer better understanding of aetiopathogenesis of OCD which allow us to develop new better treatment for OCD. Studying the first degree relatives of OCD has been the subject of few studies, and to our knowledge none of the Egyptian psychiatric studies.

Hypothesis

The main hypothesis of this study is that OCD patients and their first degree relatives have neurological soft signs and cognitive dysfunction so that they might be considered a trait marker for the disorder.

AIMS OF THE WORK

The aim of this work is to verify the hypothesis, and to answer the following questions if the hypothesis is verified:

1- Is there is a relation between neurological soft signs and cognitive dysfunction to duration of illness.

2- Is there is a relation between neurological soft signs and cognitive dysfunction to severity of symptoms.

3- Is there is a relation between neurological soft signs and cognitive dysfunction to age and gender of patients.