Cognitive Dysfunction In Patients With First And Recurrent Episodes Of Depression

Thesis

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List of Abbreviations

Abb.	Full term
ACP	American college of physicians
AD	Alzheimer's disease
CAM	*Complementary and alternative medicine*
CBT	Cognitive behavioral therapy
CBT	Cognitive behavioural therapy
CG	Control group
DHA	Docosahexaenoic acid
EC	Effortful Control
ECT	*Electroconvulsive therapy*
EFs	Executive functions
FED	First depressive episode
GAS	Global Assessment Scale
HAMD	Hamilton Depression Scale
MAO	Monoamine oxidase
MDD	Major Depressive Disorder
MDE	Major depressive episode
NART	National Adult Reading Test
NASSAs	Noradrenergic and specific serotonergic antidepressant
PFC	Prefrontal cortex
PHQ9	Patient Health Questionnaire – Nine Item
RCT	Randomized controlled trials
RED	Recurrent depressive episodes
rTMS	Repetitive transcranial magnetic stimulation
SAMe	S-adenosyl-l-methionine
SCID-I	Structured Clinical Interview for DSM-IV
SGAs	Second-generation antidepressants
SPSS	Statistical Package for Social Sciences
SSRIs	Selective serotonin reuptake inhibitor

List of Abbreviations Cont...

Abb.	Full term

TCA..... Tricyclic antidepressants
TRD..... Treatment-resistant depression
WAIS..... Wechsler adult intelligence scale
WAIS..... Wechsler Adult lntelligence Scale
WCST..... Wisconsin card sorting test
WM ..... Working memory
WMS ..... Wechsler memory scale

INTRODUCTION

Major Depressive Disorder (MDD) is a common disorder with a high rate of recurrence, chronicity, and staggering economic burden, including disability in the workforce ***(Gilmour and Patten, 2007).***

In 2010, MDD was the second leading medical cause of burden globally, with the highest estimates of disability in people of working age. The disease has shown high prevalence in certain Arabic -speaking countries ***(Ferrari et al., 2013).***

The relation between MDD and cognitive functions decline has been addressed in previous studies. Only a subset of individuals with MDD (30-40%) reach symptomatic remission after adequate treatment with a first-line antidepressant, and many patients do not reach premorbid levels of psychological functioning ***(Bortolato et al., 2016).***

Cognitive dysfunction refers to deficits in attention, verbal and nonverbal learning, short-term and working memory, visual and auditory processing, problem solving, processing speed and motor functioning. Cognitive dysfunction may be a primary mediator of functional impairment in MDD ***(McIntyre et al., 2013).***

MDD was found to have a clinically significant impact on psychomotor speed, declarative memory, working memory, executive functions and attention ***(Papakostas et al., 2014)*** and

studies even suggest that cognitive deficits might persist beyond the acute stages of illness in MDD ***(Bora et al., 2013).*** These deficits were found to be significant in both first and recurrent episodes of MDD ***(Lee et al., 2012).*** In one study of 274 subjects with major depression, 71% ranked difficulty concentrating among the top most troubling symptoms ***(Padina et al., 2009).***

Cognitive symptoms are present during 85–94 % of the length of depressive episodes and 39–44 % of the length of periods of remission. Further studies indicated that with every episode there is a decrease in cognitive function and that inter-episode cognitive function is related to the number of previous episodes ***(Murrough, et al., 2011).***

It is also apparent that, while cognitive dysfunction in MDD may improve with treatment and resolution of depressive symptoms, cognitive deficits can still be detected even in periods of symptom remission. In a 3-year, follow-up study of patients with MDD, the proportion of time with cognitive complaints was reported as 94% during acute depressive episodes; this remained at 44% despite full or partial symptom remission during treatment ***(Conradi et al., 2011).***

Hence there has been increasing recognition that symptomatic remission is an insufficient goal of treatment for MDD and that return to premorbid psychosocial functioning should be targeted ***(Zimmerman et al., 2006).***

Cognitive performance on tests of immediate memory, attention, and processing speed was reported to be inferior in patients with MDD who met criteria for remission, compared with healthy subjects ***(Baune et al., 2010).***

Meta-analyses show that cognitive deficits in executive function are still present in remitted patients, which may explain persistent psychosocial impairment in remission ***(Snyder, 2013)***.

RATIONALE OF THE STUDY

Major depressive disorder is a serious disorder with many health and morbid-related outcomes. Cognitive impairment related to major depression is a well-known phenomenon. It was suggested that these cognitive impairments are one of the main reasons for the lag between syndromal recovery and functional recovery of MDD patients, which may lead to the loss of productivity, greater healthcare costs, and an increased economic burden of the illness. The rationale of the study is to assess the cognitive deficits in the first episode of Major Depressive Disorder compared to recurrent episodes, in a sample of Egyptian patients, in symptomatic remission, and to evaluate the severity of cognitive dysfunction in each group.

Hypothesis:

There is a greater impairment in cognitive impairment in patients with recurrent episodes of depression in symptomatic remission, compared to the cognitive impairment in patients with a first episode of Major Depressive Disorder, both undergoing medical treatment.

AIM OF THE STUDY

1. To study the cognitive dysfunction in patients diagnosed with MDD.
2. To study the difference between the cognitive dysfunction in patients suffering from first compared to recurrent episodes of depression.

Chapter 1

COGNITIVE FUNCTIONS

Cognitive functions encompass reasoning, memory, attention and language and lead directly to the attainment of information, thus, knowledge. Nevertheless, endogenous factors, such as mood and physical health, can impact it tremendously ***(Roiser and Sahakian, 2013).***

A proposed classification of cognitive functions is to divide them into hot and cold cognition. It has clinical resonance as well as heuristic value. Hot cognition is defined as cognitive functions that are emotionally laden. Examples of hot cognition would include, but are not limited to, catastrophic reactions to real and / or perceived slights, anhedonia, negativistic rumination, negative recall bias, and disproportionate attention to negative stimuli. Examples of cold cognition would include, information processing speed, learning and memory, as well as attention / concentration. Neuro biologically, a discrete separation from hot and cold cognition does not exist ***(Roiser and Sahakian, 2013).***

Defining and Classifying Mental Processes:

There are three possible ways to represent the relationship between mental processes and brain processes. According to the first view, mental processes are distinct from physical (e.g., brain) processes. This is a folk psychological

view and represents a kind of dualism: there are physical entities, and there are non-physical (mental) entities, and scientifically unpopular. In contrast, the second and third views represent mental processes as a subclass of physiological (bodily) processes. The second view characterizes mental processes as a type of bodily process that is distinct from brain processes, while the third view holds that mental processes are a subtype of brain processes. Both views are consistent with what is known about the physiological basis of cognition ***(Hastings et al., 2014).***

Basic Cognitive Functions

1. Attention

Attention refers to the ability to sustain concentration on a particular object, action, or thought, and ability to manage competing demands in our environment. The ability to focus on these stimuli rather than others, ability to perform a task in the presence of distracting stimuli, sustain focus on the stimulus until it is processed, and allow for the transfer of the stimulus to higher-level processes. Attention is a basic but complex cognitive process that has multiple sub-processes specialized for different aspects of attentional processing. Some form of attention is involved in virtually all other cognitive domains, except when task performance has become habitual or automatic. Declines in attention can therefore have broad

reaching effects on one's ability to function adequately and efficiently in everyday life ***(Glisky, 2007).***

Different Divisions of Attention:

a. Selective Attention:

This term refers to the ability to select from many factors or stimuli and to focus on the one that you want while filtering out other distractions. It is considered as the earliest form of attention. Once one identifies the functions of attention, the neural correlates of these functions can be studied across species. For example, selective attention and object-based attention, which include basic discrimination functions, involve substantial portions of the cortex in humans. Even a simple shift of attention between objects activates "a large network of cortical areas". Shifting focus from one object to another is a fundamental function of attention, indispensable for selectively interpreting spatial information and without which basic navigational or visual search tasks would be impossible ***(Glisky, 2007)***.

b. Divided Attention and Attention Switching:

Is the ability to process two or more responses or react to two or more different demands simultaneously. It is usually referred to as "multi-tasking." Divided attention tasks require the processing of two or more sources of information or the