

# The Effect of Cognitive Remediation Therapy on Cognitive Flexibility, Working Memory, and Psychiatric Symptoms in Patients with Schizophrenia

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**Abstract:** Cognitive impairment is thought to be central to the pathology, and in particular in the areas of attention, memory, and executive function in patients with chronic schizophrenia. Cognitive deficits have a significant impact on the quality of life of sufferers, their symptoms and functional outcome.

**Aim:** To determine the effect of implementing cognitive remediation therapy on cognitive flexibility, working memory, and psychiatric symptoms in patients with chronic schizophrenia.

**Design:** A quasi-experimental research design (pre-test/post-test design) was used.

**Subjects:** Participants with a diagnosis of chronic schizophrenia, and a cognitive difficulty (n= 12) were randomly recruited to 24 sessions of cognitive remediation therapy (cognitive flexibility and working memory A and B modules).

**Tools:** Tools used included Wisconsin Card Sorting Test (WCST), Forward and Backward Digit Span Test, and Brief Psychiatric Rating Scale. These tools were applied twice before and after program.

**Results:** The study showed improvements in patients' performance of Wisconsin Card Sorting Test and Forward and Backward Digit Span Test, as well as in psychiatric symptoms scale. **Conclusion:** Cognitive remediation therapy can be effective in improving cognitive flexibility, working memory, and in turn psychiatric symptoms in patients with chronic schizophrenia.

**Keywords:** Cognitive Remediation Therapy, cognitive flexibility, working memory, schizophrenia, and psychiatric symptoms.

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## I. INTRODUCTION

Cognitive dysfunctions are known to be a core feature of schizophrenia. Recent researches confirmed that 65% to 85% of patients with schizophrenia have cognitive impairments (Reichenberg, 2005; Davidson & Mate 2007; Stuart & Laraia, 2013; Kontaxaki et al, 2014; Tripathi et al., 2018; Okasha et al., 2020), 75% show poor performance in planning tasks, 65% of the patients show deficits in cognitive flexibility and 65% show deficits in working memory (Morice & Delahunty, 1996). These deficits appear early in the disease course and might exist before the first positive or even negative symptoms become manifested (Niendam et al., 2003). The vulnerability-stress model of schizophrenia states that

people with schizophrenia frequently have a number of factors (such as certain genes or neuro-developmental abnormalities) which may predispose them to developing symptoms in the face of stressful events (Zubin & Spring, 1977). Cognitive deficits are thought to act as vulnerability factors, increasing the likelihood of symptoms onset or recurrence following a stressful life event (Wykes & Reeder, 2005).

Cognitive difficulties in those with a first episode of psychosis can be as severe as those who have had a diagnosis of schizophrenia for many years, and problems can span a wide range of cognitive domains (Gur et al., 2014). Schizophrenia patients with severe symptoms during their life can experience a more rapid decline in cognitive skills than normal people (Seidman et al., 2013). Among the cognitive functions, cognitive flexibility and working memory are fundamental for chronic schizophrenia.

Cognitive flexibility is the ability to appropriately adjust one's behaviour according to a changing environment, this enables an individual to work efficiently to disengage from a previous task, reconfigure a new response set, and implement this new response set to the task at hand (Dajani & Uddin, 2015). Therefore, cognitive flexibility depends on attentional processes and knowledge representation (Canas et al., 2015). People with a diagnosis of schizophrenia often struggle with sustained attention, which may make it difficult for them to concentrate on things, like the TV or what someone is saying (Liu et al., 2002). They may also have difficulties with selective attention, which may result in distractibility or perseveration (persisting with one task while neglecting another), and often struggle with divided attention (Galaverna et al., 2012).

Likewise, schizophrenia patients often struggle with both verbal and non-verbal working memory. Working memory has been described as the temporary storage and manipulation of the information necessary for such complex cognitive tasks as language comprehension, learning, and reasoning (Baddeley, 1992). One of the most important models of working memory was first proposed by Baddeley & Hitch (1974) that has later undergone considerable development by Baddeley (2000). It proposes that there are four interacting parts to working memory: three storage components "phonological loop", "visuospatial sketchpad" and "episodic buffer" which are known as "slave systems", and a system which governs them, called the "central executive". These subsystems and the central executive controller are responsible for the allocation and direction of attentional resources, the manipulation of the visual and phonological material, and the selection and execution of strategies (Baddeley, 2000).

Cognitive impairment has been noted as core component of schizophrenia. Cognitive rigidity has been found to be linked to psychiatric symptoms such as perseveration, hostility, persecutory beliefs, limited abstract reasoning, problem solving, impaired ability to empathize, and violent behaviour (Wykes et al., 2007; Omiya et al., 2016). In this respect, memory impairment is being recognized increasingly as an important feature of the neuropsychology of schizophrenia. Dysfunction of working memory, a system for the short-term storage and manipulation of information, may relate to a number of core symptoms of schizophrenia (Forbes et al., 2008).

Cognitive difficulties have a profound impact on someone's ability to function well in many aspects of everyday life. Poor cognitive skills negatively affect many factors relating to work, including *employment rates, job retention, work skills and work performance* (Bell et al., 2014; Caruana et al., 2015; Norman et al., 2015). For schizophrenia patients, the impact of cognitive problems on performance in community life is enormous. Cognitive difficulties in psychosis are associated with higher financial costs, which are in part accounted for by loss of productivity and receipt of welfare benefits (Tsang et al., 2010). Moreover, cognitive difficulties in schizophrenia have a significant impact on social functioning, the ability to interact easily and successfully with other people, and quality of life (Stouten et al., 2014; Grau et al., 2016). Unfortunately, the more aware people are of their own cognitive difficulties, the more likely they are to self-stigmatise and perceive their quality of life as poor (Shin et al., 2016).

In Cognitive Neuropsychology of Schizophrenia, different levels of treatment are present: psychotropic drugs at cerebral level, psychotherapy at clinical level and Cognitive Remediation Therapy (CRT) as a supplementary treatment at cognitive level. Interaction of each treatment at these different levels improves the help that can be given to cure psychosis. Each level of treatment is as important as the other one (Lacoste, 2015). As cognitive difficulties are remarkably common to a wide range of other mental health problems such as eating, anxiety, and mood disorders, borderline personality disorder, ADHD and brain injury, evidence is emerging that CRT might also be helpful for people with such difficulties, notably eating disorders and affective bipolar disorder (Anaya et al., 2012; Danner et al., 2015;

Strawbridge et al., 2016). Although people are actually aware of their cognitive difficulties, this subjective experience does not always well match objective measures of cognitive functioning. However, those who do notice cognitive difficulties seem to be more likely to be motivated to try therapies (e.g CRT) which can improve thinking skills (Balzan et al., 2014).

CRT is a psychological intervention which aims to help people achieve personal, recovery-based goals and to support successful engagement in their community. Rather than simply being "brain training", it fosters the transfer of new cognitive skills and strategies learned in therapy to everyday life through its personalised content and treatment plan centred around each person's recovery goals (Wykes et al., 2011). The therapist role is crucial for helping people to develop a more strategic, self-aware approach to doing things both in therapy and their everyday lives (Delahunty et al., 2000).

More specifically, CRT leads to lasting changes in the brain through neuroplasticity (physical changes in brain structure which are necessary for a newly learnt skill to last). Cognitive improvements following CRT have been associated with plastic changes such as increased blood flow to brain regions associated with cognitive skills e.g. working memory (Eack et al., 2010; Penades et al., 2013).

To achieve the previously mentioned changes / improvements, CRT uses evidence-based training techniques such as errorless learning (errors are kept to a minimum) and massed practice where tasks are done repetitively in high volume (Wykes et al., 2011). The main instructional technique used is scaffolding, this involves an instructor extending a learner's ability by providing support in those aspects of a task which the learner cannot accomplish while removing assistance in those areas where competence has been achieved (Penades et al., 2006).

Researches proposed that a CRT Program can help in improving cognitive functions and psychiatric symptoms in patients with chronic schizophrenia with long disease duration who require large doses of medication (Pillet et al., 2014; Omiya et al., 2016). The CRT was also applied and reported a positive effect on patients with depressive disorder and children with autism spectrum disorders by Tunisian researchers (Hajri et al., 2015; Hajri et al., 2016). On the national level up to the researcher's knowledge, no studies were reported using such a technique in Egypt. This was confirmed by an official letter issued from Digital Library, Alexandria University (Digital Library, 2018).

Psychiatric nurses play pivotal roles in the efficacy of evidence-based psychosocial rehabilitation and are important members of interdisciplinary teams that provide holistic health care services ranging from symptom management to facilitating rehabilitation (Mullen, 2009). Psychiatric nurses, similar to other team member members (psychiatrist, psychologists, and social workers) are also responsible for the planning and implementation of cognitive remediation therapy on patients with schizophrenia (Otong, 2003). A research team that included five trained nurses who applied Cognitive Remediation Therapy on patients with schizophrenia and schizoaffective disorders, had recommended that implementation of such intervention be integrated into the day-to-day activities of the nurses and hoped that this would be an ongoing intervention delivered to patients regularly (Dark, 2018).

#### **Aim of the study:**

Determine the effect of implementing cognitive remediation therapy on cognitive flexibility, Working memory, and psychiatric symptoms of patients with schizophrenia.

#### **The Research question:**

What is the effect of implementing a cognitive remediation therapy on cognitive flexibility, Working memory, and psychiatric symptoms of patients with schizophrenia?

## **II. MATERIALS AND METHOD**

### **A- Materials**

#### **Research design:**

A quasi-experimental research design (pre-test/post-test design) was used in this study.

#### **Setting:**

The study was conducted in the inpatient wards of EL-Maamoura Hospital for Psychiatric Medicine.

**Subjects:**

A sample of 12 randomly selected male / female patients with chronic schizophrenia who met the inclusion criteria were the subjects in this study. This number was decided upon based on logic that CRT is a manual based individual therapy, which is implemented using different techniques such as scaffolding and errorless learning.

**The subjects were selected according to following Inclusion criteria:**

- Patients diagnosed with schizophrenia by EL-Maamoura hospital medical staff.
- Duration of illness more than two years since 1<sup>st</sup> diagnosis.
- Have no history of organic brain disease or head injury.
- Have no primary diagnosis of substance abuse.
- Age between 20-50 years (to avoid the impact of aging on the cognitive ability of the study subjects).
- Completed at least a basic level of education (nine years of education).
- Able to communicate in a coherent and relevant manner.
- Not under ECT treatment.

**Tools of the study:**

Four tools were used to collect the data of this study.

**Tool I: A Socio-Demographic and Clinical Data Structured Interview Schedule:**

This interview schedule was developed by the researcher to elicit data about patient's age, sex, marital status, educational level, employment, living situation, area of residence, age of onset of schizophrenia, duration of illness, number of previous psychiatric hospitalization, and medications presently taken.

**Tool II: Wisconsin Card Sorting Test (WCST):**

The WCST was first developed by Berg (1948) as a measure of abstraction and cognitive flexibility. It was standardized by Heaton (1981). Later WCST was revised and expanded by Heaton et al (1993). The test is composed of response cards and stimulus cards. There are 128 cards divided into two identical decks of 64 cards each. Each card has one to four figures (plus sign, star, circle, or triangle) in one of four colors: red, green, yellow, blue". No two response cards have the same color, form or number". In addition to the two identical decks of response cards, four stimulus cards with the following stimulus characteristics will also be placed in front of the subject: the first will show one red triangle, the 2<sup>nd</sup> will show two green stars, the third will show three yellow crosses, and the 4<sup>th</sup> card will show four blue circles.

**Tool III: Forward and Backward Digit Span Test:**

The Forward and backward digit span test was developed by Weschler (1981) to measure immediate verbal recall, attentional capacity, and working memory. This test comprises two modalities, Digits Forward and Digits Backward in a single subtest. Digit forward is considered to measure general attention and digit backward span task measures verbal working memory. The test comprises 7 levels and each level consists of a number of digits that increases with a rate of one number by each level. The test is valid, previously applied on patients with schizophrenia and demonstrated high test-retest reliability ( $r = 0.88$ ) (Weschler, 1981). The Forward and Backward Digit Span Test has been also applied on Egyptian patients with schizophrenia (Eweida, 2017).

**Tool IV: The Brief Psychiatric Rating Scale (BPRS- version 4.0):**

The brief psychiatric rating scale (BPRS- version 4.0) is a semi-structured interview that comprises 24 items. It was developed by Ventura et al. (1993) to measure psychiatric symptoms (Ventura et al., 1993). The presence and severity of psychiatric symptoms are rated on a 7 point Likert scale ranging from 1 (not present) to 7 (extremely severe). Thus, possible scores vary from 24 to 168, with lower scores indicating less severe psychopathology. The BPRS has been found

to be valid and reliable (Ventura et al., 1993). Also, it was used and standardized in previous studies on Egyptian population (Selim, 2006; Elnakeeb, 2013). It was tested for reliability by Elnakeeb (2013), the Cronbach's alpha was 0.71.

## B. METHOD

The steps followed in the present study were:

### 1. Training steps:

The researcher undergone a period of training on Cognitive Remediation Therapy under the supervision of the CRT administrators from Institute of psychiatry, psychology & neuroscience, King's College London. The researcher received a credited certificate from the authorized college

### 2. Administrative steps:

Official written permission for conducting the study was obtained from the director of EL- Maamoura Hospital for Psychiatric Medicine and the Mental Health General Secretariat.

### 3. Preparation of the study tools:

- The Socio-Demographic and Clinical Data Structured Interview Schedule (tool I) was developed by the researcher.
- Response and Stimulus Cards (tool II) were prepared (previously described under tools).

### 4. Pilot study

- Before embarking on the actual study, a pilot study was carried out on 5 patients with schizophrenia.

### 5. Test reliability

- The internal consistency and reliability of tool (II) was tested on a sample of 7 patients with schizophrenia who met the subjects inclusion criteria (these were later excluded from the study subjects). Using Cronbach's Alpha test, the tool proved to be reliable ( $r = 0.988$ ). Tool III was tested for reliability very recently on patients with schizophrenia using test-retest reliability, the tool proved to be reliable ( $r = 0.88$ ) (Eweida, 2017).

### 6. Preparation of Cognitive Remediation Program.

- The researcher followed the Cognitive Remediation Program that was developed by Morice and Delahunty (1996) in Australia and revised by Delahunty et al. (2000) on patients with schizophrenia).
- The researcher translated the content of the program sessions into Arabic language.
- The training program was conducted through-out 24 training sessions (8 sessions for cognitive shift module, 8 sessions for working memory A module, and 8 sessions for working memory B module). Each session consumed one hour on an individual basis for each patient, 4 times per week for six weeks.
- Level of difficulty in each session varied and included numerous tasks with different skills which ranged from being very easy to difficult for the participant.

### 7. Actual study:

The actual study was gone through three phases.

#### Phase I: selection of the subjects

- Hospital wards for male and female psychotic patients were ranked randomly using simple randomization.
- Patients' medical charts in the 1<sup>st</sup> ranked ward was reviewed to identify those who meet the inclusion criteria.
- Out of those meeting the inclusion criteria, four patients were randomly selected using simple randomization.

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- Study tools (II, III) were administered on an individual basis to the selected patients using the interview method. This was done twice prior to the application of CRT training program (with two-week interval). Patients with a stable impaired perseverative error or score below 16<sup>th</sup> percentile in WCST, and low working memory score were invited to participate in cognitive flexibility, and working memory training.
- Throughout recruiting process of the study subjects, 30 patients of those meeting study inclusion criteria were subjected to study tools II, III. Out of this number 19 patients (63.3%) were cognitively impaired (eligible for CRT application). However 7 patients dropped at different stages of the training program application for various reasons (2 patients were discharged, 4 patients refused to continue, and 1 patient recommended for ECT during application program).
- Tool (I) was then applied on each of these patient.
- Tool (IV) was applied on these patients on individual basis using interview and observation techniques (participant observation was done while applying tools II and III during pretest 1 and 2, and within first session of the program).
- The CRT program was then applied on each patient on an individual basis.

### Phase II: implementing the Cognitive remediation program:

- The researcher visited the inpatient setting 4 days/ week, each session of the training intervention consumed about one hour, which increased or decreased according to patient's response.
- The researcher met each study subject on individual basis in a quiet room (doctors' room) in the assigned patient's ward.
- The researcher established rapport and explained the purpose of the study to each patient participating in program.
- The Cognitive Remediation Therapy Program was conducted by covering two modules namely "the cognitive shift module" and "the working memory (A, B) module".
- Throughout the training program, the researcher used a number of techniques with patients to keep and enhance their success and motivation high, and to allow new skills to be learned effectively, implicitly and broadly. These were: massed practice, errorless learning, scaffolding and positive reinforcement.

### Phase III: evaluation of the effectiveness of the Cognitive remediation program

At the end of the intervention a post -test was implemented using study tools (II, III, IV) for each study subject.

#### Ethical considerations:

- Study procedure was revised and approved by the Faculty of Nursing Ethical Research Committee, Alexandria University and by Human Rights Protection Committee of the General Secretariat of Mental Health in Cairo.
- Informed written consent was obtained from each patient after explanation of the aim of the cognitive remediation program.
- Confidentiality was assured for the collected data.
- Patient's privacy was respected.
- The patient's right to refuse to participate in the study or withdraw at any time was emphasized and allowed.

#### Statistical analysis was done that included:

- A. Descriptive statistics
- B. Analysis of numeric data
- C. Analysis of categorical data
- D. Linear regression analysis

III. RESULTS

Figure 1& Table 1, present subjects' scores and means of the cognitive flexibility according to their perseverative errors at pre and post intervention phases. At pre intervention phase 1, the table highlighted the total number of perseverative errors by the study subjects that ranged from 27.0 to 79.0, with a mean score of 54.8±16.5 and median of 56.0 compared to 25.0 – 80.0 with a mean score of 53.9± 17.5 and a median of 54.0 at pre intervention phase 2, with no statistical significant difference between both phases ( $Z_{wil}= 0.51, P= 0.0827$ ).

The same table shows a total number of perseverative errors among the study subjects at pre intervention phase 2 that ranged from 25.0 – 80.0 with a mean score of 53.9± 17.5 and a median of 54.0 compared to 0.0 - 53.0 , a mean score of 24.0± 18.2 and a median of 19.0 at post intervention phase. The difference between the mean scores on pre-intervention phase 2 and post intervention phase was statistically significant ( $Z_{wil}= 4.1, P= 0.001$ ), denoting great improvement in patients' cognitive flexibility.

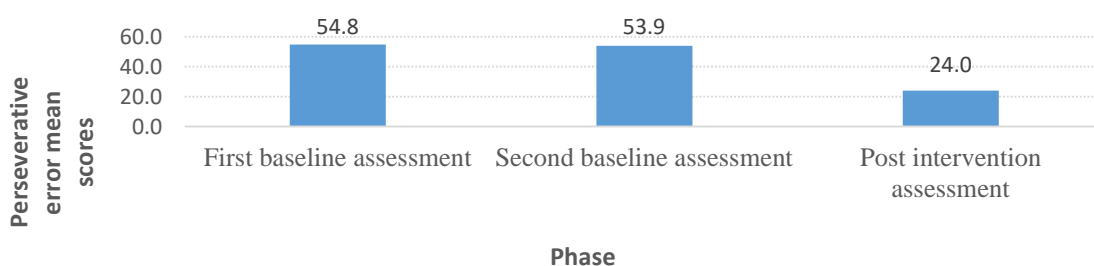


Figure (1): The study subjects cognitive flexibility mean scores according to their perseverative errors at pre and post intervention phases (WCST results).

Table (1): The study subjects cognitive flexibility scores according to their perseverative errors at pre and post intervention phases (WCST results)

Perseverative answers total	Phase			Z (P1)	Z (P2)
	Pre 1	Pre 2	Post		
Minimum	27.0	25.0	0.0		
Maximum	79.0	80.0	53.0		
Mean (SD)	54.8 (16.5)	53.9 (17.5)	24.0 (18.2)		
Median	56.0	54.0	19.0	0.51 (0.827)	4.1 (.001)*

Z: Wilcoxon test

P1: for pre 1 and pre 2

P2: for pre2 and post

\* P < 0.05 (significant)

Table 2 shows the effect of cognitive remediation program on the working memory among studied subjects at pre and post intervention phase. It was noticed from the table that before program all of the study subjects (100%) at pre 1 and pre 2 phases scored as having low working memory with no statistical significant difference between both phases ( $P= 1.000$ ). Regarding the post intervention phase, the table shows that by the end of the program all of the study subjects (100%) scored as having moderate working memory with a statistical significant difference between pre 2 and post intervention phases ( $P= 0.001$ ), reflecting the positive impact of the intervention program on patients' working memory.

Table (2): Effect of cognitive remediation program on the working memory among studied subjects (a pre and post intervention results).

Working Memory Total score (0-29)	Phase						$X^2_{mc}$ (P1)	$X^2_{mc}$ (P2)
	Pre 1		Pre 2		Post			
	No	%	No	%	No	%		
(Before program) low working memory	12	100.0%	12	100%	0	0.0%	0.0 (1.000)	9.4 (0.001)*
(By end of program) Moderate working memory	-	-	-	-	12	100.0%		

$X^2_{mc}$ : Mc-Nemar test

P1: for pre 1 and pre 2

P2: for pre2 and post \* P < 0.05 (significant)

Table 3 shows that the level of psychiatric symptoms among study subjects at pre intervention phase ranged from 77-105 with a mean score of  $88.8 \pm 9.5$  compared to 41-92 with a mean score of  $65.2 \pm 15.9$  on the post intervention phase, with a statistically significant difference ( $t=3.5, P=0.001$ )

The same table as well as figure (2) exhibit the effect of cognitive remediation program on the psychiatric symptoms among studied subjects. The table shows that before intervention all of the study subjects (100%) had moderate level of psychiatric symptoms, while on post - intervention the level of psychiatric symptoms dropped to mild level in 75.0% of the study subjects. The rest of 25% of the patients still had moderate level of psychiatric symptoms. The variation was statistically significant ( $\chi^2_{mc} = 6.9, P= 0.001$ ), indicating general decrease in psychiatric symptoms severity as a function of the cognitive remediation program.

**Table (3): Effect of cognitive remediation program on the psychiatric symptoms among studied subjects ( pre and post intervention results)**

Psychiatric symptoms	Program phase				$\chi^2_{mc} (P)$
	Pre		Post		
	No	%	No	%	
Mild	0	0.0%	9	75.0%	6.9 (.001)*
Moderate	12	100.0%	3	25.0%	
Range (24-168)	77-105		41-92		$t=3.5$ $P=0.001^*$
Mean $\pm$ SD	$88.8 \pm 9.5$		$65.2 \pm 15.9$		

$\chi^2_{mc}$ : Mc-Nemar test

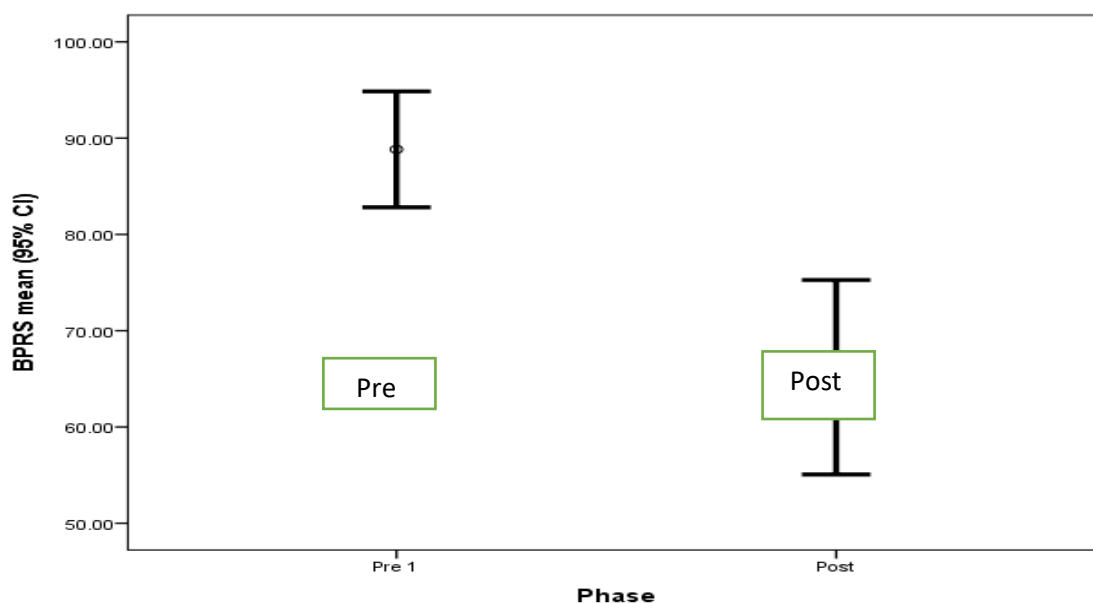
t: paired t-test

\* P < 0.05 (significant)

Mild: score range 24-71

Moderate: Score range 72-120

Severe: score range 121 – 168



**Figure (2) Effect of cognitive remediation program on the psychiatric symptoms among studied subjects (a pre and post intervention results).**

Table 4 shows relationship between studied subjects' cognitive flexibility mean scores according to their perseverative errors and their socio-demographic and clinical characteristics over the study phases. The table shows no statistically significant relation with any of the portrayed items neither on the pre intervention phase 2 nor on the post intervention. The same was also true for the relationship between subjects' working memory, psychiatric symptoms and each of socio demographic and clinical characteristics.



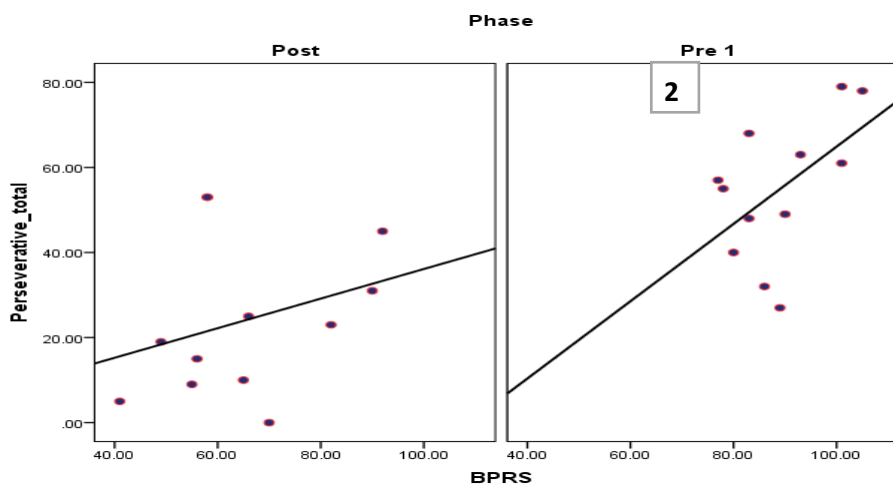
**Table (4) Relationship between studied subjects cognitive flexibility mean scores according to their perseverative errors and their socio-demographic and clinical characteristics (pre intervention phase 2 and post intervention).**

Socio-demographic and clinical data		Perseverative total (pre2)		Test (P)	Perseverative total (post)		Test(P)
		Mean	SD		Mean	SD	
Gender	Male	51.0	20.9	Z=1.5 (.177)	15.6	17.9	Z=1.5 (.177)
	Female	58.5	11.4		26.2	15.1	
Age	20-	32.0	0.0	X <sup>2</sup> =3.8 (.149)	0.0	0.0	X <sup>2</sup> =3.8 (.149)
	30-	61.0	15.4		36.0	22.9	
	40-50	55.3	16.4		18.1	9.2	
Work Status	Unemployed	56.1	16.6	Z=1.2 (.105)	23.0	16.4	Z=1.2 (.105)
	Hand workers	40.0	0.0		5.0	0.0	
Educational Level	preparatory education	60.3	19.1	X <sup>2</sup> =.35 (.840)	24.3	20.0	X <sup>2</sup> =.35 (.840)
	Secondary education	56.0	15.2		16.7	11.0	
	University education	42.0	21.2		31.0	31.1	
Marital Status	Single	53.9	18.1	Z=2.3 (.086)	18.2	13.4	Z=2.3 (.086)
	Divorced, Widowed	59.0	2.8		53.0	0.0	
Residence	Urban	55.9	19.1	Z=1.1 (.376)	18.4	14.7	Z=1.1 (.376)
	Rural	51.3	4.9		29.3	21.8	
Cohabitation	Alone	49.0	0.0	Z=.63 (.727)	25.0	0.0	Z=.63 (.727)
	with relatives	55.3	17.2		21.0	17.3	
Number of Psychiatric hospitalizations	1-	55.5	9.3	X <sup>2</sup> =1.5 (.681)	26.8	18.6	X <sup>2</sup> =1.5 (.681)
	6-	57.7	23.5		22.7	22.5	
	11-	44.0	24.0		9.0	0.0	
	16 & More	58.0	19.7		17.0	13.1	
Medication currently prescribed for the patient	Atypical Antipsychotic	54.9	16.7	Z=.81 (.497) Test (P)	24.1	17.7	Z=.81 (.497)
	Mixed Antipsychotic	54.3	19.5		14.0	12.3	

Z: Mann-Whitney test

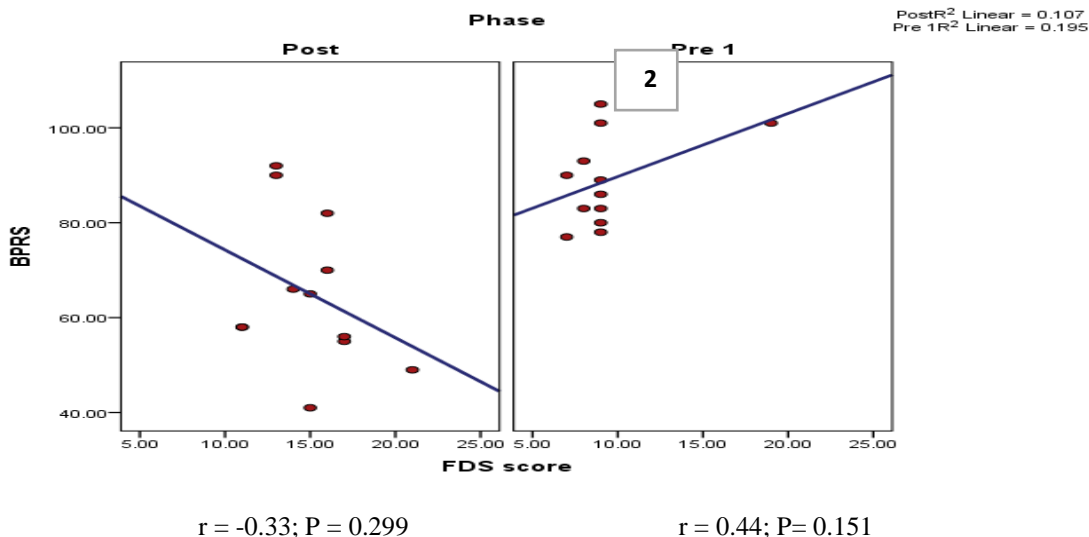
X<sup>2</sup>: Kruskal-Wallis test

Figure 3 presents a scatter diagram to describe the relation between psychiatric symptoms severity and cognitive flexibility (Perseverative error) at different study phases. At pre intervention phase 2, the figure shows an increase in psychiatric symptoms severity as well as the total number of perseverative errors, while at post intervention phase, a decrease in psychiatric symptoms and the total number of perseverative errors were noticed (neither r nor P can be calculated because it is a descriptive graph, perseverative error is a quantitative variable and psychiatric symptoms is a qualitative variable which is different from a scatter diagram for correlation).



**Figure (3) Relation between psychiatric symptoms severity and cognitive flexibility (Perseverative error) at different study phases: A scatter diagram**

Figure 4 shows a scatter diagram for correlation between psychiatric symptoms severity and working memory at different study phases. The figure presents an insignificant correlation between psychiatric symptoms severity and working memory neither at pre nor and post-intervention phases ( $r = -0.33$ ;  $P = 0.299$ ,  $r = 0.44$ ;  $P = 0.151$ , respectively)



**Figure (4) Correlation between psychiatric symptoms severity and working memory at different study phases: A scatter diagram**

Table 5 shows the variables predicting psychiatric symptoms among studied subjects according to the multiple linear regression analysis. The model accounted for 47% of variance in the studied patients with schizophrenia who had cognitive flexibility (perseverative error). Psychiatric symptoms significantly increased with the increased patients' perseverative error as one aspect of cognitive flexibility ( $p = 0.016$ ) with regression coefficient 0.51 and  $SE = 0.2$ . Other aspects of cognitive flexibility (categories achieved) as well as their working memory were not significant predictors of psychiatric symptoms in the model.

**Table (5) Variables predicting psychiatric symptoms among studied subjects according to multiple linear regression analysis**

Predictor	Unstandardized Coefficients		Standardized Coefficients	t	P-value
	B	SE	Beta		
(Constant)	63.6				
Cognitive flexibility (Categories achieved)	1.20	1.9	0.17	0.6	0.531
Cognitive flexibility (Perseverative error)	0.51	0.2	0.67	2.6	0.016*
Working memory	-0.99	0.9	-0.23	-1.1	0.276
Model Significance $R^2$	F=6.1; P=.004* 47%				

B: Regression coefficient

SE: Standard error

$R^2$ : model accuracy

#### IV. DISCUSSION

The present study revealed that patients who received Cognitive Remediation Therapy exhibited significant improvement in the mean scores of the cognitive flexibility (perseverative error and number of categories achieved) and working memory. These results may be generally attributed to the acquired competencies and skills developed in the studied patients with schizophrenia during the implementation of the cognitive flexibility and working memory modules of cognitive remediation therapy. As known, this training program encompasses a wide array of tasks that all have different cognitive skills (Sustained attention, Self-monitoring, Verbal mediation, Self-regulation of behaviour, Visual attention to

details, Perception of parts, Mental flexibility, Designing and implementation of a strategy, Prospective memory, Verbal expression, Shifting between two cognitive sets, and Mental manipulation of images).

On the same line, Wykes and Reeder (2005), Wykes et al., (2011), Cella et al. (2017), & Fan et al., (2017) confirmed the effectiveness of cognitive remediation therapy in improving clinical, cognitive, social, and functional parameters in patients with schizophrenia, both in patients in the early course and in chronic patients. Moreover, Reilly et al., (2019) ; Deste et al., (2019) found that CRT is an effective intervention for patient groups with schizophrenia experiencing severe cognitive impairments. Those who received CRT demonstrated improved global cognitive performance both at the end of treatment and follow up.

In relation to cognitive flexibility, Delahunty et al., (1996) in their study of specific cognitive flexibility rehabilitation in patients with schizophrenia, reported improvement in Wisconsin Card Sorting Test performance following the Cognitive Shift module. Wykes et al., (2007); Pillet et al. (2014) revealed that cognitive flexibility was improved with fewer perseverative errors and improvement in number of categories achieved in the WCST. Conversely, Omiya et al., (2016) in their study of "the effects of Cognitive Remediation Therapy using the Frontal/Executive Program for treating chronic schizophrenia, reported no significant improvement on WCST after implementation of CRT.

Speaking of working memory, Wykes et al. (2003) who investigated brain activation during a working memory task before and after CRT, who confirmed that normal performance on the working memory tasks were associated with frontal lobe activation, which gradually decreased over time as the participants became more skilled at the task. Participants with schizophrenia in their study showed significantly lower frontal lobe activation before CRT application that increased over time after CRT. Such findings seem to suggest that CRT effected improvement in specific neurocognitive performance, which in turn increases the efficiency of cognitive function. This was also supported by Delahunty & Morice (1996).

However, working memory for all subjects in the present study improved from low to a moderate level after conducting the CRT program. These could be explained by the fact that 8, and 9 digits in forward digit test and 5 to 8 digits in backward digits tests are reasonably difficult to remember for most of normal people and hence for studied patients with schizophrenia . This result is consistent with the findings obtained by Wykes et al., (2007) who revealed that cognitive remediation therapy is associated with durable improvements in working memory, which in turn are associated with social functioning improvements in people with schizophrenia. Similarly, Pillet et al. (2014) in their study of benefits of cognitive remediation therapy (CRT) on patients with schizophrenia with low initial memory performances, revealed a general improvement of working memory at the end of CRT program. Likewise, Omiya et al. (2016) in their study of the effects of cognitive remediation therapy using the frontal/executive program found improvement in working memory of patients with chronic schizophrenia.

The present study also showed that psychiatric symptoms (Anxiety, Depression, all negative symptoms, and most of positive symptoms) improved after implementing the cognitive remediation therapy on patients with chronic schizophrenia. This could be explained by the fact that low motivation is a symptom common in those with a diagnosis of schizophrenia, for whom it is considered a negative symptom, and is often associated with the presence of depressive symptoms (Barch & Dowd 2010). Moreover, the researcher in the present study practiced several techniques (massed practice, errorless learning, scaffolding and positive reinforcement) with patients during CRT. Knowing that in this training method the tasks are completed through the use of pencil and paper, and require patients to actively and independently perform the exercises in order to achieve the functional improvement, can lead to increment in patients' initiative and intrinsic motivation. Consequently, patients' engagement in program, feeling of success, achievement in most of tasks, and increasing patients' motivation can be reflected on patients' improvement of depressive symptoms.

Another interpretation of the statistical significant positive impact of CRT application on the patients' negative symptoms is given by Frith (1992). Given that negative symptoms have been attributed to difficulties in generating internally cued actions and intentions and to coping with information overload by avoidance. In this respect, CRT is known to aim and interfere to improve self-regulation of behavior, thus can lead to increased or better regulated self-driven behaviour and to more adaptive coping with overwhelming cognitive materials (Wykes& Reeder, 2005). This result is in accordance with other studies of Cella et al. (2014), Lanfredi et al. (2016) who found that CRT have a positive impact on negative symptoms reduction in patients with schizophrenia. In relation to this, Linke et al. (2017) in their study of effects of cognitive remediation therapy versus other interventions on cognitive functioning in schizophrenia inpatients concluded that CRT had greater effect on psychiatric symptoms reduction, namely on negative symptoms.

Furthermore, positive symptoms (Grandiosity, Suspiciousness, Hallucinations, Unusual thoughts, Bizzar Behavior) have improved after implementation of CRT program on patients in the current study. It is known that CRT is a manual based individualized therapy and all sessions of program are composed of drawings, tokens and cards work, which are colorful, attractive that grasp, engage, and stimulate patients' attention. Moreover, CRT sessions consumed a good sector of patients' time (one hour/ 4 times per week for six weeks). During such time, patients were primarily engaged, stimulated and preoccupied with real objects rather than unusual thoughts and hallucinations, had to concentrate on the required job, and to deal with the researcher's instructions i.e, deal with reality.

As related to, Wykes and Reeder (2005) and Linke et al., (2017) added and confirmed that CRT can reduce positive symptoms by encouraging reflection on thinking processes and the reappraisal of faulty attributions by reality testing and cognitive challenging. One of the schizophrenia patients' symptomatology is the perseveration of ideation. It is known that this could be a possible factor involved in the generation and maintenance of delusional systems in schizophrenia. The ability to shift such rigidity with cognitive flexibility retraining could have important implications for the treatment of chronic schizophrenia (Delahunty et al., 1996).

In general the a formentioned results were supported by Twamley et al., (2011) who reported that patients with schizophrenia who received cognitive remediation therapy have significant improvement on the positive and negative symptoms. Similarly, Pillet et al. (2014) showed a consistent improvement in positive and negative symptoms after implementation of Cognitive remediation therapy. Likewise, Farreny et al., (2016) in their study of "Baseline Predictors for Success Following Strategy-Based Cognitive Remediation Group Training in Schizophrenia", confirmed the improvement in positive, negative, and disorganized symptoms following CRT.

Conversely to the present study results, Amato et al., (2011) in their study of a randomized controlled trial of computer-assisted cognitive remediation for schizophrenia patients, observed no improvement of positive or negative symptoms in patients with schizophrenia following implementation CRT. Also, Morimoto et al., (2018) reported no evidence of significant differences between a group who received Cognitive remediation therapy and a control group regarding psychiatric symptoms.

Likewise, the present study showed that psychiatric symptoms had a statistically significant negative correlation with cognitive flexibility. This result is also supported by the multiple linear regression analysis which showed that psychiatric symptoms increased with the increased patients' perseverative error as one aspect of cognitive flexibility. Functional imaging studies have demonstrated that cognitive rigidity is consistently associated with under-activation of the fronto-striatal brain circuits such as the Anterior Prefrontal Cortex, in particular the Orbitofrontal Cortex (OFC), posterior parietal cortex (PPC) and possibly the Medial Prefrontal Cortex (MPFC). Since under-activation of those brain areas is associated with diminished cognitive flexibility (set-shifting) (Morice, 1990; Leber, 2008; Izquierdo et al., 2017).

Speaking of the aforementioned prefrontal regions, they are richly innervated by various neuromodulator systems – including those for dopamine (DA), serotonin (5- hydroxytryptamine, or 5HT), and acetylcholine – suggests that these systems have the ability to influence set-shifting, as well. This idea is strongly supported by available evidence, as both dopamine and serotonin systems are clearly implicated in both neuropsychiatric illness and set-shifting impairments. Furthermore, there is considerable evidence that cognitive flexibility (set-shifting behavior) can be influenced by dopamine and serotonin (Waltz, 2017). Several studies confirmed that abnormal recruitment of these neural circuits, contributes to the presence of both positive, negative, and disorganization symptoms in schizophrenia (Snitz, 2005; Yoon, 2008; Edwards et al., 2010). Known that CRT aims to stimulate and exercise the frontal lobe information processes directly so as to increase cognitive flexibility and working memory this can explain the improvement in cognitive flexibility and psychiatric symptoms gained in the present study

Consistent with previous result of current study, Fresco et al. (2006) reported that cognitively flexible individuals have been found to employ a greater variety of explanations for events than more rigid individuals, and have alternative attributions in different situations and this attributional flexibility is associated with endorsement of fewer symptoms of depression and anxiety. These results are in accordance with Hayes et al. (2006) who noted that greater inflexibility is related to a greater probability of having a psychiatric disorder and to greater endorsement of symptoms of depression and anxiety. In the same line, Johnson (2016) in his study of the relationship between cognitive flexibility, coping, and symptomatology in psychotherapy reported a negative relationship between cognitive flexibility and symptom severity.

Concerning working memory, the present study revealed no significant correlation between psychiatric symptoms severity and working memory at pre and post-intervention phases. This result was confirmed by Forbes et al. (2009) and Huang et al. (2019) who reported that the severity of positive or negative psychotic symptoms did not seem to affect the magnitude of performance deficit across the range of working memory tests, therefore no consistent association was noticed between psychotic symptoms profile and working memory in patients with schizophrenia. They suggested that working memory deficits relate to an aspect of the schizophrenic trait.

On the same line, Frydecka et al. (2014) using Positive and Negative Syndrome Scale (PANSS) ,observed that there is lack of association between working memory performance in patients with schizophrenia with positive and general psychopathology symptoms. This may be attributed to the fact that positive and general symptoms are associated with possibly altered activity in the areas less crucial to working memory performance, such as the hippocampus and the basal ganglia (Tamminga et al., 2010; Pankow et al., 2012; Sorg et al., 2013). On the other hand, Frydecka et al., 2014 reported only there is a negative correlation between working memory and negative symptoms. Heckers et al., (1999); Monteleone et al., (2002) suggested that negative symptoms are believed to result from decreased dopaminergic activity in the prefrontal cortex directly involved in working memory. Recently, Okasha et al., (2020) carried out a study on "Cognitive dysfunction among in patients and outpatients with schizophrenia: relationship to positive and negative symptoms". They revealed in their study that cognitive functions were negatively correlated with the positive and general symptoms of PANSS and not correlated with its negative symptoms.

On the other side, investigating the relationship between both of socio-demographic and clinical characteristics with total mean scores of cognitive flexibility and working memory among studied patients, yielded no statistically significant relation with any of the portrayed items neither on the pre intervention phase nor on the post intervention. This lack of significant relations probably reflect a fact that cognitive impairment associated with schizophrenia is independently affected by the patients' cognitive flexibility and working memory. This result is consistent with most of other studies. Wykes et al. (2011); Franck et al (2013); Bosia et al. (2014); Farreny (2016); Penadés et al.( 2016); Okasha et al.,(2020) reported that patients with schizophrenia show considerable cognitive improvement regardless of the sociodemographic and clinical characteristics (Gender, Age, Educational level, duration of illness, type and dose of antipsychotic medication) after implementing cognitive remediation therapy.

Conversely, Bowie et al. (2014) in their study of "Cognitive remediation in schizophrenia: efficacy and effectiveness in patients with early versus long-term course of illness", reported that duration of illness was inversely associated with cognitive functions. Likewise, Wykes et al. (2007) in their study of the impact of cognitive remediation therapy on patients with schizophrenia found a relationship between medication type and cognitive outcome, with the use of either clozapine or typical medication conferring a benefit not apparent in those taking atypical medications.

By the end, one can tell that the whole study results add to the growing data base for improved cognitive functioning in patients with schizophrenia, by using a neurocognitive training such as the one used in the present study (Cognitive Remediation Therapy). The results also testifies to the learning potential of this patients group as mentioned by Olbrich & Mussgay (1990); Frost et al., (1991); Tompkins et al. (1991).

## V. CONCLUSION

According to finding of the present study, it can be concluded that the Cognitive Remediation Therapy program (CRT) can contribute positively in the improvement of cognitive flexibility, working memory, and psychiatric symptoms in patients with schizophrenia. Such improvements can enhance patients' psychosocial functioning and hence potentiate the benefits to be derived from the existing rehabilitation programs (psychoeducation, psychotherapy, activities of daily living, occupational therapy..., etc).

## VI. RECOMMENDATIONS

**Accordingly the following are the main recommendations of the present study:**

- Psychiatric hospitals may consider the application of Cognitive Remediation Therapy (CRT) intervention as an integral component in the hospital routine care of patients with schizophrenia.
- Based on previous the recommendation a discharge plan for patients with schizophrenia may include tasks of CRT program to promote cognitive abilities, decrease psychiatric symptoms, and thus decrease patients' relapses and foster their adaptation back to community.

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- The CRT intervention program can be incorporated in the psychiatric hospital's protocol of care including appropriate tools needed for CRT applications (pictures, videos, cards... etc).
- Further research is clearly needed to cover and complement the following points:
  - Extend the application of CRT to cover all its modules (cognitive flexibility, working memory, and planning)
  - Extend the application of CRT to test its impact on patients' social functioning.
  - Because of limitation of time in the present study, further studies are needed.

**REFERENCES**

- [1] Amato, Th ., Bation, R., Cochet, A. Jalenques, Galland, F Elisabeth Giraud-Baro, E., Troncin, M ., Astolfi, F ., Llorca, P., Saoud, M., Brunelin, J. (2011). Arandomized, controlled trial of computer-assisted cognitive remediation for schizophrenia. *Schizophrenia Research*, 125, 284–290.
- [2] Anaya, C., Aran, A ., Mateos, J ., Wykes, T., Vieta, E., & Scott, J. (2012). A systematic review of cognitive remediation for schizo-affective and affective disorders. *Journal of Affective Disorders*, 142, 13–21.
- [3] Baddeley, A. (2000). The episodic buffer: a new component of working memory. *Trends in Cognitive Sciences*, 4(11), 417-23.
- [4] Baddely, A. (1992). Woking memory. *Science Journal*, 255, 556-559.
- [5] Balzan, R., Neaves, A., Denson, L., Liu, D., & Galletly, C. (2014). Cognitive deficit awareness in schizophrenia: absent, intact, or somewhere in-between. *Cognitive Neuropsychiatry*, 19 (6), 471–484.
- [6] Barch, D., & Dowd, E. (2010). Goal Representations and Motivational Drive in Schizophrenia: The Role of Prefrontal–Striatal Interactions. *Schizophrenia Bulletin*, 36 (5), 919–934.
- [7] Bell, M., Choi, K., Dyer, C., & Wexler, B. (2014). Benefits of Cognitive Remediation and supported employment for schizophrenia patients with poor community functioning. *Psychiatry Services*, 56(4), 449-475.
- [8] Berg, E. (1948). A Simple Objective Technique for Measuring Flexibility inThinking. *The Journal of General Psychology*, 39, 15-22.
- [9] Bosia, M., Zanolettica, A., Spangaro, M., Buonocore, M., Bechia, M., Cocchia, F., Pirovano, A., Lorenza, C., Bramantid, P., Smeraldia, E., & Roberto Cavallaro, R. (2014). Factors affecting cognitive remediation response in schizophrenia: The role of COMT gene and antipsychotic treatment. *Psychiatry Research*, 217, 9–14.
- [10] Bowie, C., Grossman, M., Gupta, M. Oyewumi, K., & Harvey, P. (2014). Cognitive Remediation in schizophrenia: efficacy and effectiveness in patients with early versus long term course of illness. *Early Intervention in Psychiatry*, 8, 32–38.
- [11] Cañas, J., Fajardo, I., & Salmerón, L. (2015). Cognitive flexibility. *Research Gate*, 296-301. Available at: <https://www.researchgate.net/publication/272022148> (Retrieved on 20/6/2017).
- [12] Caruana, E., Cotton, S., Killackey, E., & Allott, K. (2015). The relationship between cognition, job complexity, and employment duration in first-episode psychosis. *Psychiatric Rehabilitation Journal*, 38(3), 210–217.
- [13] Cella, M., Reeder, C., & Wykes, T. (2014). It is all in the factors: Effects of cognitive remediation on symptom dimensions. *Schizophrenia Research* 156, 60–62.
- [14] Cella, M., Stahl, D., Morris, S., Keefe, R., Bell, M., & Wykes, T. (2017). Effects of cognitive remediation on negative symptoms dimensions: exploring the role of working memory. *Psychological Medicine*, 47, 2593–2601.
- [15] Dajani, D., & Uddin, L. (2015). Demystifying cognitive flexibility: Implications for clinical and developmental neuroscience. *Trends in Neurosciences*, 38(9), 571-578.
- [16] Danner, U., Dingemans, A., & Joanna Steinglass, J. (2015). Cognitive remediation therapy for eating disorders. *Wolters Kluwer Health, Inc.*, 28(6), 468-472.

**International Journal of Novel Research in Healthcare and Nursing**

 Vol. 8, Issue 1, pp: (636-654), Month: January - April 2021, Available at: [www.noveltyjournals.com](http://www.noveltyjournals.com)

- [17] Dark, F., Meredith Harris, M., Jones, V., Newman, E., & Whiteford, H. (2018). Implementing cognitive remediation and social cognitive interaction training into standard psychosis care. *BMC Health Services Research*, 18(458), 1-7.
- [18] Davidson, M., & Matei, V. (2007). Cognitive functioning as an endophenotype to investigate schizophrenia. *Revista Română de Psihiatrie*, 9 (3), 1-11.
- [19] Delahunty, A., Morice, R. (1996). Rehabilitation of frontal/executive impairments in schizophrenia. *Australian and New Zealand Journal of Psychiatry*, 30, 760-767.
- [20] Delahunty, A., Morice, R., Frost, B. (1996). Specific cognitive flexibility rehabilitation in schizophrenia. *Psychological Medicine*, 23, 221-27.
- [21] Delahunty, A., Reeder, C., Wykes, T., Morice, R., & Newton, E. (2000). Cognitive Remediation Therapy. In: Wykes, T., Reeder, C. (2005). *Cognitive remediation therapy for schizophrenia theory and practice*, New York, Routledge.
- [22] Deste, G., Barlati, S., Galluzzo, A., Corsini, P., Valsecchi, P., Turrina, C., & Antonio Vita, A. (2019). Effectiveness of Cognitive Remediation in Early Versus Chronic Schizophrenia: A Preliminary Report. *Frontiers in Psychiatry*, 10, 1-6.
- [23] Digital Library Unit. Institute of Graduate Studies and Research. 2018. Alexandria University.
- [24] Eack, Sh., Hogarty, G., Cho, R., Prasad, K., Greenwald, D., Hogarty, S., & Keshavan, M. (2010). Neuroprotective effects of cognitive enhancement therapy against gray matter loss in early schizophrenia. *Arch Gen Psychiatry*, 67(7), 674-682.
- [25] Edwards, B., Barch, D & Braver, T. (2010). Improving prefrontal cortex function in schizophrenia through focused training of cognitive control. *Front. Hum. Neuroscience*. 4, 32-40.
- [26] Elnakeeb, M. (2013). The relationship of social cognition and psychotic symptoms with social functioning of schizophrenic patients. Unpublished Doctorate Dissertation. Faculty of Nursing, Alexandria University, 28-9.
- [27] Eweida, R. (2017). Problem solving ability and working memory capacity of patients with schizophrenia: the effect of Problem Solving Training Intervention. Unpublished Doctorate Dissertation. Faculty of Nursing, Alexandria University, 2017, 27.
- [28] Fan, Q., Liao, L., & Pan, G. (2017). The application of cognitive remediation therapy in the treatment of mental disorders. *Shanghai Archives of Psychiatry*, 29(6), 373-375.
- [29] Farreny, A., Aguado, J., Corbera, S., Susana Ochoa, S., Ramos, E & Usall, J. (2016). Baseline predictors for success following strategy-based cognitive remediation group training in schizophrenia. *The Journal of Nervous and Mental Disease*, 1-5.
- [30] Forbes, N., Carrick, L., McIntosh, A., & Lawrie, S. (2008). Working memory in schizophrenia: a meta-analysis. *Psychological Medicine*, 39, 889-905.
- [31] Forbes, N., Carrick, L., McIntosh, A., & Lawrie, S. (2009). Working memory in schizophrenia: a meta-analysis. *Psychological Medicine*, 39, 889-905.
- [32] Franck, N., Duboc, C., Sundby, C., Isabelle Amado, I., Wykes, T., Demily, C., Launay, C., Roy, V., Bloch, P., Willard, D. Todd, A., Petitjean, F., Foullu, S., Briant, P., Grillon, M., Deppen, P., Hélène Verdoux, H., Bralet, M., Dominique Januel, D., Riche, B., Roy, P., & Vianin, P. (2013). Specific vs general cognitive remediation for executive functioning in schizophrenia: A multicenter randomized trial. *Schizophrenia Research*, 147, 68-74.
- [33] Fresco, D., Williams, N., & Nugent, N. (2006). Flexibility and negative affect: examining the associations of explanatory flexibility and coping flexibility to each other and to depression and anxiety. *Cogn Ther Res*, 30, 201-210.

**International Journal of Novel Research in Healthcare and Nursing**

 Vol. 8, Issue 1, pp: (636-654), Month: January - April 2021, Available at: [www.noveltyjournals.com](http://www.noveltyjournals.com)

- [34] Frith, D. (1992)a. The cognitive neuropsychology of schizophrenia. Hove, UK, Lawrence Erlbaum Associates. In: Wykes, T., Reeder, C. (2005). Cognitive remediation therapy for schizophrenia theory and practice, New Yourk, Routlege.
- [35] Frost, B., Morice, R., Delahunty, A., Gulliver, S., Ryan, M., Frampton, G., Connolly, S. & Hunter, M. (1991). Neurocognitive and psychosocial rehabilitation of chronic schizophrenia: a clinical study. In Brain Impairment: Proceedings of the Fifteenth Brain Impairment Conference, 49-57.
- [36] Frydecka, D., Eissa, A., Hewedi, D., ManalAli, M., Drapała, J., Misiak, B., ska1, E., Joseph, R., Phillips, J., Ahmed, A., & Moustafa, A. (2014). Impairments of working memory in schizophrenia and bipolar disorder: the effect of history of psychotic symptoms and different aspects of cognitive task demands.
- [37] Galaverna, F., Morra, C., & Bueno, A. (2012). Attention in patients with chronic schizophrenia: Deficit in inhibitory control and positive symptoms. *Eur. J. Psychiat*, 26(3), 185-195.
- [38] Grau, N., Abadal, E., Usall, J., Barajas, A., Butjosa, A., Dolz, M., Baños, I Sánchez, B., Rodríguez, M., Pelaez, T., Sammut, S., Carlson, J., Ramos, E., & Ochoa, S. (2016). Influence of cognition, premorbid adjustment and psychotic symptoms on social functioning in first episode psychosis. *Psychiatry Research*, 121, 1-16.
- [39] Gur, R., Calkins, M., Theodore, D., Satterthwaite, Th., Ruparel, K., Bilker, W., Moore, T., Savitt, A., Hakonarson, H., & Gur, R. (2014). Neurocognitive Growth Charting in Psychosis Spectrum Youths. *JAMA Psychiatry*, 71(4), 366-374.
- [40] Hajri, M., Abbes, Z., Yahia, H., Ouanes, S., Halayme, S., Bouden, A., Marbet, A., & Amado, I. (2016). Effects of Cognitive Remediation Therapy in children with autism spectrum disorder. *International journal of science and research*, 5(7), 7-12.
- [41] Hajri, M., Abbes, Z., Yahia, B., Boudali, M., Halayme, S., Othman, S., Bouden, A., & Ouanes, S. (2015). Effects of Cognitive Remediation in patients with mood disorder. *European psychiatry*, 30(1), 28-31.
- [42] Hayes, S., Luoma, J., Bond, F., Masuda, A., Lillis, J. (2006). Acceptance and commitment therapy: Model, processes, and outcomes. *Behaviour Research and Therapy*, 44, 1-25.
- [43] Heaton, R. (1981). Wisconsin Card Sorting Test Manual. In: Ozonoff, S. (1995). Reliability and validity of the Wisconsin Card sorting Test in studies of autism. *Neuropsychology Journal*, 9(4), 491-500.
- [44] Heaton, R., Chelune, G., Tallery, J., Kay, G., & Curtiss, G. (1993). Wisconsin Card Sorting Test Manual: revised and expanded. Psychological Assessment Resources. In: Ozonoff, S. (1995). Reliability and validity of the Wisconsin Card sorting Test in studies of autism. *Neuropsychology Journal*, 9(4), 491-500.
- [45] Heckers, S., Goff, D., Schacter, D., Savage, C., Fischman, A., Alpert, N., & Rauch, S. (1999). Functional imaging of memory retrieval in deficit VS non deficit schizophrenia. *Arch Gen Psychiatry*, 56, 1117-1123.
- [46] Huang, A., Rogers, B., Anticevic, A., Blackford, J., Stephan Heckers, S., & Woodward, N. (2019). Brain function during stages of working memory in schizophrenia and psychotic bipolar disorder. *Neuropsychopharmacology*, 44, 2136 – 2142.
- [47] Hussien, M. (2018). Professor of Biostatistics. Higher Institute of Public Health; personal communication.
- [48] Izquierdo, A., Brigman, J., Radke, A., Rudebeck, P., & Holmes, A. (2017). The neural basis of reversal learning: An updated perspective. *Neuroscience*, 345, 12–26.
- [49] Johnson, B. (2016). The relationship between cognitive flexibility, coping, and symptomatology in psychotherapy. Master Thesis, Faculty of the Graduate School, Marquette University.
- [50] Lacoste, L. (2015). Cognitive remediation to take care of schizophrenic patients today. *Neural Disord Journal*, 3(1), 1-4.



- [51] Lanfredi, M., Deste, G., Ferrari, C., Barlati, S., Magni, L., Roberta Rossi, R., Peri, L., Bonomi, M., Rossi, G., & Vita, A. (2016). Effects of cognitive remediation therapy on neurocognition and negative symptoms in schizophrenia: an Italian naturalistic study. *Cognitive Neuropsychiatry*, 1-17.
- [52] Leber, A., Turk-Browne, N., Chun, M. (2008). Neural predictors of moment-to-moment fluctuations in cognitive flexibility. *Proc Natl Acad Sci USA*, 105(36), 13592- 13597.
- [53] Linke, M., Jankowski, K., Wichniak, A., Jarema, M., & Wykes, T. (2017). Effects of cognitive remediation therapy versus other interventions on cognitive functioning in schizophrenia inpatients. *Neuropsychological Rehabilitation*, 1-13.
- [54] Liu, Sh., Chiu, C., Chang, C., Hwang, T., Hwu, H., & Chen, W. (2002). Deficits in Sustained Attention in Schizophrenia and Affective Disorders: Stable Versus State-Dependent Markers. *American Journal of Psychiatry*, 159, 975–982.
- [55] Monteleone, P., Lieto, A., Martiadis, V., Bartoli, L., & Maj, M. (2002). Correlations between negative symptoms and peripheral G protein levels in mononuclear leukocytes of deficit and non-deficit schizophrenics. *Eur Arch Psychiatry Clin Neurosci*, 252, 214–218.
- [56] Morice, R. (1990). Cognitive inflexibility and pre-frontal dysfunction in schizophrenia and mania. *Br J Psychiatry*, 157, 50-54.
- [57] Morice, R., & Delahunty, A. (1996). Frontal/executive impairments in schizophrenia. *Schizophrenia Bulletin*, 22(1), 125-137.
- [58] Morimoto, T., Matsuda, Y., Matsuoka, K., Yasuno, F., Ikebuchi, E., Kameda, H., Taoka, T., Miyasaka, T., Kichikawa, K., & Kishimoto, T. (2018). Computer-assisted Cognitive Remediation Therapy increases hippocampal volume in patients with schizophrenia: a randomized controlled trial. *BMC Psychiatry*, 18(83), 1- 8.
- [59] Mullen, A. (2009). Mental health nurses establishing psychosocial interventions within acute inpatient settings. *International Journal of Mental Health Nursing*, 18, 83–90.
- [60] Niendam, T., Bearden, C., Rosso, I., Sanchez, L., Hadley, T., Naechterlein, K., Cannon, T. (2003). A prospective study of childhood Neurocognitive functioning in schizophrenic patients and their siblings. *AMJ Psychiatry*, 160, 2060-2062.
- [61] Norman, R., Carr, J., & Manchanda, R. (2015). Cognition and the prediction of functioning in patients with a first treated episode of psychosis: A prospective study. *Schizophrenia Research*, 1-5.
- [62] Okasha, T., Hanan Hussein, H., Shorub, E., Nagi, H., Moustafa, A., & El-Serafi, D. (2020). Cognitive dysfunction among in patients and outpatients with schizophrenia: relationship to positive and negative symptoms. *Middle East Current Psychiatry*, 27(58), 1-7.
- [63] Olbrich, R. & Mussgay, L. (1990). Reduction of schizophrenia deficits by cognitive training: an evaluative study. *European Archives of Psychiatry & Neurological Sciences* 239, 366-369.
- [64] Omiya, H., Yamashita, K., Miyata, T., Hatakeyama, Y., Miyajima, M., Yambe, K., Matsumoto, I., Mastui, M., Toyomaki, A., & Denda, K. (2016). The effect of cognitive remediation therapy using the frontal executive program for treating chronic schizophrenia. *The open psychology Journal*, 9, 121-28.
- [65] Otong, D. (2003). Psychosocial rehabilitation. *The Nursing Clinics of North American*, 38, 151-160.
- [66] Pankow, A., Knobel, A., Voss, M., & Heinz, A. (2012). Neurobiological correlates of delusion: beyond the salience attribution hypothesis. *Neuropsychobiology*, 66, 33–43.
- [67] Penadés, R., Pujol, N., Catalán, R., Masana, G., Rizo, C., Bargalló, N., Rodríguez, A., Piñeiro, D., Miquel Bernardo, M., Carme Junqué, C. (2016). Cortical thickness in regions of frontal and temporal lobes is associated with responsiveness to cognitive remediation therapy in schizophrenia. *Schizophrenia Research*, 171, 110–116.

**International Journal of Novel Research in Healthcare and Nursing**

 Vol. 8, Issue 1, pp: (636-654), Month: January - April 2021, Available at: [www.noveltyjournals.com](http://www.noveltyjournals.com)

- [68] Penades, R., Pujol, N., Catalan, R., Massana, G., Rametti, G., Garcia-Rizo, C., Bargallo, N., Gasto, C., Bernardo, M., & Junque, C. (2013). Brain effects of cognitive remediation therapy in schizophrenia: a structural and functional neuroimaging study. *BIOL Psychiatry*, 73, 1015–1023.
- [69] Penadés, R., Rosa Catalán, R., Salamero, M., Boget, T., Puig, O., Guarch, J., & Gastó, C. (2006). Cognitive remediation therapy for outpatients with chronic schizophrenia: a controlled and randomized study. *Schizophrenia Research*, 87, 323–331.
- [70] Pillet, B., Morvan, Y., Todd A., Franck, N., Duboc, C., Grosz, A., Laanay, C., Demily, C., Gaillard, R., Krebs, M., & Amado, I. (2014). Cognitive remediation therapy benefits more to patients with schizophrenia with low initial memory performance. *An international Multi-Disciplinary Journal*, 1-8.
- [71] Reichenberg, A. (2005). Cognitive impairment as a risk factor for psychosis. *Dialogues in Clinical Neuroscience*, 7(1), 31-38.
- [72] Reilly, K., Donohoe, G., Sullivan, D., Coyle, C., Corvin, A., Flynn, P., Donnell, M., Galligan, T., Connell, P., & Kennedy, H. (2019). A randomized controlled trial of cognitive remediation for a national cohort of forensic patients with schizophrenia or schizoaffective disorder. *BMC Psychiatry*, 19(27), 1-12.
- [73] Seidman, L., Cherkerzian, S., Goldstein, J., Agnew-Blais, J., Tsuang, M., & Buka, S. (2013). Neuropsychological performance and family history in children at age 7 who develop adult schizophrenia or bipolar psychosis in the New England family studies. *Journal of Psychological Medicine*, 1-13.
- [74] Selim, A. (2006). Development of a risk symptom list for prediction of psychotic inpatient's aggression. Unpublished Doctorate Dissertation. Faculty of Nursing, Alexandria University, 27.
- [75] Shin, Y., Joo, Y., & Kim, J. (2016). Self-perceived cognitive deficits and their relationship with internalized stigma and quality of life in patients with schizophrenia. *Neuropsychiatric Disease and Treatment*, 12, 1411–1417.
- [76] Snitz, B. Lateral and medial hypo-frontality in first-episode schizophrenia: functional activity in a medication-naive state and effects of short-term atypical antipsychotic treatment. (2005). *Am. J. Psychiatry*, 162, 2322–2329.
- [77] Sorg, C., Manoliu, A., Neufang, S., Myers, N., Henning Peters, H., Schwerthoffer, D., Scherr, M., Muhlau, M., Claus Zimmer, C., Drzezga, A., Hans Forstl, H., Bauml, J., Eichele, T., Wohlschlagler, A., & Valentin Riedl, V. (2013). Increased intrinsic brain activity in the striatum reflects symptom dimensions in schizophrenia. *Schizophrenia Bulletin*, 39(2), 387–395.
- [78] Stouten, L., Veling, W., Laana, W., Helma, M., Gaag, M. (2014). Psychotic symptoms, cognition and affect as predictors of psychosocial problems and functional change in first-episode psychosis. *Schizophrenia Research*, 158, 113–119.
- [79] Strawbridge, R., Fish, J., Halari, R., John Hodso, J., Reeder, C., Macritchie, K., McCrone, P., Wykes, T., & Young A. (2016). The Cognitive Remediation in Bipolar (CRiB) pilot study: study protocol for a randomised controlled trial. *Bio Med Central*, 17, 1-9.
- [80] Stuart, G., & Laraia, M. (2013). Principles and psychiatric nursing. 10th ed. St. Louis, Mosby, 79-81.
- [81] Tamminga, C., Stan, A., & Wagner, A. (2010). The hippocampal formation in schizophrenia. *Am J Psychiatry*, 167, 1178–1193.
- [82] Tompkins, L., Goldman, R. & Axelrod, B. (1991). Modifying the Wisconsin Card Sorting Test performance of schizophrenic patients. *American Journal of Psychiatry*, 148, 1613.
- [83] Tripathi, A., Kar, S & Shukla, R. (2018). Cognitive deficits in schizophrenia: understanding the biological correlates and remediation strategies. *Clinical Psychopharmacology and Neuroscience*, 16(1), 7–17.
- [84] Tsang, H., Leung, A., Chung, R., Morris Bell, M., & Cheung, W. (2010). Review on vocational predictors: a systematic review of predictors of vocational outcomes among individuals with schizophrenia. *Australian and New Zealand Journal of Psychiatry*, 44, 495–504.

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- [85] Twamley, E., Burton, C., & Vella, L. (2011). Compensatory cognitive training for psychosis: who benefits? who stays in treatment?. *Schizophrenia Bulletin*, 37(2), 55–62.
- [86] Ventura, J., Lukoff, D., Nuechterlein, K., Liberman, R., Green, M., & Shaner, A. (1993). Appendix 1: Brief Psychiatric Rating Scale (BPRS) Expanded version (4.0) scales, anchor points and administration manual. *International Journal of Methods in Psychiatry*, 3, 227–44.
- [87] Waltz, J. (2017). The Neural Underpinnings of Cognitive Flexibility and their Disruption in Psychotic Illness. *Neuroscience*, 345, 203–217.
- [88] Weschler, D. (1981). Weschler Memory scale. In: Ostrosky, F., & Lozano, A. (2006). Digit Span: effect of education and culture. *International Journal of psychology*, 41(5), 333-341.
- [89] Wykes, T., Huddy, V., Cellard, C., McGurk, S., & Czobor, P. (2011). A Meta-Analysis of Cognitive Remediation for Schizophrenia: Methodology and Effect Sizes. *American Journal of Psychiatry*, 168 (5), 472–485.
- [90] Wykes, T., Reeder, C. (2005). *Cognitive remediation therapy for schizophrenia theory and practice*, New York, Routledge.
- [91] Wykes, T., Reeder, C., Landau, S., Everitte, B., Knapp, M, patel, A., & Romeo, R. (2007). Cognitive remediation therapy in schizophrenia. *British Journal of Psychiatry*, 190, 421-27.
- [92] Wykes, T., Reeder, C., Williams, C., Corner, J., Rice, C., & Everitt, B. (2003). Are the effects of Cognitive Remediation Therapy (CRT) durable? Results from an exploratory trial in schizophrenia. *Schizophrenia Research*, 6, 163–174.
- [93] Yoon, J. (2008). Association of dorsolateral prefrontal cortex dysfunction with disrupted coordinated brain activity in schizophrenia: relationship with impaired cognition, behavioral disorganization, and global function. *Am. J. Psychiatry*, 165, 1006–1014.
- [94] Zubin, J& Spring, B. Vulnerability-A new view of schizophrenia. (1977). *Journal of Abnormal Psychology*, 86(2),103-26.