Clin Schizophr Relat Psychoses
Volume 16:S3, 2022
Doi: 10.3371/CSRP.OGSA.071422

Clinical Schizophrenia & Related Psychoses

Research Article

Hybrid Open Access

Dysexecutive Behavior in First-Episode Schizophrenia

Gricel Orellana[1,2*], Andrea Slachevsky[3,4,5] and Fernando Henriquez[3,4,5,6]

[1]*Departamento de Psiquiatría Oriente, Universidad de Chile, Santiago, Chile*

[2]*Comité de Ética de la Investigación en Seres Humanos, Universidad de Chile, Santiago, Chile*

[3]*Clínica de Memoria y Neuropsiquiatría (CMYN), Servicio de Neurología, Hospital del Salvador y, Universidad de Chile, Santiago, Chile*

[4]*Centro Gerociencias, Salud Mental y Metabolismo (GERO), Santiago, Chile*

[5]*Laboratorio de Neuropsicología y Neurociencias Clínicas (LANNEC), Programa de Fisiopatología-ICBM, Departamento de Ciencias Neurológicas Oriente y Neurociencias, Universidad de Chile, Santiago, Chile*

[6]*Laboratory for Cognitive and Evolutionary Neuroscience (LaNCE), Departamento de Psiquiatría, Pontificia Universidad Católica de Chile, Santiago, Chile*

Abstract

Background: Dysexecutive syndrome is a prominent and functionally significant cognitive feature of schizophrenia. This study assesses and correlates executive function (EF) deficits and dysexecutive behavior (DB) in first-episode schizophrenia (FES) patients and healthy participants.

Methods: We evaluated 22 FES patients (aged 17–29 years, history of single episode of schizophrenia, treated with atypical antipsychotics) and 20 controls matched for gender, age, and education. EF was evaluated using the Modified Six Elements Test (MSET), Modified Wisconsin Card Sorting Test (M-WCST), and Frontal Assessment Battery (FAB). DB was evaluated using the Dysexecutive Questionnaire (DEX) and Behavioral Dysexecutive Syndrome Inventory (BDSI).

Results: FES patients had marked dysexecutive behaviors and executive function impairments as compared to controls. Our findings suggest that executive function scores on standardized neuropsychological tests may be ecologically valid predictors of dysexecutive behavior.

Conclusion: DB is common during first-episode schizophrenia and may be a primary impairment throughout disease progression. The present results inform clinical practice by providing insight into first-episode schizophrenia specific features of dysexecutive behavior. Understanding the associations between executive function tests and dysexecutive behaviors helps to explain the social adjustment disorders associated with schizophrenia. This knowledge may be used to improve diagnostic and therapeutic tools; for example, clarifying the implications of specific DEX and BDSI dimensions could increase the efficacy of individual or familial psychotherapy and cognitive rehabilitation interventions.

Keywords: Schizophrenia • Psychosis • Executive function • Dysexecutive behavior • Cognition

Introduction

Schizophrenia is a mental illness that affects 1% of the world population and has severe, deleterious effects on quality of life. Symptoms appear early in life, and current treatments cannot offer full recovery [1]. The disease is characterized by multiple cognitive impairments, including executive function disorders [2,3]. Many of the psychosocial problems associated with schizophrenia are attributable to these cognitive deficiencies [4-7].

Neuropsychological and neurocognitive paradigms have become increasingly valuable in identifying the dysfunctional structures and putative brain systems underlying the cognitive and behavioral disorders associated with schizophrenia [8]. These paradigms rely on clinical tests to precisely characterize neurocognitive abnormalities. Recent research has expanded upon previous psychological findings by using functional neuroimaging to compare patients with healthy controls and to validate results in other populations with brain disorders [9]. Studying neurocognitive performance in schizophrenia has made it possible to identify central cognitive deficits that may explain a significant proportion of the disease's social and vocational morbidity [10,11].

Traditionally, most studies on cognition in this syndrome have used heterogeneous samples of adults with chronic schizophrenia and a long history of somatic treatments, including electroconvulsive therapy. The effects of age, other clinical symptoms, illness duration and severity, adverse lifestyle that increase the burden of cardiometabolic problems and treatments confound findings on the nature of the neurocognitive dysfunction. Over the past 15-20 years, interest in researching the clinical and neurocognitive characteristics of early schizophrenia has grown, as this approach minimizes the interpretive difficulties associated with studying chronically ill patients [12].

The EF deficits characteristic of schizophrenia is also apparently present in adolescents at risk of developing the disease (ultra-high-risk patients), patients with a first outbreak, and even first-degree relatives of patients [13-15]. Patients with a FES commonly experience mild-to-moderate EF impairment [16]. In older patients, cognitive impairments typically evolve into more severe symptoms, including deterioration of EF. Dysexecutive syndrome is characterized by impaired frontal control over behavior, with symptoms such as impulsivity, difficulty planning, reduced attention, decreased strategic self-regulation, and memory problems. This syndrome produces DB and/ or deficits in neuropsychological test which measure EF. DB is measure with standardized questionnaires designed to assess everyday changes in cognition, emotion, and behavior, for example DEX. EF impairments are most obvious when patients must manage complex, open-ended, and socially ambiguous situations [17]. The assessment of EF is with some well-studied tests, like MWCST. It is important that we attempt to define the most typical dysexecutive symptoms in FES, as these complaints may underlie many problems that patients face during everyday life, even during very early stages. Moreover, executive dysfunction is

***Corresponding Author:** Gricel Orellana, Departamento de Psiquiatría Oriente, Universidad de Chile, Santiago, Chile; E-mail: gricel.orellana@gmail.com*

Received date: 13 Jun, 2022, Manuscript No. CSRP-22-67598; **Editor assigned:** 16 Jun, 2022, PreQC No. CSRP-22-67598(PQ); **Reviewed:** 01 Jul, 2022, QC No. CSRP-22-67598; **Revised:** 08 Jul, 2022, Manuscript No. CSRP-22-67598(R); **Published:** 14 Jul, 2022; DOI: 10.3371/CSRP.OGSA.071422.

strongly linked to the psychosocial impairment characteristic of the disease. Despite its central role in schizophrenia, few studies have analyzed DB in FES [16].

The DB described in FES is thought to be related to prefrontal cortex abnormalities, but a more detailed evaluation of these behaviors would be useful; therefore, characterizing this deficit was a major focus of this study. Our hypothesis was that FES patients would show marked DB as compared to healthy controls on standardized questionnaires, as well as impaired EF, including reduced strategic self-regulation. We further hypothesized that there would be correlations between EF tests and DB in the FES group.

Materials and Methods

Participants

Twenty-two FES participants took part in this study. FES patients were recruited between 260 inpatients and outpatients from Psychiatry Services of Hospital Barros Luco Trudeau and Hospital Salvador in Santiago, Chile. Only 22 FES patients met the clinical and DSM-IV-TR criteria for schizophrenia in the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I). Nineteen FES patients were paranoid, two disorganized, and one catatonic. They were evaluated by expert academic psychiatrists during a period ranging from 1 to 36 months after clinical diagnosis with no history of other episodes prior to or after diagnosis. Patients were rated on the Positive and Negative Syndrome Scales (PANSS) after the episode. Their scores on the Positive Syndrome Scale ranged from 7 to 13 (mean=8.5 ± 2.0) and on the Negative Syndrome Scale ranged from 7 to 28 (mean=16.8 ± 6.2), corresponding to mild schizophrenia (Table 1). Patients were clinically stable throughout the study evaluation period and were treated a single atypical antipsychotic Medication: Risperidone in fourteen (4.5-9 g/day), olanzapine in three (20–30 mg/day), clozapine in four (125-550 mg/day), and quetiapine in one patient (dose: 250 mg/day). Computed cerebral tomography, made by expert neurologists, showed no brain abnormalities in 20 patients; the remaining two refused the scan. The FES patients showed no significant extrapyramidal symptoms as measured by the Extrapyramidal Symptom Rating Scale (ESRS) (scores in our sample were 0–10 out of a maximum score of 175) and reported no vision or hearing problems. Each participant verbally confirmed understanding of the procedures and tasks. All evaluations were carried out in the University of Chile, Faculty of Medicine, and Department of Psychiatry.

Twenty healthy control participants, matched with FES patients by age, gender, and education level, were enrolled. For both FES and control participants, exclusion criteria were (a) brain disease other than schizophrenia, (b) IQ less than or equal to 79, (c) substance abuse, or (d) electroconvulsive therapy. The biomedical research ethics committee of the University of Chile, Faculty of Medicine, approved the study. All participants signed the informed consent form before the evaluation and consented to the anonymized publication of their results.

Clinical and cognitive assessment

Clinical evaluation of FES was performed in three sessions. In the first session, the SCID-I was used to verify the clinical diagnosis, and the PANSS was administered to measure positive and negative symptoms. Global cognition was tested in the second session, using the Dementia Rating Scale (DRS) [18] and Raven's Progressive Matrices (RPM) [19]. In the third session, ESRS was performed.

For the cognitive evaluation of EF and DB, the M-WCST [20], FAB, and MSET were used to evaluate EF. The FAB consists of 6 subtests of frontal-lobe functions: (1) Conceptualization and Abstract Reasoning (similarities); (2) Mental Flexibility (verbal fluency); (3) Motor Programming and Executive Control of Action (Luria motor sequences); (4) Resistance to Interference (conflicting instructions); (5) inhibitory control (go/no-go test); and (6) Environmental Autonomy (prehension behavior). Each subtest is scored from 3 (better score) to 0, for a maximum score of 18. [21]. this study marks the first application of the FAB in a FES sample. The MSET consists of three types of tasks (dictation, simple arithmetic, and picture naming), each with two subtasks. Dictation requires participants to tell a story on a specific topic; simple arithmetic includes 60 questions; and picture-naming includes 60 brightly colored pictures to be identified in writing. Participants are instructed to attempt all six subtasks within the allotted 10 minutes and told not to move directly from subtask A to B within a given task. A digital timer is provided for participants to monitor their time. Four scores were calculated for the MSET: (1) subtasks completed; (2) rule breaks; (3) deviations from optimal per-task time allocation (time error); and (4) summary score (total profile score) [22,23].

Finally, two DB measures, the DEX and BDSI, were given to both the participant and a reliable informant. The DEX is a 20-item questionnaire designed to assess everyday changes in cognition, emotion, and behavior after an acquired brain injury or trauma. The DEX is completed by the patient (self-rating; DEX-S) and a person who knows the patient well, such as a partner or close family member ("significant other;" DEX-SO) [24,25]. The difference between DEX-S and DEX-SO scores reflects awareness of the deficit (DEX-A). Burgess et al. [23] grouped the questionnaire items into 5 behavioral dimensions or factors: Factor 1 (Inhibition): response suppression problems, impulsivity, no concern for others' feelings, and no concern for social rules, disinhibition, impaired abstract reasoning, and restlessness. Factor 2 (Intentionality): planning problems, poor decision-making, and lack of insight, distractibility, and knowing-doing dissociation. Factor 3 (Executive Memory): confabulation, temporal sequencing problems, and perseveration. Factor 4 (Positive Affect): variable motivation, aggression, and euphoria. Factor 5 (Negative Affect): shallow affect, apathy. We recorded total DEX-SO, DEX-S, and DEX-A scores, as well as scores for each item and factor. Higher scores indicate greater levels of behavioral disorder [23]. We used the BDSI, a structured-informant interview, to assess for behavioral changes after the first episode of schizophrenia. The test covers 12 domains: (1) global hypoactivity with apathy-abulia; (2) difficulties in anticipation, planning and initiation of activities; (3) disinterest and indifference to his/her own concern and others; (4) hyperactivity-distractibility-psychomotor instability; (5) irritability-impulsivity-aggressiveness; (6) euphoria, emotional lability, and moria; (7) stereotyped and perseverative behavior; (8) environmental dependency; (9) anosognosia-anosodiaphoria; (10) spontaneous confabulations; (11) social behavior disorders; and (12) disorders of sexual, eating, and urinary behaviors [24]. The reliable informant was an individual who interacted with the patient daily and had apparently normal intellectual function with no history of severe psychiatric disease. This study marks the first application of the BDSI in a sample of FES patients. We performed two questionnaires to measure DB as the validity of the DEX and BDSI is yet to be evaluated in FES and using two questionnaires enhances the reliability of our results.

Healthy controls were evaluated in two sessions. In the first session, absence of mental disorder was verified using the SCID-I, and global cognition was tested using the DRS and RPM. In the second session, control participants were tested with the same EF and DB instruments as the patients with schizophrenia, except for the PANSS and ESRS.

Statistical analysis

Statistical analyses were performed using SPSS Statistics 21. The demographic, clinical, and global cognition data for the FES and control groups, including gender, age, education level, DRS and RPM scores, were subjected to independent-samples t-tests (alpha level=.05; two-tailed). MSET, FAB, M-WCST, DEX, and BDSI scores for the FES and control groups were also subjected to independent-samples t-tests (alpha level=.05; two-tailed). Effect sizes (Cohen's d statistic) were also calculated to determine the magnitude of the differences between groups. According to Cohen, effect sizes between 0.2 and 0.49 are considered small; between 0.5 and 0.79, moderate; and 0.8 and above, large.

For both the FES and control participants, we used Pearson's correlation coefficients to analyze the relationships between total and subtotal scores in MSET, M-WCST, FAB and total and subtotal scores in DEX and BDSI.

Results

Demographic and clinical data

Table 1 provides the demographic and clinical data for both groups. There were no significant sex, age and education year's differences between FES and control groups. Global cognition results are also shown in Table 1. DRS and RPM scores were significantly lower in the FES group.

Executive function tests

The tests used have validity criteria, which is an indicator that the test measures what it claims to measure, usually obtained by comparing the performance of the new test with a gold standard.

The average MSET total profile score was 2.50 (SD=1.22, range 0–4) for the FES patients and 3.90 (SD=0.31, range 3–4) for controls. Significant differences were observed between FES and control participants for MSET: Total Profile, Subtasks Completed, and Rule Breaks. There were no significant differences between groups for MSET: Picture Naming A, Picture Naming B, Arithmetic A, Arithmetic B, Dictation A, or Dictation B times. The FES patients completed fewer subtasks and committed more rule breaks than controls but did not take significantly longer than controls to complete any subtask (Table 2).

FAB: Total, Conceptualization, Motor Programming, Resistance to Interference, and Inhibitory Control scores were significantly lower in FES patients than controls (Table 3).

FES patients had significantly worse scores for M-WCST: Categories Completed, Total Errors, Failures to Maintain Set, Perseverative Errors, and Cards Used (Table 4).

Dysexecutive behavior

The dysexecutive questionnaire results are presented below. The questionnaires used have a previously studied validity criterion.

The t-tests showed significant differences between the FES and control participants for BDSI, DEX-SO, and DEX-S total scores. There were no significant differences in DEX-A scores between groups (Table 5).

Table 1. Demographic and clinical data for FES and control groups.

	FES		Control		t/ χ^2	p
	Mean	SD	Mean	SD		
Sex (female/male)	9/13		8/12		0.059[a]	0.952
Age (years)	21.8	3.5	20.3	3.2	1.463	0.151
Education (years)	12.1	2.4	13.1	2.2	1.224	0.228
DRS	131.7	8.3	141.7	1.6	5.5	0
RPM	24.9	11.4	55.6	3.1	8.2	0
PANSS: Positive	8.5	2	NA	NA	NA	NA
PANSS: Negative	16.8	6.2	NA	NA	NA	NA
PANSS: General	26.36	5.9	NA	NA	NA	NA
Psychopathology						
PANSS: Total	51.66	11.48	NA	NA	NA	NA

Note: a: Chi-square; FES: First-Episode Schizophrenia; DRS: Dementia Rating Scale; RPM: Raven's Progressive Matrices; PANSS: Positive and Negative Syndrome Scales.

Table 2. MSET scores for FES and control groups.

	FES		Control		t	p	Effect size (d)[a]
	Mean	SD	Mean	SD			
MSET: Total profile score	2.5	1.22	3.9	0.31	5.185	0	-1.573
MSET: Subtasks completed	4.95	1.53	6	0	3.212	0.004	-0.97
MSET: Rule breaks	0.73	1.2	0.05	0.22	-2.593	0.016	0.788
MSET: Picture naming A time	175	133.36	121.5	47.55	-1.762	0.089	0.534
MSET: Picture naming B time	82.23	63.82	104.75	43.38	1.348	0.186	-0.413
MSET: Dictation B time	37.82	78.32	49.95	39.57	0.624	0.536	-0.195
MSET: Arithmetic A time	108.23	79.28	103.05	41.44	-0.261	0.795	0.082
MSET: Arithmetic B time	109.95	110.78	114.2	66.43	0.152	0.88	-0.046
MSET: Dictation A time	46.14	63.45	47.95	37.08	0.112	0.912	-0.035

Note: a: Cohen´s d; FES: First-Episode Schizophrenia; MSET: Modified Six Elements Test.

Table 3. FAB scores for FES and control groups.

	FES		Control		t	p	Effect size (d)[a]
	Mean	SD	Mean	SD			
FAB: Total score	14.77	2.25	17.55	0.76	5.468	0	-1.655
FAB: Conceptualization	2	0.97	2.9	0.3	4.107	0	-1.253
FAB: Inhibitory control	2.23	1.11	3	0	3.266	0.003	-0.981
FAB: Resistance to interference	2.68	0.65	3	0	2.309	0.034	-0.696
FAB: Motor programming	2.73	0.55	3	0	2.324	0.033	-0.694
FAB: Mental flexibility	2.18	0.8	2.65	0.75	3.116	0.057	-0.606
FAB: Environmental autonomy	3	0	3	0	--	--	--

Note: a: Cohen´s d; FES: First-Episode Schizophrenia; FAB: Frontal Assessment Battery.

Table 4. M-WCST scores for FES and control groups.

	FES		Control		t	*p*	Effect size (d)[a]
	Mean	SD	Mean	SD			
M-WCST: Total errors	13.91	9.11	1.65	1.78	-6.18	0	1.868
M-WCST: Categories completed	4	1.8	6	0	5.21	0	-1.571
M-WCST: Failures to maintain set	2.82	2.68	0.2	0.52	-4.48	0	1.357
M-WCST: Perseverative errors	3.82	4.46	0.25	0.64	3.71	0.001	1.12
M-WCST: Cards used	43.82	8.52	37.9	2.31	-3.13	0.005	0.948

Note: a: Cohen´s d; FES: First-Episode Schizophrenia; M-WCST: Modified Wisconsin Card Sorting Test.

Table 5. DEX and BDSI total scores for FES and control groups.

	FES		Control		t	*p*	Effect size (d)[a]
	Mean	SD	Mean	SD			
DEX-S	19.82	7.72	11.55	7.79	-3.45	0.001	1.066
DEX-SO	20.05	11.1	10.8	8.46	-3.014	0.004	0.937
DEX-A	0.18	13.28	-0.75	6.84	-0.289	0.78	0.088
BDSI	34.36	22.13	6.4	8.66	-5.483	0	1.664
M-WCST: Cards used	43.82	8.52	37.9	2.31	-3.13	0.005	0.948

Note: a: Cohen´s d; FES: First-Episode Schizophrenia; DEX: Dysexecutive Questionnaire; DEX-SO Significant Other; DEX-S: self-rating; DEX-A: Awareness of Deficit; BDSI: Behavioral Dysexecutive Syndrome Inventory.

The t-tests also showed several significant differences between the FES and control participants for individual items. Specifically, the two groups differed significantly on several DEX-SO items (restlessness, planning problems, poor decision-making, lack of insight, temporal sequencing problems, and apathy) and factors (intentionality, executive memory, and negative affect). Moreover, the two groups differed significantly on various DEX-S items (impaired abstract reasoning, planning problems, and lack of insight, confabulation, and temporal sequencing problems) and two DEX-S factors (intentionality and executive memory) (Table 6).

Finally, the two groups differed significantly for numerous BDSI items (global hypoactivity with apathy-abulia; difficulties in anticipation, planning and initiation of activities; disinterest and indifference to his/her own concern and others; hyperactivity-distractibility-psychomotor instability; euphoria, emotional lability, and moria; stereotyped and perseverative behavior; anosognosia-anosodiaphoria; spontaneous confabulations; and disorders of sexual, eating, and urinary behavior) (Table 7).

These results indicate that patients demonstrate DB after a single episode of schizophrenia.

Finally, to evaluate the relationship between DB (as measured by the DEX and BDSI) and EF (as assessed using the MSET, FAB and M-WCST) in FES patients, we analysed the correlations between pairs of variables.

Correlations between dysexecutive behavior and executive function tests

The ordinal neuropsychological variables were subjected to bivariate analysis using Pearson's correlation coefficient to evaluate for relationships between DB and EF. Correlations were made only between total and subtotal scores that were statistically significant between patients and controls.

First, to evaluate the relationship between DB (measured by DEX and BDSI total and subtest scores) and impaired strategic self-regulation (measured by MSET total score) in FES patients, we analyzed correlations between various pairs of variables. There were no significant correlations between total DEX-S, total DEX-SO, or total BDSI and total MSET (DEX-S: r=-0.050, p=0.824, DEX-SO: r=-0.398, p=0.067 and BDSI: r=-0.218, p=0.330). As for the subtests, no statistically significant correlations were found between the subtests of the MSET (subtasks completed and rule breaks) and the DEX (SO and S) and the BDSI. Overall, there was no relationship between strategic self-regulation and DB in FES patients.

Table 6. Differences between FES and controls for DEX-SO and DEX-S items and factors.

	FES		Control		t	*p*	Effect size (d)[a]
	Mean	SD	Mean	SD			
DEX-SO: Lack of insight	1.59	1.18	0.35	0.58	-4.368	0	1.334
DEX-SO: Intentionality factor	6.73	4.14	2.8	2.31	-3.839	0.001	1.172
DEX-SO: Temporal sequencing problems	0.5	0.67	0	0	-3.487	0.002	1.055
DEX-SO: Apathy	1.82	1.26	0.65	0.99	-3.361	0.002	1.032
DEX-SO: Poor decision-making	1.64	1.09	0.8	0.69	-2.985	0.005	0.921
DEX-SO: Executive memory factor	1.14	1.55	0.2	0.41	-2.727	0.012	0.829
DEX-SO: Negative affect factor	2.91	1.74	1.6	1.67	-2.482	0.017	0.768
DEX-SO: Restlessness	1	1.02	0.4	0.5	-2.444	0.02	0.747
DEX-SO: Planning problems	1.64	1.5	0.75	0.97	-2.299	0.027	0.705
DEX-S: Executive memory factor	2.55	1.79	0.65	0.81	-4.48	0	1.368
DEX-S: Confabulation	1	0.93	0.15	0.37	-3.977	0	1.201
DEX-S: Lack of insight	1.18	0.73	0.35	0.67	-3.825	0	1.184
DEX-S: Temporal sequencing problems	0.86	0.77	0.15	0.37	-3.872	0.001	1.175
DEX-S: Impaired abstract reasoning	1.18	1.01	0.3	0.47	-3.69	0.001	1.117
DEX-S: Intentionality factor	5.77	2.47	3	2.62	-3.525	0.001	1.088
DEX-S: Planning problems	1.32	1.25	0.3	0.66	-3.347	0.002	1.02

Note: a: Cohen´s d; FES: First-Episode Schizophrenia; DEX: Dysexecutive Questionnaire; DEX-SO Significant Other; DEX-S: self-rating.

Table 7. Differences between FES and controls on BDSI items.

	FES		Control		t	*p*	Effect size (d)[a]
	Mean	SD	Mean	SD			
Global hypoactivity with apathy-abulia	3.86	3.39	0.5	1.4	-4.278	0	1.295
Difficulties in anticipation, planning and initiation of activities	2.91	2.93	0.35	0.74	-3.963	0.001	1.198
Disorders of sexual, eating, and urinary behavior	1.23	1.97	0	0	-2.916	0.008	0.883
Euphoria, lability, and moria	0.68	1.04	0.05	0.22	-2.776	0.011	0.838
Stereotyped and perseverative behavior	2.14	2.34	0.55	1.47	-2.66	0.012	0.814
Disinterest and indifference to one's own concern and other	2.68	2.77	0.85	1.63	-2.641	0.012	0.805
Anosognosia and anosodiaphoria	1.14	1.67	0.25	0.55	-2.353	0.027	0.716
Spontaneous confabulations	0.82	1.68	0	0	-2.284	0.033	0.69
Hyperactivity-distractibility-psychomotor instability	1.59	2.79	0.2	0.89	-2.217	0.036	0.671

Note: a: Cohen´s d; FES: First-Episode Schizophrenia; BDSI: Behavioral Dysexecutive Syndrome Inventory

To evaluate the relationship between DB (measured by DEX and BDSI total and subtest scores) and impaired EF (measured by FAB total and subtest scores), we analyzed correlations among other variable pairs. In sum, there were no significant correlations between total DEX-S, total DEX-SO, total BDSI scores and total FAB scores (DEX-S: r=-0.192, p=0.392, DEX-SO: r=-0.286, p=0.196 and BDSI: r=-0.175, p=0.437).

When we examined subtest scores, we found statistically significant correlations between DEX-SO: Temporal Sequencing Problems and total FAB, as well as DEX-SO: Negative Affect Factor and total FAB (r=-0.457, p=0.032; r=-0.456, p=0.033, respectively).

There were also significant correlations between DEX-SO: Temporal Sequencing Problems and FAB: Conceptualization as well as DEX-SO: Executive Memory Factor and FAB: Conceptualization (r=-0.453, p=0.044; r=-0.472, p=0.027, respectively).

There was also significant correlation between DEX-SO: Negative Affect Factor and FAB: Motor Programming (r=-0.474, p=0.026). No statistically significant correlations were found between the FAB (total score and subscales) and the DEX-S (total scale and subscales).

The BDSI: Difficulties in Anticipation, Planning and Initiation of Activities was correlated with FAB: Motor Programming (r=-0.460, p=0.031). There was also significant correlation between BDSI: total score and FAB: Inhibitory Control (r=-0.461, p=0.031). These findings indicate that more pronounced DB was associated with worse EF (as measured by the FAB) in the FES patients.

To evaluate relationships between DB (measured DEX and BDSI total and subtest scores) and impaired EF (measured by M-WCST total and subtest scores), we analyzed a final set of variable pairs. There were no significant correlations between total DEX-S, total DEX-SO, total BDSI scores and M-WCST: Categories Completed (DEX-S: r=-0.219, p=0.327, DEX-SO: r=-0.258, p=0.247, BDSI: r=-0-026, p=0.907).

For the DEX-S, there was a significant correlation between total DEX-S and M-WCST: Perseverative Errors (r=0.512, p=0.015).

There were also significant correlations between DEX-S: Impaired Abstract Reasoning and M-WCST: Categories Completed, Total Errors, and Perseverative Errors (r=-0.447, p=0.037, r=-0.423, p=0.050, r=-0.464, p=0.030, respectively).

There was also a significant correlation between DEX-S: Executive Memory Factor and M-WCST: Perseverative Errors (r=0.621, p=0.002). In terms of DEX-SO subtests, we found statistically significant correlations between DEX-SO: Temporal Sequencing Problems and M-WCST: Categories Completed, Total Errors and Perseverative Errors (r=-0.472, p=0.027; r=0.482, p=0.023, r=0.604, p=0.003, respectively). There were significant correlations between DEX-SO: Executive Memory Factor and M-WCST: Categories Completed, Total Errors, and Perseverative Errors (r=-0.477, p=0.025; r=0.550, p=0.008, r=0.678, p=0.001, respectively). Finally, there were no significant correlations between BDSI total or subtest and M-WCST scores. These findings indicate that more marked DB was associated with greater EF impairment (as measured by the M-WCST) in our FES group. Taken together, the results suggest that results of neuropsychological tests of EF such as the M-WCST, and FAB may be ecologically valid predictors of some DB, especially symptoms detectable by caregivers.

Discussion

Dysexecutive syndrome is characterized by impaired frontal control over behavior, with symptoms such as impulsivity, difficulty planning, reduced attention, decreased strategic self-regulation, and memory problems. This syndrome produces DB and/or deficits in neuropsychological test which measure EF. DB is measure with standardized questionnaires designed to assess everyday changes in cognition, emotion, and behavior. This study showed that patients have deficits in DEX and BDSI, validated questionnaires to characterize the DB, which affects everyday life in FES. This is the first time that the latter questionnaire has been applied in a FES population. This research assesses executive dysfunction of FES patients after initial stabilization with atypical antipsychotic medications. Patients showed impaired performance on tasks requiring self-regulation (MSET) and FAB and M-WCST as compared to healthy controls. Moreover, we found that DEX and BDSI scores were correlated with EF test. Finally, patients did not appear to lack awareness of their deficits (measured as the difference between DEX-S and DEX-SO results).

Dysexecutive behavior

Problems in DB are common clinical observations in FES, and we believe that standardized testing for this syndrome should be a routine part of clinical psychiatric practice. Various questionnaires have been designed to measure the impact of dysexecutive syndrome on daily life and overcome the low sensitivity of standard neuropsychological tests. The DEX from the Behavioral Assessment of the Dysexecutive Syndrome [23,24] and the BDSI from the Groupe de Réflexion sur l'Évaluation des Fonctions Exécutives [25] probe for symptoms that reflect DB in everyday life. In designing this study, we hypothesized that FES patients would receive scores indicative of DB on such questionnaires.

To test this hypothesis, we applied validated DEX and BDSI questionnaires to a group of patients with FES and to a control group. We found that there were significant differences between the patient and control groups in terms of total and subtotals scores for both instruments. This result supports our hypothesis; patients with FES showed evidence of DB.

The BDSI has excellent diagnostic accuracy for executive disorders in mild-to-moderate Alzheimer's disease, stroke, and traumatic brain injury [26-28]. This study marks the first application of this instrument in FES. We found statistically significant differences between patients and controls for most items on the instrument, suggesting that it is a sensitive test for DB in FES. Only three questions showed no significant differences between patients and controls. The first pertained to emotional symptoms (irritability-impulsivity-aggressiveness) that are clinically more typical of bipolar disorder than schizophrenia. The second, environmental autonomy is associated with catatonic symptoms, which are rare in FES. The third items address severe and chronic behavioral problems, which are also rare in this kind of patients.

In terms of the DEX, this study is the first to analyze not only total score but also item and factor scores in a FES population. The main behavioral problems reported by informants on the DEX-SO were related to the intentionality factor (including lack of insight, poor decision-making and planning problems); executive memory factor (temporal sequencing problems and confabulation); negative affect factor (apathy); and restlessness. On the DEX-S, the main behavioral problems recognized by the patients were related to the executive memory and intentionality factors and the impaired abstract reasoning item. These problems are common clinical complaints in FES and may partially explain the problems with school, work, and general social participation that this population experiences. As the above results indicate, there was significant overlap between symptoms detected by caregivers and self-reported problems. Studies using the DEX with chronic schizophrenia populations have reported that the total DEX-S score is typically lower than the total DEX-SO score (indicating incomplete awareness of impairment), and that only the latter score differs significantly from results for controls [29]. Our study, in contrast, found that early-stage FES patients were generally aware of their deficits, suggesting that insight may deteriorate later in disease progression. This finding also separates FES from numerous neurological disorders associated with significant anosognosia.

Executive function

FES patients have been shown to suffer EF deficits such as difficulty with rule shifts, planning, and coordination of two competing tasks. These deficits are consistent across patients, suggesting that the impairment is intrinsic to the disease [9,30,31]. Given the above, it would be reasonable to imagine that FES patients would score different on EF tests than healthy controls. Accordingly, we found a detectable deficit even with a brief test such as the FAB. This study marks the first application of this test in a sample of FES patients. Patients showed difficulty with conceptualization, motor programming, resistance to interference, and inhibitory control items on the FAB. These findings are consistent with results from studies using other tests, which have reported abnormal verbal fluency scores in FES and chronic schizophrenia [32]. This result suggests that the FAB might have utility as a routine clinical test in this population, except for the environmental autonomy subtest. Patients with neurological disorders such as Alzheimer's disease, frontotemporal dementia, and amyotrophic lateral sclerosis have also been found to have abnormal FAB scores [21,33]. However, studies with greater numbers of patients and in various stages of disease evolution are necessary to confirm the utility of the FAB in cognitive evaluation of FES.

EF involves such abilities as abstract reasoning, concept formation, decision-making, and planning of behavior. Based on a rule-learning paradigm, which invokes these abilities, the M-WCST is one of the most widely applied neuropsychological measures of EF [34]. The M-WCST is particularly sensitive to lesions of the dorsolateral prefrontal cortex (DLPFC) and upper medial regions of the prefrontal cortex. Importantly, reductions in DLPFC gray matter volume are significantly more pronounced in schizophrenia patients with greater executive dysfunction as measured by the M-WCST [17]. However, the M-WCST should be used with caution as a frontal measure because retro-Rolandic cortex lesions, such as hippocampal lesions, have also been associated with impairments, especially perseverative errors. Chronic schizophrenic and FES patients show difficulty with inhibiting previously learned responses and shifting attention towards relevant stimuli; that is, they perseverate on an answer already noted to be incorrect. The poor performance of patients with schizophrenia may reflect a difficulty in inhibiting inappropriate responses [17]. We also explored the executive dysfunction associated with FES using the M-WCST; as widely described in the literature, patients demonstrated numerous problems in carrying out the study tasks. In our sample, the FES patients committed more total errors, failures to maintain set and perseverative errors than controls. Patients also used more cards to complete the M-WCST than the controls.

EF impairment is a cognitive deficit central to the symptomatology of schizophrenia. However, traditional neuropsychological tests of EF may not be sensitive enough to capture everyday dysexecutive problems in FES. These tests were originally designed to evaluate neurological patients and may therefore miss psychiatric-related cognitive deficits. Qualitative information on EF is also important for diagnosis and treatment in psychiatric populations [35]. The MSET, which requires patients to plan, organize, and monitor behaviour over a brief period while carrying out a simple task, provides some qualitative data and is often used to measure EF in neurological patients [36]. Our FES group performed more poorly than controls on MSET tasks. Specifically, patients completed fewer tasks and broke more rules; in other words, they showed impaired self-regulation. Shallice and Burgess emphasize that few neuropsychological tests require patients to organize or plan their behavior over long stretches of time or prioritize among competing tasks [37] even though this type of executive ability is an important component of many real-life activities. Our results indicate that patients already show impairment in this area after a single episode of schizophrenia despite stabilization with medication. Our results are consistent with studies in chronic, treated FES patients [29,35,38,39] and one study of unmedicated FES patients [40] that report impaired performance on the MSET. The literature is inconsistent in terms of the longitudinal evolution of self-regulation problems, and the specific cognitive deficit underlying the impairment remains unclear. Patients may lack the ability to perform the number of tasks required, for example, or they may perseverate on a single task, break the stated rules, or deviate from optimal distribution of time spent per task. Therefore, it is crucial that we continue to explore MSET as a test of EF in schizophrenia. A prior study evaluated EF over the course of disease progression, applying the MSET in medication-naïve patients after a first episode of schizophrenia and then following the patients for several years. Consistent with our results, FES patients demonstrated impairment as compared to controls on the MSET. Importantly, this impairment persisted from the medication-naïve state to clinical stabilization and throughout the three years following the first psychotic episode, despite improved performance on a conventional executive test (M-WCST). MSET performance was not related to intelligence, education level, changes in symptoms, age of onset, or duration of untreated psychosis. Furthermore, better MSET performance during the medication-naïve state predicted improvements in negative and positive symptoms over the three-year study period. These findings suggest that impaired self-regulation, as measured by the MSET, is a primary deficit in schizophrenia that begins early in the course of the illness and remains present irrespective of clinical status for at least three years following the first episode [41]. The Chinese version of the task has been adapted for use in patients with first episode and chronic schizophrenia and has been tested in healthy adults in Hong Kong, with results indicating adequate sensitivity to deficits in attention allocation and planning [40,42,43]. In one study, impaired attention allocation and planning at illness onset (FES), as measured by the MSET, were associated with risk of residual semantic disorganization after one year [44]. We propose that clinicians adopt this simple test as part of routine evaluation of FES.

Correlations between dysexecutive behavior and executive function tests

The literature indicates that many EF tests show only moderate ecological validity when used to predict individual functional capacity [45]. Therefore, it is important to assess whether our EF tests, MSET, FAB and M-WCST, have ecological relevance in our sample.

Ecological validity, that is, the applicability of test results to real-life function, has become a major focus of neuropsychological research. Characterizing EF deficits is critical to predicting functional capacity in FES [30,45]; if we assume that MSET, FAB an MWCST are valid measure of EF and that the DEX and BDSI questionnaires are valid measures of the DB encountered in everyday life, we expect strong correlation among the measures.

a) MSET: In designing this trial, we hypothesized that self-regulation would correlate with more quantitative measures of DB in a sample of FES patients. However, we did not find any correlations between MSET and dysexecutive questionnaire scores. This finding is consistent with results in chronic FES and distinguishes this population from neurological patients, in whom the two measures are typically linked [29].

Total BDSI and DEX scores provide an overall measure of DB, including the numerous dimensions that might reflect underlying cognitive processing deficits. Burgess et al. identified at least 5 behavioral dimensions addressed by the DEX, such as inhibition and intentionality [24]. The negative result here suggests that a more precise analysis of cognition in FES might require teasing out, with a large sample, the relationships among strategic self-regulation and the specific dimensions and items on the dysexecutive questionnaire.

One possible explanation for the scarce correlations here is that while many persons diagnosed with FES might indeed have EF deficits, some of their behavioral symptoms may be unrelated to executive deficits. Alternatively, the symptoms may be associated with executive deficits not addressed by the MSET. These symptoms would in any case cause problems for the patient in everyday life and therefore be detectable by the DEX and BDSI. This topic merits further exploration. It is also possible that FES patients might have EF impairments but no obvious symptoms of DB. By the same token, many FES patients demonstrate moderate or marked memory impairments on standardized tests, yet family members and caregivers rarely report this symptom [29].

b) FAB: EF is primarily associated with the frontal lobes. Scores for all six FAB subtests are significantly correlated with frontal metabolism in patients with frontal lobe damage according to PET studies [17]. Our study demonstrates for the first time in schizophrenia that the EF deficit assessed by the FAB also correlates with dysexecutive questionnaire results. Specifically, we found a statistically significant correlation between total BDSI and FAB inhibitory control scores. Difficulty inhibiting inappropriate responses and controlling impulsiveness are common clinical observations in FES, and this impairment likely underlies some of the behavioral problems that these patients experience. We found that motor programming performance as measured by the FAB (in which the patient must remain attentive to the examiner's movements for several minutes and copy movement) was statistically correlated with BDSI: difficulties in anticipation, planning, and initiation of activities.

Performance on total FAB and FAB: Conceptualization (which requires abstract reasoning) may predict behavioral problems related to DEX-SO: Temporal Sequencing Problems (patient mixing events with each other and confusing the order in which they occurred), and DEX-SO: Executive Memory factor (which includes confabulation and temporal sequencing problems) and Negative Affect factor (which includes shallow affect, apathy).

These results suggest that the FAB could be a valid and ecologically relevant and might have utility as a routine clinical test in this population, except for the environmental autonomy subtest (FAB: Prehension Behavior), which is more frequent in neurological patients.

c) M-WCST: Our study is the first to explore correlations between the deficits identified using the M-WCST and the results of dysexecutive questionnaires in FES. One study in the literature reports a correlation between M-WCST total errors and DEX total score in chronic FES, but the authors did not specify the type of DEX used [46].

In our study, correlation analysis indicated statistically significant relationships between various aspects of M-WCST performance and DB. In terms of the DEX-S, there was a significant correlation between M-WCST: Perseverative Errors and total DEX-S. This result likely reflects the fact that the FES assesses many of the executive dysfunctions commonly associated with frontal injuries, such as perseverative deficits, incoherent actions, and unstructured behaviors. Moreover, M-WCST: Perseverative Errors may also predict behavioral problems in FES related to the DEX-S: Executive Memory factor and DEX-SO: Executive Memory factor. These findings would seem to be related to the role of EF in memory, especially given that markedly perseverative patients tend to be those who confabulate [24].

We found strong correlations between M-WCST performance and DB. In contrast, the associations between psychiatric symptoms (positive, negative, etc.) and cognitive performance on this executive test were typically weak, suggesting relative independence of these disease processes [34].

Our study revealed various significant correlations between EF tests and DB. However, the cognitive tests explained only a small percentage of the variance in the behavioral assessments. In considering what other factors might explain this variance, it is important to keep in mind that DB may be linked to many factors not evaluated in this study:

• Performing activities of daily living in the context of FES requires self-motivation and persistence, which is supplied by the examiner in the study setting.

• Multiple and idiosyncratic real-life environmental demands, as well as the compensatory strategies used to address them, can affect the validity of neuropsychological tests in evaluating EF as related to activities of daily living [45].

• EF tests do not require patients to organize their behavior over long periods of time or prioritize competing tasks to the degree that real-life tasks demand.

• The tests are performed in a highly structured environment, unlike real-life situations in disorganized environments.

Moreover, reducing complex human behaviors to a test score or questionnaire item limits our insight into the nature of the deficit. EF implies integration and monitoring of cognitive functions, meaning that qualitative as well as quantitative measures (such as a description of how the patient performs the task) are needed to comprehensively characterize the executive deficit. Therefore, directly measuring those processes would significantly improve EF evaluation [45,46]. Our results support our hypothesis; however, future studies are needed to identify the role of the various factors in everyday function and to confirm the ecological validity of the neuropsychological tests used to explore EF.

Antipsychotics

While our sample of FES patients were treated with different atypical antipsychotics, studies involving cognitive testing with currently treated, previously treated, and never-treated patients have reported similar results regardless of medication status, suggesting that antipsychotics have a relatively minor effect on most neuropsychological functions, although there are some conflicting results in the literature [8,47-49]. We believe that the disordered behavior observed in this study is likely to reflect dysfunction attributable to the FES itself rather than side effects of the medications.

Neuropsychological heterogeneity

The pathophysiology of FES seems to involve many different degrees and types of global and/or specific cognitive deficits, including varying levels of problems with attention, EF, and memory. In general, the cognitive function of patients with FES is better than that of chronic patients. This cognitive heterogeneity was observed in our study for performance on the

MSET and global cognition tests. For instance, while the MSET is sensitive to deficits in abilities traditionally categorized as EF [29], some of the FES patients in our sample (approximately 27%) performed within normal limits. These results are consistent with other studies of FES that also reported cognitive heterogeneity [50-53].

Cognitive deficits can be considered central to schizophrenia, as they are present from the onset of the first episode-ruling out the possibility that the symptoms are completely attributable to illness duration, aging, psychosocial deprivation, cardio metabolic disease, institutionalization, or intensive treatments (electroconvulsive therapy)- and persist throughout the duration of the disease. The confounding cognitive effects of these other factors are a major problem in most neuropsychological studies of schizophrenia and may partially explain the heterogeneity of findings for this population. Therefore, we and numerous other investigators suggest that future research should focus on the population of first-episode patients, as their condition is more likely to reflect the true pathophysiology of this severe brain disorder.

Conclusion

Patients with schizophrenia demonstrate significant abnormalities in DB. Syndrome dysexecutive manifests as DB, which may underlie the many of the problems that patients face in their daily lives. A better understanding of DB may help us to understand the social adjustment disorders associated with schizophrenia and thereby improve our diagnostic and therapeutic tools. For example, clarifying the interpretation of specific DEX and BDSI dimensions in our schizophrenic patients could increase the efficacy of individual and/or familial psychotherapy interventions and cognitive remediation. There is no cure for dysexecutive syndrome, but there are therapies to help patients cope with their symptoms. This syndrome affects several brains functions and varies from person to person. Because of this variance, successful therapy tends to include multiple methods.

Further studies are needed to explore the evolution of DB throughout the course of the disease and to document responses to pharmacological and non-pharmacological treatments. Investigating the longitudinal course of executive dysfunction in schizophrenia is also important because this dysfunction is already present in children who go on to develop schizophrenia. Moreover, maturation of EF extends into young adulthood.

Executive control is required for planning, decision-making, error detection, responding to new events, and inhibiting habitual behaviors. We propose that FES patients show a specific pattern of executive dysfunction related to executive control. This study focused partially on the strategic self-regulation deficit, defined as the inability to regulate behavior in accordance with goals and internally generated limits. Our findings suggest impaired self-regulation in FES may be interpreted as a lack of executive control over thoughts and actions, potentially explaining some of the dysexecutive symptoms observed in our FES sample. Moreover, our research advances by using for the first time specific and validated user-friendly questionnaires to test executive function, such as the FAB. FAB might have utility as a routine clinical test in schizophrenia.

This study is relevant to public health, as understanding the associations between EF (control) and DB (such as planning problems) informs clinical practice, providing insight into FES-specific features of DB. EF is crucial for many aspects of daily functioning; therefore, DB has a significant impact on academic, vocational, emotional, social, and adaptive functioning. In this study, we observed that FES patients demonstrate a diversity of DB. Our findings suggest that the dysexecutive deficit may be a central impairment throughout disease progression.

Declarations

Ethics committee and consent to participate

Our protocol was performed in accordance with the relevant guidelines and regulations from the Chilean Ethics Committee.

Approved by Comité de Ética de Investigación en Seres Humanos (CEISH) Facultad de Medicina, Universidad de Chile; N°2232 date 09/28/2005

Email: comiteceish@med.uchile.cl

All participants signed the informed consent form before the evaluation and consented to the anonymized publication of their results.

Consent for publication

NA

Availability of data and material

All data generated or analysed during this study are included in this published article.

Competing interests

There are no potential conflicts of interest to report for the authors or other contributors.

Funding

FH is supported by Grants

From ANID-Subdirección de Capital Humano/Doctorado Nacional/2021-21211349. AS is partially supported by ANID / FONDAP /15150012; ANID/ Fondecyt Regular/ 443865; 1210176; 1210195 & 1191726 ; ANID/ PIA/Anillos ACT210096; ANID / FONDEF / ID20i10152 & MULTI-PARTNER CONSORTIUM TO EXPAND DEMENTIA RESEARCH IN LATIN AMERICA (ReDLat), supported by the National Institutes of Aging of the National Institutes of Health under award number R01AG057234, an Alzheimer's Association grant (SG-20-725707-ReDLat), the Rainwater Foundation, and the Global Brain Health Institute.

The content is solely the responsibility of the authors and does not represent the official views of the National Institutes of Health, Alzheimer's Association, Rainwater Charitable Foundation, or Global Brain Health Institute.

Authors' contributions

All authors participated in the study conception and design; data collection, analysis, and interpretation; and manuscript drafting. Furthermore, all authors have read, critically reviewed, and approved the final manuscript.

Acknowledgements

We would like to thank our study participants as well as the University of Chile staff members who edited this manuscript.

References

1. Andreasen, Nancy C. "Schizophrenia: The fundamental Questions." *Brain Res. Rev* 31(2000): 106-112.
2. Joyce, Eileen M, and Jonathan P. Roiser. "Cognitive Heterogeneity in Schizophrenia." *Curr Opin Psychiatry* 20(2007): 268-272.
3. Park, Sohee, and Diane C. Gooding. "Working Memory Impairment as an Endophenotypic Marker of A Schizophrenia Diathesis." *Schizophr Res Cogn* 1(2014): 127-136.
4. Fioravanti, Mario, Olimpia Carlone, Barbara Vitale and Maria Elena Cinti, et al. "A Meta-Analysis of Cognitive Deficits in Adults with a Diagnosis of Schizophrenia." *Neuropsychol Rev* 15(2005): 73-95.

5. Davis, Kenneth L, ed. Neuropsychopharmacology: the Fifth Generation of Progress: An Official Publication of the American College of Neuropsychopharmacology. *Lippincott Williams & Wilkins*, 2002.
6. Green, Michael F, Keith H. Nuechterlein, James M. Gold and Deanna M. Barch, et al. "Approaching a Consensus Cognitive Battery for Clinical Trials in Schizophrenia: the Nimh-Matrics Conference to Select Cognitive Domains And Test Criteria." *Biol Psychiatry* 56(2004): 301-307.
7. Heydebrand, Gitry, Marc Weiser, Jonathan Rabinowitz and Anne L. Hoff, et al. "Correlates of Cognitive Deficits in First Episode Schizophrenia." *Schizophr Res* 68(2004): 1-9.
8. Heinrichs, R. Walter, and Konstantine K. Zakzanis. "Neurocognitive Deficit in Schizophrenia: a Quantitative Review of the Evidence." *Neuropsychology* 12(1998): 426-445.
9. Pantelis C, Stephen JW and Maruff P. In Cognitive Deficits in Brain Disorders, Eds. J.e. Harrison and A.m. Owen. London: Martin Dunitz. Schizophr (2002): 217-248.
10. Addington, Jean, and Donald Addington. "Neurocognitive and Social Functioning in Schizophrenia." *Schizophr Bull* 25(1999): 173-182.
11. Orellana, Gricel, Andrea Slachevsky, and Marcela Peña. "Executive Attention Impairment in First-Episode Schizophrenia." *BMC psychiatry* 12(2012): 1-9.
12. Mesholam-Gately, Raquelle I, Anthony J. Giuliano, Kirsten P. Goff and Stephen V. Faraone, et al. "Neurocognition in First-Episode Schizophrenia: a Meta-Analytic Review." *Neuropsychology* 23(2009): 315.
13. Kuperberg, Gina, and Stephan Heckers. "Schizophrenia and Cognitive Function." *Curr Opin Neurobiol* 10(2000): 205-210.
14. Breton, Florence, Aurélie Planté, Cindy Legauffre and Nastassja Morel, et al. "The Executive Control of Attention Differentiates Patients with Schizophrenia, Their First-Degree Relatives And Healthy Controls." *Neuropsychologia* 49(2011): 203-208.
15. Freedman, David, and Alan S. Brown. "The Developmental Course of Executive Functioning in Schizophrenia." *Dev Neurosci* 29(2011): 237-243.
16. Flashman, Laura A. "Disorders of Awareness in Neuropsychiatric Syndromes: an Update." *Curr. Psychiatry Rep* 4(2002): 346-353.
17. Orellana, Gricel, and Andrea Slachevsky. "Executive Functioning in Schizophrenia." *Front Psychiatry* 4(2013): 35.
18. Mattis, Steven. Dementia Rating Scale: Professional Manual. Psychological Assessment Resources, Incorporated, 1988.
19. Raven JC, Court JH, Raven J. Test De Matrices Progresivas. Escalas Coloreada, General and Avanzada. Manual. Buenos Aires: Paidós (1993).
20. Nelson, Hazel E. "A Modified Card Sorting Test Sensitive to Frontal Lobe Defects." *Cortex* 12(1976): 313-324.
21. Slachevsky, Andrea, Juan Manuel Villalpando, Marie Sarazin and Valerie Hahn-Barma, et al. "Frontal Assessment Battery and Differential Diagnosis of Frontotemporal Dementia and Alzheimer Disease." *Arch. Neurol* 61(2004): 1104-1107.
22. Burgess, P, N. Alderman, J. Evans and B. Wilson, et al. "Modified Six Elements Test. Behavioral Assessment of the Dysexecutive Syndrome." (1996).
23. Wilson, Barbara A, Jonathan J. Evans, Nick Alderman and Paul W. Burgess, et al. "Behavioural Assessment of the Dysexecutive Syndrome." *In Methodology of Frontal and Executive Function* (2004): 240-251.
24. Burgess, Paul W, Nick Alderman, JON. Evans and Hazel Emslie, et al. "The Ecological Validity of Tests of Executive Function." *J Int Neuropsychol Soc* 4(1998): 547-558.
25. Godefroy, Olivier, Philippe Azouvi, Philippe Robert and Martine Roussel, et al. "Dysexecutive Syndrome: Diagnostic Criteria and Validation Study." *Ann. Neurol.* 68(2010): 855-864.
26. Beilen, Marije van, Frederiec K. Withaar, Ed H. van Zomeren and Robert J. van den Bosch, et al. "Deviant Strategy on the Modified Six Elements Test in Patients With Schizophrenia." *J. Clin. Neuropsychol.* 20(2006): 469-479.
27. Bertens, Dirk, Nikita Frankenmolen, Danielle HE Boelen and Roy PC Kessels, et al. "Validity of an Adapted Scoring Method for a Modified Six Elements Test in Individuals with Brain Injury." *Arch Clin Neuropsychol.* 30(2015): 122-129.
28. Shallice, TIM, and Paul W. Burgess. "Deficits in Strategy Application following Frontal Lobe Damage in Man." *Brain* 114(1991): 727-741.
29. Evans, JJ, SE Chua, PJ McKenna, and BA Wilson. "Assessment of the Dysexecutive Syndrome in Schizophrenia." *Psychol. Med.* 27(1997): 635-646.
30. Ihara, H., G. E. Berrios, and P. J. McKenna. "Dysexecutive Syndrome in Schizophrenia: a Cross-Cultural Comparison Between Japanese and British Patients." *Behav. Neurol.* 12(2000): 209-220.
31. Jovanovski, Diana, Konstantine K. Zakzanis, Donald A. Young, and Zachariah Campbell. "Assessing the Relationship Between Insight and Everyday Executive Deficits in Schizophrenia: a Pilot Study." *Psychiatry Res.* 151(2007): 47-54.
32. Chan, Raymond CK, Eric YH Chen, and CW Law. "Specific Executive Dysfunction in Patients with First-Episode Medication-Naive Schizophrenia." *Schizophr. Res.* 82(2006): 51-64.
33. Liu, Kristy CM, Raymond CK Chan, Kevin KS Chan and Jennifer YM Tang, et al. "Executive Function in First-Episode Schizophrenia: a Three-Year Longitudinal Study of An Ecologically Valid Test." *Schizophr. Res.* 126(2011): 87-92.
34. Chan, RCK, EYH. Chen, EFC. Cheung, and HK Cheung. "Executive Dysfunctions in Schizophrenia." *Eur Arch Psychiatry Clin Neurosci* 254(2004): 256-262.
35. Chan, Raymond CK, Eric YH Chen, Eric FC Cheung and Ronald YL Chen, et al. "The Components of Executive Functioning in a Cohort of Patients with Chronic Schizophrenia: a Multiple Single-Case Study Design." *Schizophr. Res.* 81(2006): 173-189.
36. Xu, Jia-Qi, Christy Lai-Ming Hui, Julia Longenecker and Edwin Ho-Ming Lee, et al. "Executive Function as Predictors of Persistent Thought Disorder in First-Episode Schizophrenia: a One-Year Follow-Up Study." *Schizophr. Res.* 159(2014): 465-470.
37. Godefroy, Olivier, Olivier Martinaud, Marc Verny and Chrystèle Mosca, et al. "The Dysexecutive Syndrome of Alzheimer's Disease: the Grefex Study." *J Alzheimers Dis* 42(2014): 1203-1208.
38. Azouvi, Philippe, Claire Vallat-Azouvi, Pierre-Alain Joseph and Thierry Meulemans et al. "Executive Functions Deficits After Severe Traumatic Brain Injury: the Grefex Study." *J. Head Trauma Rehabil.* 31(2016): E10-E20.
39. Roussel, Martine, Olivier Martinaud, Hilde Henon and Martine Vercelletto, et al. "The Behavioral and Cognitive Executive Disorders of Stroke: the Grefex Study." 11(2016).
40. Molina, Alberto García, Javier Tirapu Ustárroz, and Teresa Roig Rovira. "Validez Ecológica En La Exploración De Las Funciones Ejecutivas." *Anales de Psicología/Annals of Psychology* 23(2007): 289-299.
41. Snyder, Hannah R, Akira Miyake, and Benjamin L. Hankin. "Advancing Understanding of Executive Function Impairments and Psychopathology: Bridging the Gap Between Clinical and Cognitive Approaches." *Front. Psychol.* 6(2015): 328.
42. Diamond, Adele. "Executive Functions." Annual review of psychology 64(2013): 135.
43. Keefe, R, and C. Eesley. "Neurocognitive Impairments in: Lieberman Ja, Stroup Ts, Perkins Do, Editors. Textbook of Schizophrenia." (2006): 245-260.
44. Nidos, Andreas, Dimitrios S. Kasselimis, Panagiotis G. Simos and Michael Rentzos, et al. "Frontotemporal Dysfunction in Amyotrophic Lateral Sclerosis: a Discriminant Function Analysis." *Neurodegener. Dis.* 16(2016): 140-146.
45. Nieuwenstein, Mark R, André Aleman, and Edward HF De Haan. "Relationship Between Symptom Dimensions and Neurocognitive Functioning in Schizophrenia: a Meta-Analysis of Wcst and Cpt Studies." *J. Psychiatr. Res.* 35(2001): 119-125.
46. Vugt, Lydia Krabbendam Marjolein E, and de Mayke MA Derix Jelle Jolles. "The Behavioural Assessment of The Dysexecutive Syndrome As a Tool to Assess Executive Functions in Schizophrenia." *J. Clin. Neuropsychol.* 13(1999): 370-375.
47. Harvey, Philip D, and Margaret M. McClure. "Pharmacological Approaches to the Management of Cognitive Dysfunction in Schizophrenia." *Drugs* 66(2006): 1465-1473.
48. Daban, Claire, Isabelle Amado, Marie-Chantal Bourdel and Henri Loo, et al. "Cognitive Dysfunctions in Medicated and Unmedicated Patients with Recent-Onset Schizophrenia." *J. Psychiatr. Res.* 39(2005): 391-398.
49. Moustafa, Ahmed A, Julia K. Garami, Justin Mahlberg and Jan Golembieski, et al. "Cognitive Function in Schizophrenia: Conflicting Findings and Future Directions." *Rev Neurosci* 27(2016): 435-448.
50. Joyce, Eileen M, Sam B. Hutton, Stanley H. Mutsatsa, and Thomas RE Barnes. "Cognitive Heterogeneity in First-Episode Schizophrenia." *Br J Psychiatry* 187(2005): 516-522.

51. Heilbronner, Urs, Myrto Samara, Stefan Leucht and Peter Falkai, et al. "The Longitudinal Course of Schizophrenia Across the Lifespan: Clinical, Cognitive, and Neurobiological Aspects." *Harv. Rev. Psychiatry.* 24(2016): 118-128.

52. Spikman, Jacoba M, Danielle HE Boelen, Kirsten F. Lamberts and Wiebo H. Brouwer, et al. "Effects of a Multifaceted Treatment Program for Executive Dysfunction After Acquired Brain Injury on Indications of Executive Functioning in Daily Life." *J. Int. Neuropsychol.* Soc 16(2010): 118-129.

53. Thai, Maria Lotus, Anna Krogh Andreassen, and Vibeke Bliksted. "A Meta-Analysis of Executive Dysfunction in Patients with Schizophrenia: Different Degree of Impairment in the Ecological Subdomains of the Behavioural Assessment of the Dysexecutive Syndrome." *Psychiatr. Res.* 272(2019): 230-236.

How to cite this article: Orellana, Gricel, Andrea Slachevsky and Fernando Henriquez. " Dysexecutive Behavior in First-Episode Schizophrenia." *Clin Schizophr Relat Psychoses* 16S (2022). Doi: 10.3371/CSRP.OGSA.071422