# DISCRIMINATION LEARNING AND SET-SHIFTING IN SCHIZOPHRENIA: ASSOCIATIONS WITH NEGATIVE SYMPTOMS

**CAMELIA DEAC[1], RODICA MACREA[2], CODRUȚA ALINA POPESCU[3], IOANA VALENTINA MICLUȚIA[4]**

*[1]PhD candidate "Iuliu Haţieganu" University of Medicine and Pharmacy Cluj-Napoca, Community Mental Health Centre Cluj-Napoca, [2,3,4]"Iuliu Haţieganu" University of Medicine and Pharmacy Cluj-Napoca*

***Keywords:*** *schizophrenia, discriminative learning, attentional-set shifting, negative symptoms*

***Abstract:*** *Background: Working Memory deficits are considered a cardinal cognitive feature of schizophrenia. The intradimensional/extradimensional (IDED) task assesses different forms of learning from feedback. Attentional set-shifting deteriorates over time in schizophrenia. Aims: In this study, we compared the performance of patients with schizophrenia with that of healthy controls on tests of executive functioning and verbal memory in order to identify specific impairments in executive functioning and the relationship between executive function and memory performance. We then compared the performance of patients with or without negative symptoms. Method: 138 outpatients with a diagnosis of schizophrenia and 43 healthy controls were tested with tests of verbal memory and executive function (RAVLT and IED) Results: Significant group differences were observed in cognitive performance. Schizophrenic patients showed impairment in executive function and verbal memory in comparison with healthy control subjects. Patients showed impaired set-shifting that correlated with verbal memory. Conclusions: Impaired performance can be attributed to negative symptoms. Our findings suggest that patients with schizophrenia can learn and generalize rules but are inflexible when rules change, reflecting both reduced responsiveness to negative feedback and difficulty in switching attention. This profile seems to represent a stable trait of the illness.*

***Cuvinte cheie:*** *schizofrenie, învăţare discriminativă, comutarea setului atenţional, simptome negative*

***Rezumat:*** *Introducere: Deficitul memoriei de lucru este considerat a fi o caracteristică principală în schizofrenie. Testul de comutare a setului intra/ extradimensional evaluează diferite forme de învăţare. Comutarea setului atenţional se deteriorează în timp în schizofrenie. Scop: În acest studiu comparăm performanţa unui grup de pacienţi cu schizofrenie cu cea a unui grup de subiecţi sănătoşi la testele care evaluează funcţia executivă şi memoria verbală cu scopul de a identifica deteriorări specifice în funcţiile executive şi relaţia între funcţia executivă şi performanţele mnezice. Apoi vom compara performanţa pacienţilor cu schizofrenie cu şi fără simptome negative. Metoda: 138 pacienţi cu diagnostic de schizofrenie şi 43 de subiecţi sănătoşi au fost testaţi cu teste care evaluează memoria verbală şi funcţia executivă (RAVLT si IED). Rezultate: Diferenţe semnificative au fost observate în ceea ce priveşte performanţa cognitivă. Pacienţii cu schizofrenie prezentau deteriorări ale funcţiei executive şi memoriei verbale în comparaţie cu subiecţii sănătoşi. Pacienţii prezentau deteriorarea comutării setului atenţional corelat cu memoria verbală. Concluzii: Deteriorarea performanţelor poate fi atribuită simptomelor negative. Descoperirile noastre sugerează că pacienţii cu schizofrenie pot învăţa şi generaliza reguli dar sunt inflexibili când regulile se schimbă, reflectând pe de o parte reducerea responsivităţii la feed-back negativ şi dificultăţile de comutare a atenţiei. Acest profil pare să fie o caracteristică stabilă a bolii.*

## INTRODUCTION

Working Memory deficits are considered a cardinal cognitive feature of schizophrenia.(1) Being able to learn by experience is crucial for successful adaptation to a changing environment. Patients with schizophrenia show learning impairments on episodic memory tasks (2) but less is known about how learning is shaped by positive and negative feedback.(3) Executive function refers to a constellation of higher-level cognitive abilities that enables an individual to plan and execute goal-directed operations (4) and includes distinct components of response inhibition, working memory, cognitive flexibility, and interference control.(5) These superordinate cognitive-control mechanisms are therefore involved in the flexible and adaptive regulation of goal-directed behavior, particularly in novel situations for which automated behavioural routines are neither available nor appropriate.(6) Strong correlations between executive impairments and negative symptoms and/or disorganization symptoms have been reported by a study among chronically hospitalized patients.(7) A meta-analysis (8) further supported the significant associations of both negative and disorganized, but not positive, symptoms with impairments on tests of executive functioning.

## PURPOSE

In this study, we compared the performance of patients with schizophrenia with that of healthy controls on tests

[1]Corresponding author: Camelia Deac, Aleea Padin, Nr. 20, Ap. 25, Cod 400517, Cluj Napoca, România, Tel: +0741 030 066, E-mail: camelia.deac@yahoo.com
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of executive functioning and verbal memory in order to identify specific impairments in executive functioning and the relationship between executive function and memory performance. We then compared the performance of patients with or without negative symptoms.

## METHODS

**Subjects**

138 outpatients with a diagnosis of schizophrenia were recruited from the Community Mental Centre Cluj-Napoca. The diagnosis of schizophrenia was determined according to the criteria of the ICD-10. Subjects with neurological illness or head trauma, a history of alcohol or drug abuse, an estimated IQ below 70 were excluded from the study or age under 18 or over 60 years old were excluded from the study. Patients with schizophrenia were divided into the '"with negative symptoms group" and "without negative symptoms group" according to PANNS negative score below or above 19. A group of 43 control participants was recruited from a community sample with no psychological background. Exclusion criteria for the controls included a history of mental illness within first-degree relatives and the presence of a medical illness that might impair cognitive functioning.

**Measures**

**Clinician-rated measures**

The Romanian version of the PANSS (9) was used to measure the psychopathology of patients. Patients who scored higher than 19 on PANSS negative scales were included in the negative symptoms subgroup of schizophrenia.

**Neuropsychological assessment**

**Intradimensional/Extradimensional Shift (IED)** from Cambridge Neuropsychological Test Automated Battery (CANTAB) (10) and **RAVLT** (The Rey Auditory Verbal Learning Test (11) were used for neuropsychological assessment.

The IED subtest is a computer touch-screen adaptation of the Wisconsin Card Sorting Test that assesses the ability to shift attentional sets. The task is graded according to level of difficulty; it begins with a simple visual-discrimination task and then gradually increases in complexity. The following measures were derived from this test: Number of stages completed (1–9); Total errors; Pre-ED errors (errors prior to the extradimensional shift); EDS errors (errors at the extradimensional shift).

For the IDED task, subjects learn a series of visual discriminations in which one of two stimuli is correct. Feedback from the computer indicates whether a choice is correct (green tick, high tone) or incorrect (red cross, low tone). The rule is changed after six consecutive correct choices. If the learning criterion is not achieved within 50 trials, the test is discontinued. Stage 1 (simple discrimination [SD]) requires learning of the correct stimulus from a choice of two shapes; at Stage 2 (simple reversal [SR]) the previously irrelevant shape becomes correct. At Stage 3 (compound discrimination [C_D]) a second dimension (line) is introduced alongside the shape dimension with each of the two stimuli containing a shape and line; subjects need to continue selecting the shape dimension. At Stage 4 (compound discrimination [CD]), the lines are superimposed onto shapes in each stimulus, and responding to the previous shape is required. At Stage 5 (compound reversal [CR]) the previously incorrect shape now becomes the correct response. Thus, at stages 1–5, the exemplars are the same, and subjects are required to respond to the same dimension of shape. Stage 6 (intradimensional shift [IDS]) tests the veracity of rule learning as new compound line and shape exemplars are introduced, but the same dimension (shape) remains correct. Selection of the previously incorrect shape pattern is required at Stage 7 (intradimensional reversal [IDR]). Stage 8 tests attentional set-shifting (extradimensional shift [EDS]) as the previously irrelevant dimension (line) now becomes relevant, and one of the line patterns becomes the correct response. At Stage 9 required response. The various stages of this task require simple discrimination learning, compound discrimination learning, abstraction, attentional set-shifting, and reversal learning.

The Rey Auditory Verbal Learning Test (11) uses a simple format in which the client is asked to remember a list of 15 unrelated words (List A) repeated over five different trials. The client is then presented with another list of 15 unrelated words (List B), which serves to potentially interfere with previous learning, followed by a request to recall as many of the words from the original list as possible. After a 30-minute delay, the client is again asked to recall words from the original list (List A), following which he or she is asked to recognize as many words as possible in a list that includes words from the original list. As a result, a wide diversity of functions can be assessed. These include short-term auditory-verbal memory, rate of learning, learning strategies, retroactive and proactive interference, presence of confabulation or confusion in memory processes, retention of information, and differences between learning and retrieval. The entire procedure takes 10 to 15 minutes.

**Data analysis**

The data were analyzed using SPSS version 20 for OS 10.8.5. Analysis of variance (ANOVA) or chi-square tests were performed to compare demographic and neuropsychological variables.

## RESULTS

**Demographic and clinical variables**

The demographic data obtained from the schizophrenia group and the healthy controls are presented in table no. 1 and table no. 2. The three groups did not significantly differ in sex and age.

**Table no. 1 Demographic and clinical variable**

| | **Schizophrenia with negative symptoms** | **Schizophrenia without negative symptoms** | **Healthy controls** | | p |
|---|---|---|---|---|---|
| Gender (males) | 15.4 % | 15.1 % | 25.6 % | Chi-square 2.42 | >.05 |
| Age (years) | 39.3 | 37.7 | 36.14 | F 2.3 | >.05 |
| PANSS negative | 24.6 | 14.5 | | | |

*Comparison of neurocognitive functioning among those with negative symptoms schizophrenia or without negative symptoms schizophrenia and healthy controls*

The scores for executive functioning and for verbal memory are presented in table no. 2 and table no. 3. Significant group differences were observed in cognitive performance. Schizophrenic patients showed impairment in executive function and verbal memory in comparison with healthy control subjects. In terms of executive functioning, we found significant group differences in the IED total errors, adjusted total errors, pre-ED errors, and EDS errors. Post-hoc analyses indicated that those with negative symptoms schizophrenia exhibited more total and pre-ED errors on the IED than did normal controls. In terms of memory, schizophrenic patients performed worse than the healthy subjects.

**Table no. 2. Executive function**

| | | Schizophrenia with negative symptoms (SN) N=65 | Schizophrenia without negative symptoms (SWN) N=73 | Healthy Controls (HC) N=43 | F | p | Post-hoc Dunnet T3 | P |
|---|---|---|---|---|---|---|---|---|
| IED | Stage completed | 8.51 | 8.82 (.03) | 9 (0) | 7.961 | <.001 | SN< SWN | <.001 |
| | Total errors | 19.82 (3.6) | 18.7 (4.2) | 9.16 (3.93) | 14.396 | <.001 | SN=SWN | >.05 |
| | Pre-ED errors | 8.71 (2.5) | 8.53 (3.3) | 4.91 (2.2) | 8.875 | <.001 | SN=SWN | >.05 |
| | EDS errors | 9.42 (2.3) | 6.86 (1.3) | 2.95 (.21) | 9.606 | <.001 | SN< SWN | <.001 |

**Table no. 3. Verbal memory**

| | Schizophrenia with negative symptoms (SN) N=65 | Schizophrenia without negative symptoms (SWN) N=73 | Healthy Controls (HC) N=43 | F | p | Post-hoc Dunnet T3 | P | |
|---|---|---|---|---|---|---|---|---|
| RAVLT | First trial memory score | 5.5 (1.81) | 6.35(1.62) | 8.9 (2.33) | 44.188 | <.001 | SN< SWN | <.001 |
| | Second trial memory score | 7.6 (1.79) | 8.60(1.27) | 11.76 (1.79) | 48.984 | <.001 | SN< SWN | <.001 |
| | Retroactive inference | 8.9 (1.86) | 9.53 (1.42) | 13.74 (1.57) | 86.834 | <.001 | SN=SWN | >.05 |
| | Proactive inference | 9.87 (1.33) | 10.26(1.03) | 13.65 (1.57) | 42.832 | <.001 | SN=SWN | >.05 |
| | Retrieval | 11.47 (2.44) | 12.36 (2.99) | 13.4 (1.69) | 12.49 | <.001 | SN< SWN | <.001 |
| | Total | 52.2769 (5.33) | 56.75(12.34) | 74.32 (6.5) | 76.553 | <.001 | SN< SWN | <.001 |

Overall, the observed group differences can be attributed to impaired performance among negative symptoms schizophrenia when compared with the performance of healthy controls.

## DISCUSSIONS

In the present study, we compared the executive functioning and verbal memory of normal controls with that of patients with schizophrenia. We further examined how impaired executive functioning in patients was associated with severity of psychopathology.

Our results suggest that schizophrenic patients with negative symptoms are likely to exhibit poorer performance on tests of executive functioning and verbal memory than are normal controls. These results are consistent with the results of previous studies.(12)

Our findings suggest that patients with schizophrenia can learn and generalize rules but are inflexible when rules change, reflecting both reduced responsiveness to negative feedback and difficulty in switching attention.

This profile seems to represent a stable trait of the illness.

## CONCLUSIONS

Schizophrenic patients showed impairment in executive function and verbal memory in comparison with healthy control subjects. Impaired performance can be attributed to negative symptoms.

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