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RESEARCH PAPER

# ARE EXECUTIVE FUNCTIONS DEFICITS IN EARLY-ONSET CHRONIC SCHIZOPHRENIA MORE SEVERE THAN IN ADULT-ONSET CHRONIC SCHIZOPHRENIA?

Beata Hintze, Magdalena Rowicka, Anna Barczak

## Abstract

*Objective*: The research on the age of schizophrenia onset and cognitive impairments leads to contradictory conclusions. It is still unknown whether neurocognitive deficits in early-onset schizophrenia (EOS) are more intense than adulthood-onset schizophrenia (AOS). The study aimed to examine specific aspects of the executive functions of chronic outpatients with different ages of schizophrenia onset.

*Method*: Two clinical groups (EOS and AOS) consisted of 60 chronic outpatients with schizophrenia recruited from the community-based support system. The executive functions were measured with the Wisconsin Card Sorting Test (WCST), Trail Making Test A&B (TMT A&B), verbal fluency task (VFT), and the N-back test. Obtained results were compared to control groups consisting of 40 healthy subjects, matched with age, sex, and years of education, respectively.

*Results*: There were no differences in various aspects of executive dysfunctions between EOS and AOS outpatients. The outpatients in general, had lower scores than healthy controls regardless of their age of symptom onset. The most important finding suggests that some cognitive domains (visual working memory and processing speed) in presented schizophrenia patients were similar to those in healthy controls.

Despite the demographic differences, both clinical groups present the same level of executive functioning. In addition, similar to the healthy participants, the outpatients had no problems in working memory and processing speed.

*Conclusions*: These observations suggest that EOS might not be associated with more severe cognitive deterioration. Moreover, the stabilization or improvement of their functioning might be linked with long-term psycho-social rehabilitation and modern pharmacotherapy.

**Key words**: early-onset schizophrenia, adulthood-onset schizophrenia, executive dysfunction, community-based support systems

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## Introduction

Schizophrenia is considered a neurodevelopmental, mental disorder in which numerous structural and functional brain changes are observed (Giraldo-Chica et al., 2018; Rao et al., 2015). Central nervous system development anomalies are reflected in the formation of specific cognitive deficits.

Executive functions, including working memory, cognitive flexibility, inhibition, volition, planning, thinking, and self-monitoring, also encompass emotional and social abilities crucial for independent daily functioning, quality of life, school, and job success (Hwang et al., 2019). Disorders of working memory and executive functions, which are associated with frontal lobe dysfunctions, especially their prefrontal areas, are considered the most characteristic of schizophrenia (Wolf et al., 2015). Moreover, their impairment is one the most prominent deficits in schizophrenia, a significant predictor of functional outcome in patients. Thus, the dysexecutive syndrome is often considered strategic in terms of diagnosis and the different forms of interventions (Berberian et al., 2019).

Schizophrenia, starting during the adolescence period (early-onset schizophrenia, EOS), is still considered a more severe form of psychosis compared to adult-onset schizophrenia (AOS) (Armando et al., 2015; Coulon et al., 2020). Studies comparing the course and psychopathological manifestation of the disease have shown that EOS is characterized by a greater degree of neurodevelopmental disturbances, intensification of negative symptoms, cognitive deficits, a longer period of untreated psychosis, and a more frequent burden of schizophrenia in the family (Budisteanu et al., 2020). Long-term observations also point to worse long-term social functioning than for AOS patients (Caldiroli,



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et al., 2018; Grover, et al., 2019). A significant proportion of EOS patients had delayed psychomotor development (including walking), impaired visual-motor coordination, stereotypic movements, language, and speech disorders, along with delayed speech, social isolation, and withdrawal together with lower school competencies prior to the psychosis onset (Arango, et al., 2014; Budisteanu et al., 2020). An analysis of the 21 long-term studies on long-term outcome prognosis in EOS (Clemmensen, et al., 2012) showed worse results in those patients than other psychotic disorders. A group of people with EOS from the so-called "good outcome" was the least numerous (15.4%) in contrast to the so-called "poor outcome" (60.1%). During the 10-year follow-up, over half of the EOS patients had reduced functioning, which was already about 67% poor outcome in the following years of observation. With the increase in the number of years of illness, a good outcome was observed in a smaller percentage of people (about 12%). The authors emphasized that the early onset of schizophrenia has a worse outcome and prognosis than onset in adulthood. Different results from those cited above were also reported. A follow-up study after seven years in people with the first psychotic episode of the schizophrenia spectrum showed that patients with early-onset psychosis (EOP) had significantly fewer positive symptoms, better global, social, occupational, and community functioning than patients with adult-onset psychosis (AOP). The group with EOP also achieved significantly better results in their professional work and had a more favorable course of the disease with fewer psychotic episodes (Amminger et al., 2011).

Research indicates that cognitive dysfunctions are crucial for the course of schizophrenia (Berberian et al., 2019; Green, 2016). Some of the results showed that the onset of the disease within adolescence is related to the deterioration of cognitive functioning throughout the disease, thus with a worse prognosis, compared with cases beginning in adulthood (Grover, et al., 2019). Other reports did not confirm such relationships, especially in the first years of the diseases (Hintze, 2012; Holmén et al., 2012). Studies comparing the level of cognitive dysfunction between patients with the first episode and patients with multiple episodes are contradictory because some studies suggest a difference between them, and others point to no differences. Some studies have confirmed that cognitive dysfunction intensifies with subsequent episodes and a growing number of years of psychosis (Herold et al., 2021). Others indicate the stabilization of cognitive disorders (Bergh et al., 2016; Rund et al., 2015), while others suggest the possibility of improving the range of cognitive functioning (Kida et al., 2020). Therefore, the dynamics of cognitive dysfunction in EOS are still unknown. Overall, the patients with schizophrenia had cognitive deficits up to 2 standard deviations below the general population (Girdler et al., 2019).

Schizophrenia, specifically with severe cognitive impairment, contributes to the deterioration of the psycho-social functioning of patients. Therefore, it implies the necessity of long-term integrated therapy and comprehensive treatment. Community-based support systems (CBSS) allow for psycho-social rehabilitation after stays in medical institutions and enhance the recovery process. Such forms of support, like community self-help centers and occupational therapy workshops, are focusing on improvement of the independent everyday functioning, prevention of relapse and rehospitalizations, development of resources, and preparation for professional work by acquiring new social skills (Asher et al., 2017).

The study aimed to examine specific aspects of executive function of chronic outpatients with early-onset schizophrenia (EOS) and adulthood-onset schizophrenia (AOS) from the community-based support systems compared to age-matched healthy controls.

## Methods

### *Participants*

The schizophrenia outpatients were recruited from various forms of community-based support systems, such as occupational therapy workshops, services of community self-help centers, and community treatment teams. Inclusion criteria were as follows: outpatients with schizophrenia with at least ten years of illness (min 10– max 23 years), clinically stable. Exclusion criteria were abuse of or addiction to alcohol and other psychoactive substances, the co-occurrence of severe neurological or somatic diseases (such as diabetes, hypertension, coronary artery disease), intellectual disability.

Sixty outpatients with the diagnosis of paranoid schizophrenia (F20.0 according to ICD-10) participated in the study. These subjects were enrolled in two clinical subgroups (30 participants each), by the period of onset in adolescents (under 18, EOS – early-onset schizophrenia) and adulthood (over 18, AOS – adult-onset schizophrenia). All patients had a history of the condition for at least ten years. Before the start of the study, these diagnoses were confirmed by properly licensed psychiatrists. In both groups, outpatients were mostly treated with second-generation antipsychotic medications (EOS 83.3%; AOS 83.4%): olanzapine, risperidone, quetiapine, clozapine, sulpiride, amisulpride, aripiprazole, ziprasidone. From the first generation, antipsychotic medications following substances were reported: fluanxol, perazine, haloperidol. Most participants from both groups were on polytherapy. There was a significant difference in monotherapy, as in the AOS group, treatment with one antipsychotic was more often (26.7% EOS, 40% AOS $Chi^2$ (1) = 4.42 p = 0.036). The percentage of the familial burden of schizophrenia in the groups was similar, and 33.3% in EOS and 40% in AOS ($Chi^2$ (1) = 1.12 p = 0.290) had a family history of schizophrenia.

Healthy control subjects, age, sex, and years of education matched to the studied groups recruited healthy volunteers enrolled through advertisements. They all underwent detailed assessment, and the presence of psychiatric disorders, severe medical conditions, or cognitive impairment was an exclusion. Control groups (20 subjects each) were selected for clinical groups (EOS and AOS) to assess the level of performance of tests in the computer version (Wisconsin Card Sorting Test -WCST and N-back) and another for Trail Making Test A&B -TMT A&B and verbal fluency task -VFT.

### *Measurements*

**Neuropsychological tests**

Following neuropsychological methods were used:

1. Wisconsin Card Sorting Test Computer Version 4 Research Edition (WCST: CV4) (Heaton et al., 1993) was used to measure executive functions, set-shifting in particular. The following parameters were considered: percentage of total errors, percentage of perseverative and non-perseverative errors, percentage of conceptual level responses, number

of correctly completed categories, and trials to complete the first category.
2. N-back test (Coppola 1-back version) (1999) was used for the evaluation of visual working memory. The measured parameters included the percentage of correct responses and the mean reaction time.
3. Trail Making Test part A and B (TMT A & B); part A was used to assess the psychomotor speed and part B to evaluate visuospatial working memory and the ability to shift strategies; the test measured the time of completion (in seconds), and two additional indicators considered a good measure of executive control, relatively free from the influence of psychomotor speed (TMT B execution time - TMT A execution time [B - A]; TMT B execution time: execution time TMT A [B: A]) (Periáñez et al., 2007).
4. Verbal Fluency Task (VFT) in Polish version (Wysokiński et al., 2010), with two semantic categories: names of animals and names of sharp objects, and a phonetic one: words beginning with the letter "k" This method was used to assess verbal aspects of executive functions. The result of VFT is the number of correct words generated for each of the categories during 60 seconds. In addition, the total sum of words in all categories (total fluency) was also evaluated.

### *Clinical measures*

The assessment of schizophrenic symptoms (positive, negative, and general psychopathology) was conducted with the validated Polish version (Rzewuska, 2002) of the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987), assessment of the level of symptomatic remission (numerical criterion) and the level of symptomatic remission developed by The Remission in Schizophrenia Working Group (Andreasen et al., 2005). In addition, psycho-social functioning was evaluated with GAF - Global Assessment of Functioning (American Psychiatric Association, DSM-V, 2013).

### *Ethics*

The study complied with the ethical standards constituted in the 1995 Helsinki Declaration. Therefore, the Ethics Committee approved the study design of the Maria Grzegorzewska University in Warsaw, Poland (32-2011/2012). All participants (outpatients and controls) signed an informed consent and were informed of their right to withdraw their consent at any time, without consequences.

### *Statistical analysis*

The statistical description includes means, standard deviation, and percentage frequency. A significance level of $p < 0.05$ was adopted. The analysis of the shape of the distribution of variables was checked using the Kolmogorov - Smirnov test. The logarithmic transformation was used to normalize the variable distributions. One-way analysis of variance (ANOVA) was used to assess the significance of differences between the means. In the case of variables whose distributions differed significantly from the normal distribution, non-parametric Mann-Whitney tests were used. The analyses were carried out using IBM SPSS Statistics 22. The sample sizes (n=50) were estimated to satisfy the standard power and alpha conditions (alpha=.05, two tails, and power =.80) with effects sizes of $eta^2$=0.15.

## Results

### *Sample characteristics*

The EOS group consisted of nine women and 21 men. The average period of functioning outside psychiatric hospitalization was about 27 months. Healthy controls for WCST and N-back (20 subjects) consisted of nine women and 11 men and for TMT and VFT (20 subjects) consisted of seven women and 13 men.

The AOS group consisted of 16 women and 14 men. The average period of functioning outside psychiatric hospitalization among the AOS patients was about 26 months. Healthy controls for WCST and N-back (20 subjects) consisted of ten women and ten men and for TMT and VFT consisted of 11 women and nine men (see **tables 1-3** for sociodemographic details).

Patients with schizophrenia differed significantly in the demographic factors. Outpatients with EOS, compared to those with AOS, were, as expected, significantly younger. They were also less educated than the AOS group, with a shorter employment period and a more extended period of disability pension (Table 1). Clinically, both groups had similar severity in positive, negative, and general psychopathological symptoms, numerical values of symptomatic remission index (Andreasen et al., 2005), general functioning (GAF),

**Table 1.** *Characteristics of the EOS and AOS groups*

| Demographic and clinical characteristics | EOS M (*SD*) | AOS M (*SD*) | test *F*(df)/ *Z* | *p*-value |
|---|---|---|---|---|
| Age | 32.78 (4.14) | 39.41 (6.36) | *F*(1,58) = 22.91 | *p < 0.001* |
| Education (years) | 13.23 (3.13) | 15.83 (2.34) | *F*(1,58) = 13.32 | *p < 0.01* |
| Period of disability (years) | 11.27 (5.99) | 6.78 (5.71) | *F*(1,58) = 8.79 | *p < 0.001* |
| Employment (years) | 3.06 (4.27) | 8.78 (5.47) | *Z* = –4.33 | *p < 0.001* |
| Age at onset (years) | 16.13 (0.90) | 24.83 (4.90) | *F*(1,58) = 91.25 | *p* < 0.001 |
| Duration of disease (years) | 16.33 (4.06) | 14.60 (3.44) | *F*(1,58) = 3.18 | *p* = 0.079 |
| Hospitalizations (number) | 8.63 (5.20) | 7.06 (4.48) | *F*(1,58) = 1.56 | *p* = 0.216 |
| PANSS dimensions - total | 67.47 (19.12) | 62.70 (14.25) | *F*(1,58) = 1.19 | *p* = 0.278 |
| Positive Symptoms | 13.70 (4.29) | 13.87 (4.96) | *F*(1,58) = 0.19 | *p* = 0.889 |
| Negative Symptoms | 19.53 (7.34) | 17.13 (5.41) | *F*(1,58) = 2.07 | *p* = 0.155 |
| General Symptoms | 34.23 (10.74) | 31.70 (7.41) | *F*(1,58) = 1.13 | *p* = 0.292 |
| GAF | 56.13 (12.43) | 60.07 (11.00) | *F*(1,58) = 1.68 | *p* = 0.199 |
| Level of symptomatic remission | 18.83 (6.81) | 17.23 (4.92) | *F*(1,58) = 1.09 | *p* = 0.301 |

number of hospitalizations, and duration of psychosis.

Outpatients with EOS compared to their control groups had fewer years of education, and no differences were found between the AOS and their controls in terms of education.

versus 76.7% in the AOS subjects. In the N-back test, the error-free performance was slightly worse in the EOS (46.7%, versus 60%). The TMT results in both groups point to executive control disorders - the time of performing Part B is over 2.5 times longer than Part

**Table 2.** *Characteristics of clinical and the healthy controls for WCST and N-back*

| Groups | Age M (SD) | Test *t* (df) | Years of education | Test *t* (df) |
|---|---|---|---|---|
| EOS | 32.78 (4.14) | *t* (48) = 0.86 | 13.23 (3,13) | *t* (48) = -4.36 |
| Controls I | 31.60 (5.51) | p=0.393 | 16.60 (1,79) | p< 0.001 |
| AOS | 39.41 (6.36) | *t* (48) = -1.47 | 15.83 (2,34) | *t* (48) = -0.43 |
| Controls II | 42.25 (7,18) | p=0,148 | 16.10 (1,86) | p =0.671 |

**Table 3.** *Characteristics of clinical and the healthy controls for TMT and VFT*

| Groups | Age M (SD) | Statistic value *Z* | Years of education | Statistic value *Z* |
|---|---|---|---|---|
| EOS | 32.78 (4.14) | *Z* = -0.28 | 13.23 (3,13) | *Z* = -4.32 |
| Controls I | 32.85 (5.51) | p=0.781 | 17.40 (1,60) | p< 0.001 |
| AOS | 39.41 (6.36) | *Z* = -1.65 | 15.83 (2,34) | *Z* = -0.62 |
| Controls II | 39.15 (10.90) | p=0,100 | 15.30 (2.23) | p =0.533 |

### *Performance on neurocognitive tests*

The EOS group performed significantly lower in all parameters of WCST (percentage of total perseverative and non-perseverative errors, percentage of conceptual level responses, correctly completed categories, and needed more cards to complete the first category) compared to their controls. In TMT B, the EOS subjects were significantly slower and less effective in control indicators than their age-matched healthy group. They produced overall fewer words (sum of 3 categories) than healthy participants and in each measured category separately. No significant differences were found between the EOS and controls in N-back and TMT A tasks (table 4).

The AOS group performed significantly lower in WCST in all parameters, in VFT in 2 categories (animals and words beginning with the letter "k") than healthy controls. In the WCST, AOS outpatients had a significantly higher percentage of total perseverative and non-perseverative errors, a lower percentage of conceptual level responses, and correctly completed categories. They required more cards to complete the first category compared to healthy controls. In the verbal fluency task, the AOS produced a similar number of sharp objects but scored significantly lower than their controls in the rest of the categories and the total sum of 3 categories. No significant differences were observed between the AOS and healthy controls in N-back, TMT A & B, and the Part B to Part A indicators (Table 4).

A comparison between the EOS and the AOS failed to find differences in neuropsychological measures. A large scatter of raw results was noted in both groups, which proves their similar diversity in terms of variables analyzed (similar values of standard deviations) (Table 5).

It is worth mentioning that in the WCST, most of the participants completed all of the required categories. It suggests the relatively persevered executive functions. In the EOS group, 73% of people achieved six categories A. In the assessment of verbal fluency, both groups examined provided significantly more animal names than words beginning with the letter "k" and sharp objects, which in turn were the least numerous category (Wilcoxon test for dependent samples: animals - words with the letter k for EOS Z = -3.41 p = 0.001; for AOS Z = -3.74 p <0.001; Student's t-test for dependent samples: animals - sharp objects: for EOS t (29) = 10.41 p <0.001; for AOS t (29) = 12.37 p <0.001; Wilcoxon test for dependent samples: words beginning with the letter k - sharp objects : for EOS Z = -4.40 p <0.001; for AOS Z = -4.43 p <0.001).

## Discussion

The research results indicate that outpatients with long-term schizophrenia, regardless of the age of onset, have a similar level of executive functioning (no statistically significant differences in the performance of neuropsychological measures). It confirms recent reports suggesting the lack of cognitive differences in this regard between patients with long-term schizophrenia with different onsets (Coulon et al., 2020; Vernal et al., 2020). Obtained results contrast to the data pointing to a correlation between worse cognitive and executive functions and early onset of schizophrenia (Caldiroli et al., 2018; Grover et al., 2019).

As expected, schizophrenia subjects showed significantly poorer performance in some of the neurocognitive measures. Compared to their control groups, outpatients had significantly lower scores in all parameters of the WCST. Furthermore, they made a higher total percentage of errors, including perseverative and non-perseverative ones. In addition, their scores on conceptual level response-ability were lower; they had managed to complete fewer categories and needed more trials to complete the first category compared to the healthy controls. A similar WCST performance in EOS and AOS corresponds to the available study results (Hintze, 2012; Holmén et al.,

**Table 4.** *Results in WCST, N-back, TMT, VFT in the clinical groups compared healthy controls*

| Neurocognitive tests WCST/N-back/ FVT | EOS M (*SD*) | HC $^{EOS}$ M (SD) | AOS M (*SD*) | HC $^{AOS}$ M (SD) | EOS vs HC$^{EOS}$ test *F*(df)/ *Z*, *eta*$^2$ *p* - value | AOS vs HC$^{AOS}$ test *F*(df)/ *Z*, *eta*$^2$ *p* - value |
|---|---|---|---|---|---|---|
| WCST % total errors | 23.00 (9.65) | 16.85 (5.35) | 22.87 (10.91) | 15.20 (5.13) | $^{ln}F$(1.48) = 6.03 $p$ = 0.018 *eta*$^2$ = 0.112 | $^{ln}F$(1.48) =8.05 $p$ = 0.007 *eta*$^2$ = 0.144 |
| WCST % perseverative errors | 11.50 (6.21) | 8.25 (2.67) | 12.47 (6.98) | 7.65 (2.52) | $^{ln}F$(1,48) = 4.74$p$ = 0.034 *eta*$^2$ = 0,090 | $F$(1,48) = 10.29 $p$ = 0.002 *eta*$^2$ = 0.176 |
| WCST % nonperseverative errors | 11.43 (5.47) | 8.55 (3.15) | 10.27 (5.17) | 7.65 (2.96) | $F$(1,48) = 4.53 $p$ = 0.038 *eta*$^2$ = 0.086 | $^{ln}F$(1,48) = 4.19 $p$ = 0.046 *eta*$^2$ = 0.080 |
| WCST % conceptual level responses | 71.67 (13.28) | 79.80 (8.08) | 70.87 (15.79) | 82.50 (7.32) | $^{ln}F$(1,48) = 4.57 $p$ = 0.038 *eta*$^2$ = 0.087 | $^{ln}F$(1,48) = 6.50 $p$ = 0.014 *eta*$^2$ = 0.119 |
| WCST categories completed | 5.53 (1.01) | 6.00 (0.00) | 5.47 (1.18) | 6.00 (0.00) | $Z$ = –2.30 $p$ = 0.022 | $Z$ = –2.30 $p$ = 0.022 |
| WCST trials to complete 1st category | 15.87 (5.70) | 11.80 (2.73) | 16.07 (7.24) | 12.50 (3.10) | $Z$ = –2.35 $p$ = 0.019 | $Z$ = –1.82 $p$ = 0.069 |
| N-back % number correct | 84.67 (19.91) | 90.00 (12,68) | 89.07 (15.33) | 91.00 (11.67) | $^{ln}F$ (1,48) = 0.37 $p$ = 0.545 | $^{ln}F$ (1,48) =0.06 $p$ = 0.816 |
| N-back reaction time (msec) | 744.83 (320.65) | 773.55 (240.50) | 685.67 (319.60) | 850.30 (233.91) | $F$(1,48) = 0.11 $p$ = 0.744 | $F$ (1,48) = 3.90 $p$ = 0.054 *eta*$^2$ = 0.075 |
| TMT A – sec. | 30.30 (16.48) | 26.15 (10.53) | 30.43 (12.03) | 28.20 (10.00) | $^{ln}F$(1,48) = 0.76 $p$ = 0.386 | $^{ln}F$(1,48) = 0.47 $p$ = 0.496 |
| TMT B – sec. | 75.97 (41.93) | 49.25 (15.80) | 75.70 (36.94) | 67.30 (20.37) | $^{ln}F$(1,48) = 9.78$p$ = 0.003 *eta*$^2$ = 0.169 | $^{ln}F$(1,48) = 0.33 $p$ = 0.567 |
| TMT B–A | 45.67 (33.56) | 23.10 (11.56) | 45.27 (31.31) | 39.10 (19.46) | $Z$ = –3.49 p <0.001 | $Z$ = –0.28 p = 0.781 |
| TMT B: A | 2.67 (1.11) | 2.01 (0.59) | 2.55 (0.95) | 2.59 (0.93) | $Z$ = –2.58 p=0.010 | $Z$ = –0.24 p = 0.812 |
| VFT names of animals 60 sec. | 20.63 (5.99) | 28.70 (5.34) | 20.33 (5.07) | 26.45 (5.57) | $F$(1,48) = 23.70 $p$ < 0.001 *eta*$^2$ = 0.331 | $F$(1,48) = 16.14 $p$ < 0.001 *eta*$^2$ = 0.251 |
| VFT words beginning with the letter "k"60 sec. | 16.9 (5.17) | 20.60 (5.11) | 15.06 (4.31) | 19.10 (5.28) | $^{ln}F$(1,48) = 6.34 $p$ = 0.015 eta2 = 0.117 | $F$(1,48) = 9.00 $p$ = 0.004 *eta*$^2$ = 0.158 |
| VFT names of sharp objects 60 sec. | 10.20 (3.14) | 12.00 (3.78) | 10.00 (3.43) | 10.80 (3.78) | $F$(1,48) = 3.34 $p$ = 0.074 *eta*$^2$ = 0.065 | $F$(1,48) = 0.60 $p$ = 0.442 |
| Total number of words 3 category | 48.03 (110.1) | 61.30 (9.92) | 45.06 (9.74) | 56.85 (12.25) | $F$(1,48) = 18.82 $p$ < 0.001 *eta*$^2$ = 0.282 | $F$(1,48) = 14.27 $p$ < 0.001 *eta*$^2$ = 0.229 |

For the interpretation of Eta squared *eta*$^2$ > 0.01 is a small effect; *eta*$^2$> 0.06 is a medium effect; *eta*$^2$ > 0.14 is a large effect.
$^{Ln}$ – logarithmized results

2012), which did not confirm the impact of the age of onset on the level of assessed cognitive functioning in the first years of the disease. The lack of such differences between clinical groups with long-term schizophrenia may be related to treatment with atypical antipsychotic drugs (MacKenzie et al., 2018). However, the mean results of completed categories of the WCST in our outpatients are significantly better than recently published data on chronic schizophrenia patients with a similar disease duration period (Wei et al., 2020). One possible explanation is participating in community-based support systems, which might have a beneficial impact on executive functioning.

In the VFT, the EOS group achieved significantly lower results than the healthy control in the sum of all tasks and particular categories. The AOS patients,

**Table 5.** *Results in WCST, N-back, TMT, VFT tests in the EOS and AOS groups tested*

| Neurocognitive tests WCST/N-back/ FVT/CVLT | EOS *N* = 30 M (*SD*) | AOS *N* = 30 M (*SD*) | test *F*(df)/ *Z*, *p* - value |
|---|---|---|---|
| WCST % total errors | 23.00 (9.65) | 22.87 (10.91) | $^{ln}F(1,58) = 0.07$ $p = 0.799$ |
| WCST % perseverative errors | 11.50 (6.21) | 12.47 (6.98) | $^{ln}F(1,58) = 0.27$ $p = 0.603$ |
| WCST % nonperseverative errors | 11.43 (5.47) | 10.27 (5.17) | $F(1,58) = 0.72$ $p = 0.399$ |
| WCST % conceptual level responses | 71.67 (13.28) | 70.87 (15.79) | $^{ln}F(1,58) = 0.06$ $p = 0.808$ |
| WCST categories completed | 5.53 (1.01) | 5.47 (1.18) | $Z = –0.06$ $p = 0.952$ |
| WCST trials to complete 1st category | 15.87 (5.70) | 16.07 (7.24) | $Z = –0.04$ $p = 0.970$ |
| N-back % number correct | 84.67 (19.91) | 89.07 (15.33) | $^{ln}F(1,58) = 0.72$ $p = 0.400$ |
| N-back reaction time (msec) | 744.83 (320.65) | 685.67 (319.60) | $F(1,58) = 0.51$ $p = 0.477$ |
| TMT A – sec. | 30.30 (16.48) | 30.43 (12.03) | $^{ln}F(1,58) = 0.21$ $p = 0.652$ |
| TMT B – sec. | 75.97 (41.93) | 75.70 (36.94) | $^{ln}F(1,58) = 0.01$ $p = 0.909$ |
| TMT B–A | 45.67(33.56) | 45.27 (31.31) | $Z = –0.04$ $p = 0.965$ |
| TMT B : A | 2.67 (1.11) | 2.55 (0.95) | $Z = –0.39$ $p = 0.695$ |
| TMT B–A/A | 1.67 (1,11) | 1.55 (0.95) | $Z = –0.39$ $p = 0.695$ |
| VFT names of animals 60 sec. | 20.63 (5.99) | 20.33 (5.07) | $F(1,58) = 0.04$ $p = 0.835$ |
| VFT words beginning with the letter “k”60 sec. | 16.9 (5.17) | 15.06 (4.31) | $^{ln}F(1,58) = 1.71$ $p = 0.196$ |
| VFT Names of sharp objects 60 sec. | 10.20 (3.14) | 10.00 (3.43) | $F(1,58) = 0.06$ $p = 0.815$ |
| Total number of words - 3 categories | 48.03 (110.1) | 45.06 (9.74) | $F(1,58) = 1.22$ $p = 0.274$ |

($^{Ln}$ – logarithmized results)

similarly to the EOS group, had lower results than the healthy control in two out of three categories ("animals" and "k" words) and the total fluency score (the sum of all words). These results suggested a poorer level of some aspects of executive functioning in outpatient groups than healthy controls. The outpatients were similar in terms of verbal fluency performance. Most words were generated in the 'animals' category, and the least – in the 'sharp objects' one. Such distribution is typical for controls and patients' populations in Poland (Ponichtera-Kasprzykowska et al., 2019). Data on verbal fluency in people with schizophrenia often show a reduced ability to generate words according to the phonetic and/or semantic criteria, with errors in the type of perseverations and inclusions, which is associated with dysfunction of the frontal and temporal lobes in the brain (Landrø & Ueland, 2008; Onishi et al., 2019). However, not all researchers agree on the existence of verbal fluency deficits in patients with schizophrenia, regardless of the endophenotype (EOS compared to AOS) (Grover, et al., 2019). Moreover, in some cases (the phase of stabilization of psychopathological symptoms), no deterioration of phonemic or semantic fluency is observed, as in a healthy population (Batty et al., 2015). Regardless of the significant differences between clinical groups and their controls, the obtained verbal fluency scores in our outpatients suggest relatively intact verbal productivity of all categories compared to schizophrenic patients according to the recent Polish data (Krukow et al., 2017).

Verbal fluency scores depend on speed processing (Brébion et al., 2018), and our outpatients showed no slowing compared to the healthy group. Furthermore, we found no difference in the time of TMT A execution. Among outpatients, only the EOS group had longer performance times of TMT B and the lower control indicators compared to healthy controls. Recent meta-analyses suggest that all schizophrenia patients, regardless of the endophenotype, are characterized by a deficit in processing speed (Laere et al., 2018) which was not present in our population. Moreover, recent data suggest that executive functioning is related to speed processing (Thuaire et al., 2020). It is worth mentioning that the outpatients described, as noted above, had relatively good executive functioning.

Working memory impairment is considered a significant cognitive deficit among schizophrenia patients. Due to dysfunctions of its network (Wu &

Jiang, 2020), mainly in the prefrontal cortex (Kumar et al., 2021), it was somewhat surprising that we failed to observe it in our participants. The outpatients had similar levels of visual working memory as healthy individuals, and no differences were noted between EOS and AOS subjects in the 1-back task scores. Several factors are probable to consider in terms of lack of working memory problems. It includes the specific as well as non-specific effects of CBSS (e.g., through behavioral activation or increased motivation) (Cassetta et al., 2018), antipsychotic treatment (Guo et al., 2019). Possibly, it had contributed to fewer hospitalizations and fewer severe negative symptoms, as the latter is suggested to be related to visual working memory impairment (Zhang et al., 2018).

Current data suggest that only some dimensions of executive functions, mainly in spatial working memory measured by TMT B, are severely impaired in psychotic patients compared to healthy subjects (Hwang et al., 2019). Other researchers emphasized that abnormalities in the performance of TMT B are stable over time, which is why they can be treated as a characteristic feature of schizophrenia, regardless of the illness duration, level of education, or being an inpatient/ outpatient (Laere et al., 2018). It contrasts with the other data suggesting that executive functioning measured by TMT might be intact (Yu et al., 2016). Published studies assessing performance in control indicators point to the significant deficit in patients with schizophrenia. The greatest problems of TMT B execution time are observed in patients with a family history compared to people without genetic load (on average over 2.5 times longer) (Birkett et al., 2008; Periáñez et al., 2007). Similar values of index B: A were obtained in the present study - EOS 2.67 and AOS 2.55. One explanation for this finding is the speed processing discussed above, measured by TMT A execution time, leading to discrepancies. Compared to relatively spared visual working memory, the scores of control indicators corroborate the more recent data on the primary but limited to specific domains executive functions. It seems that the executive control, but not all executive functions, were disturbed in our outpatients, which was also found in recent data (Joo et al., 2020).

The lack of often reported severe executive deficits could probably be due to an explanation of a combination of active participation in community-based support systems, already mentioned above, and modern pharmacological treatment (Sidana et al., 2018). Another significant factor is that the outpatients have achieved symptomatic remission. These conclusions are consistent with the sparse research that assessed the executive functions in fully and partially remitted schizophrenia outpatients, indicating no significant differences in the executive functioning of fully remitted outpatients and healthy controls (Braw et al., 2012). Thus, it proves the importance of negative symptoms in determining executive dysfunction in schizophrenia. Moreover, it also shows a substantial role in long-term therapeutic efforts.

The similar performance profiles of WCST, N-back, TMT, and VFT between the presented groups from EOS and AOS after many years of treatment, with significant differences in demographic factors (such as years of education, years of professional work, and duration of retirement) may be due to many reasons. Moreover, several aspects of executive functions such as working memory, processing speed, and set-shifting were similar to those in healthy people. Thus, these data suggested relatively intact/undisturbed domains of executive functions in both clinical groups but deficits of others (executive control, set-shifting).

It seems that, apart from the use of modern pharmacotherapy, participation in the community-based support systems and achieving symptomatic remission are the most important factors. Due to the main aim of preparing outpatient for occupational activity through the acquisition of new social skills and developing the ability to live independently by using skills training for daily activities, participation in CBSS is crucial. Social skills training contributes to improving such skills as problem-solving, coping with stress, and interpersonal communication. It also indirectly influences the improvement of executive functions. Such an explanation seems probable to research the neurobiological basis of psychotherapy (Javanbakht & Alberini, 2019). Studies of the influence of therapeutic interactions on central nervous system (CNS) function have shown changes in activity in the dorsolateral prefrontal cortex. Changes in this area of the CNS confirm the beneficial effect on executive functions (e.g., Frewen et al., 2008; Haut et al., 2010). Social skills training is also related to learning processes, so it can be assumed that they influence the processes of neurogenesis that are associated with neuroplasticity (Kang et al., 2016). Neurogenesis is of exceptional importance in compensatory processes (Moreno-Jiménez, et al., 2019). These findings are treated as a neurophysiological basis for the application of cognitive training in schizophrenia. Therefore, the continuation of therapeutic and rehabilitation training after hospital stays outside medical centers impacts the activity positively in many areas, including indirectly on cognitive functioning (Mayer-Amberg et al., 2016). Most of the participants examined achieved the numerical criterion of symptomatic remission (a complete remission) and had a long period without psychiatric hospitalization. Our observations are consistent with other results regarding the lack of differences in executive functioning between EOS and AOS. A meta-analysis showed that the outcomes of schizophrenia, remission status, the severity of psychopathological symptoms, and social and occupational functioning of patients after a long-term illness only slightly depend on the age of the disease onset. In EOS, on the other hand, occupational rehabilitation and employment are of particular importance for the outcome, which is in line with other researchers' reports (Immonen et al., 2017).

## Conclusions and limitations

The age of onset for schizophrenia does not differentiate outpatients in terms of cognitive functioning, which constitutes one of the most significant findings from our study. The long-term form of schizophrenia with an early onset does not have to be associated with the progression of executive dysfunction. It indirectly proves the need for integrated and long-term interventions, both pharmacological and environmental, along with cognitive ones. Those actions can positively affect the functioning of people with schizophrenia, regardless of the initial severity of symptoms associated with the age of schizophrenia onset.

It is worth emphasizing that the outpatients described were clinically high-functioning, free from other often observed problems such as substance abuse and comorbid somatic conditions. Therefore, their scores can be different from data from numerous studies on the general schizophrenia population. In contrast to published research, our outpatients

presented relatively spared executive functioning, attention, speed processing, and working memory. Thus, early therapeutic strategies, comprehensive pharmacological and non-pharmacological treatments, and social interventions, along with community cased support systems involvement seems to be beneficial and promising in terms of long-term outcome in patients with early-onset schizophrenia.

Relatively small samples of outpatients might be problematic, but this is partially due to the selection of chronic outpatients without severe somatic illnesses such as diabetes or hypertension, which often occur after years of treatment. Another limitation of the research is the lack of data on the duration of untreated psychosis. The next limitation of this research is the difference in years of education between the EOS and control groups. It was impossible to recruit healthy people in the age range adapted to EOS but with fewer years of education.

The advantage of this study is that it provides new and partially contradicting data on research on patients with different onsets of schizophrenia.

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