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The associations of negative and disorganization symptoms with verbal fluency in schizophrenia: the mediation effect of processing speed and cognitive flexibility

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Abstract

Background Psychopathological symptoms appear important for cognitive functions in schizophrenia. Nevertheless, the factors and their impact on relationships between negative or disorganization symptoms and verbal fluency are still debatable. The preliminary objective of the study was to compare verbal fluency, including clustering and switching as cognitive strategies, executive functions, and processing speed between individuals with schizophrenia (SZ) and healthy controls (HC). The main aim of the study was to investigate mediation models and identify whether relationships between negative and disorganization symptoms and verbal fluency in schizophrenia are mediated by cognitive flexibility and processing speed.

Methods Semantic (animal and fruit) and phonemic (letter k and letter f) fluency tasks, the Berg Card Sorting Test (BCST), and the Color Trails Test (CTT) were administered in the SZ group (n = 108) and a matched HC group (n = 108). The Positive and Negative Syndrome Scale (PANSS) was applied to measure psychopathological symptoms in schizophrenia patients.

Results SZ produced fewer words, had larger cluster size, and fewer switches in semantic fluency than HC. Moreover, the SZ group had longer completion time in CTT 1 and CTT 2 and higher percent of perseverative and non-perseverative errors in BCST than HC. Three mediation models demonstrated good fit indices, suggesting that processing speed and cognitive flexibility were significant mediators for relationships between: (1) psychopathological symptoms and productivity or semantic clustering in animal fluency; (2) negative symptoms and productivity in semantic or phonemic fluency; and (3) disorganization symptoms and productivity in semantic fluency.

Conclusions Individuals with schizophrenia are characterized by a specific performance profile on verbal fluency tasks. They manifest poor productivity and problems using cognitive strategies for semantic fluency. Referring to executive functioning, schizophrenia patients exhibit decreased cognitive flexibility, problem-solving, and formulating concepts, as well as slow processing speed. It was found that processing speed and cognitive flexibility may be

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understood as the neuropsychological mechanisms modifying the relationships between negative symptoms, disorganization symptoms, and semantic and phonemic fluency. Therefore, these results provide a foundation for including cognitive flexibility and processing speed in cognitive remediation for schizophrenia patients.

Keywords Verbal fluency, Clustering, Switching, Executive functions, Cognitive flexibility, Processing speed, Psychopathological symptoms, Schizophrenia

Background

Currently, schizophrenia is considered a spectrum disorder [1], and the cognitive dysfunctions revealed in its clinical picture have an essential impact on functional outcomes [2, 3]. Thus, it is crucial to better understand the specificity of cognitive deficits and the nature of the complex relationships between psychopathological symptoms and cognitive impairments due to treatment outcomes [4].

Verbal fluency refers to a set of cognitive and linguistic functions that facilitate information retrieval from memory and it is known to be impaired in the course of schizophrenia [5–8]. Cognitive processes—in particular, executive functions (such as initiation, planning, monitoring, and inhibition of irrelevant words)—are involved in searching one's mental lexicon based on cues and associations with a probe and recent retrievals [9]. Fluency is typically assessed in terms of either semantic or phonemic fluency. Studies mostly find that individuals with schizophrenia score better in semantic than phonemic fluency but lower for both than healthy controls [10-13].

Verbal fluency is typically assessed by measuring productivity; however, more comprehensive evaluation includes the cognitive strategies of clustering (producing words within clusters or categories) and switching (shifting effectively from one subcategory or cluster to another) [14]. Clustering and switching abilities involve not only executive functions but also the integrity and functional organization of short-term and long-term semantic memory systems for both semantic and phonemic fluency. Semantic clustering seems to be more important than phonemic for the efficient search of a mental lexicon, independently of the kind of imposed criterion (semantic or phonemic). Recent meta-analysis results indicate that individuals with schizophrenia have smaller numbers of clusters and switches in semantic fluency compared to healthy controls [7]. However, this paper focuses only on semantic fluency and the number of clusters. Other researchers indicate that mean cluster size is a better measure of semantic memory and mental lexicon, since it is relatively independent of word production [15–18]. Sokołowski et al. [19] suggested using average cluster size or number of switches divided by the sum of correct responses (proportion indicator).

The investigation of clustering and switching strategies has identified some features of verbal fluency impairment in schizophrenia. Nevertheless, research results regarding such cognitive strategies are inconsistent. Some studies confirmed reduced switches and clusters in semantic and phonemic fluency in individuals with schizophrenia [20-22] or fewer switches but normal clusters [23-25]. Other studies indicated normal numbers for both strategies and additionally for mean cluster size [26]. Beilen et al. [27] found smaller mean cluster size for semantic fluency in schizophrenia; Zakzanis et al. [28] obtained similar results for phonemic fluency. However, other authors did not confirm these results [29-31]. Differences in cognitive strategies may disappear when controlling for total words [21, 32] or they may remain significant only for mean cluster size in semantic fluency [20]. It seems that both semantic and executive deficits can decrease verbal fluency performance in schizophrenia.

Several important neuropsychological factors may have a crucial role in verbal fluency among individuals with schizophrenia [33]. Firstly, processing speed and executive deficits have been recognized as important in schizophrenia [34-36], which is confirmed by several meta-analyses [5, 6, 11, 37–39]. Additionally, some previous studies revealed that processing speed play the mediating role for the relationships between schizophrenia symptoms, brain connectivity, and executive functions [40, 41]. Studies have also demonstrated associations of semantic and phonemic fluency with processing speed [27, 42-44] and executive functions, including cognitive inhibition and working memory [45-48] in schizophrenia. Recently, relationships of verbal fluency with cognitive flexibility, concept formation, and cognitive inhibition have also been shown in healthy participants [49, 50]. However, little is known about the relationships between these cognitive functions and cognitive strategies (clustering and switching) for verbal fluency among individuals with schizophrenia. Only Savla et al. [51] found a link between information processing speed and switches in semantic fluency in a clinical sample. In healthy individuals, Unsworth et al. [52] confirmed that working memory is a significant predictor of number of clusters, while both working memory and processing speed are significant for number of switches.

Verbal fluency impairments in schizophrenia may be related to psychopathological symptoms. At the clinical level, negative and disorganization symptoms are associated with verbal fluency [53]. The meta-analysis conducted by Henry and Crawford [13] found a relationship of negative symptoms with phonemic fluency as well as of negative and positive symptoms with semantic fluency. Furthermore, only a few studies reported relationships between psychopathological symptoms, cognitive strategies such as clustering and switching, and the number of switches in phonemic fluency [25] or between negative symptoms and switching in semantic fluency [31, 54]. Some authors have not found a link between psychopathological symptoms and cognitive strategies [23, 26].

Finally, negative and disorganization symptoms also appear crucial for other cognitive functions in schizophrenia, particularly processing speed and executive functions, which has been confirmed in various studies [55, 56] as well as in meta-analyses [53, 57]. Therefore, considering the presence of relations between psychopathological symptoms, verbal fluency, processing speed, and executive functions, it can be assumed that there are more complex relationships between these variables, including mediating factors. It has been suggested that in the relationships between negative symptoms, working memory [58], and verbal fluency [59], processing speed plays a mediating role in schizophrenia. Similarly, there may be a relationship between negative and disorganization symptoms and verbal fluency via executive functions and information processing speed. If such mediating effects were confirmed, efforts to improve verbal fluency should be directed at improving processing speed and executive functions rather than alleviating psychopathological symptoms.

Taking the above findings into account, this study was designed to fill the gap in the literature regarding the complexity and character of verbal fluency problems in schizophrenia by investigating productivity and cognitive strategies (clustering and switching) in semantic and phonemic fluency as well as executive functions, processing speed, and their associations with psychopathological symptoms. The preliminary aim was to compare verbal fluency, including cognitive strategies, executive functions, and processing speed between participants with schizophrenia and healthy controls. The main objective of the study was to examine mediation models to test if the relationships between negative or disorganization symptoms and verbal fluency (including clustering and switching) are mediated by cognitive flexibility and processing speed in schizophrenia patients.

Material and methods Participants

One hundred and eight participants diagnosed with schizophrenia (SZ) and 108 healthy controls (HC) took part in this study. The diagnosis was confirmed by properly licensed psychiatrists using a structured clinical interview according to ICD-10 diagnostic criteria (WHO [60]). All participants were non-consanguineous and right-handed. SZ individuals were recruited from inpatients, day treatment patients, and outpatients at three psychiatric wards. The inclusion criteria required SZ participants to be aged 18-60 years old, comprehend the test procedure, and be in a stable clinical state assessed by psychiatrists. The exclusion criteria were craniocerebral injuries, severe somatic diseases (e.g., cancer), dementia, or substance use disorders. All participants with SZ were taking neuroleptic medication and were clinically stable when neuropsychological assessments were performed for the current study.

HC were individuals without mental or neurological disorders (verified by interview), matched in terms of sex, age, and education. Students and employees of local universities disseminated information about the recruitment of controls. The inclusion and exclusion criteria for HC were the same as the criteria for the SZ group, with the exception of the clinical parameters pertaining to schizophrenia. No recruited individual was excluded from the study based on the exclusion criteria.

The data were collected from two research projects, which had the same inclusion and exclusion criteria. All participants signed written consent to take part in the study. Both study protocols were approved by local bioethics committees. Both studies were carried out in accordance with the Helsinki Declaration II.

Neuropsychological assessment Verbal Fluency Test

Participants performed four fluency tasks in Polish: two each for semantic and phonemic fluency [14]. In each task, participants had one minute to generate as many words as possible in the given category without repeating items. Audio was recorded for all responses with the participant's consent and transcribed for further analysis. Productivity was measured by the total words. Cognitive strategies were assessed using the total switches and the mean cluster size in each task. The technique for calculating the strategies is presented in more detail in the Supplementary Materials and in our previous work [19].

Berg Card Sorting Test

Executive functions were assessed using a computerized version of the Berg Card Sorting Task (BCST) provided by the Psychology Experiment Building Language (PEBL [61]). The version used in this study consists of a 64-card deck with each card containing a unique combination of quantities, shapes, and colors. The participant's task is to discover which quality is the currently operating rule, based on trial and error, using feedback received after each card is sorted. After 10 cards have been chosen successfully, the sorting rule changes (without the participants' knowledge), which also indicates the completion of the first set. Following the data of Polgár et al. [62], concept formation was measured using the percent of perseverative errors, and problem-solving was measured using the percent of non-perseverative errors.

Color Trails Test

The Color Trails Test (CTT [63]), Polish adaptation by Lojek and Stańczak [64], was used to assess processing speed and cognitive flexibility. Each participant performed two parts of the test: CTT 1, in which one is required to trace 25 consecutive numbered circles marked on a page; and CTT 2, which also requires the participant to trace circles numbered from 1 to 25, alternating between two colors. Both time-related indices were analyzed in this study.

Clinical assessment

The Positive and Negative Syndrome Scale (PANSS [65]), Polish adaptation [66], was used to measure the severity of psychopathological symptoms in SZ participants. Following the suggestions of Shafer and Dazzi [67], five psychopathological dimensions were distinguished: positive, negative, disorganization, affect, and resistance. Due to the purpose of the study, we only analyzed negative and disorganization symptoms as predictors of verbal fluency in schizophrenia.

Statistical analysis

Statistical analysis was conducted using IBM SPSS 28 and IBM AMOS 7. Continuous variables were presented as means (M) and standard deviations (SD). The normalities of distributions were tested with the Shapiro–Wilk test as well as skewness and kurtosis values. It was assumed that skewness and kurtosis values between -2 and +2 indicated normal distributions [68]. Logarithmic or Box-Cox transformation was conducted for most variables (except total words in verbal fluency) to achieve normality [69]. To assess differences in demographic variables, Student's *t* test and the chi-square test were performed. Differences between groups in verbal fluency, executive functions, and processing speed were analyzed with a 2 (groups) \times 2 (type of tasks) two-way mixed analysis of variance (ANOVA). To determine the magnitudes of effect sizes for differences, Cohen's d or η^2 were used [70]. G*Power software was used to estimate the sensitivity analysis for mixed ANOVA, indicating that a mixed ANOVA with 216 participants across the two groups would be sensitive to effects of $\eta^2 = 0.015$ with 95% power (p = 0.05), meaning that our study would not be able to reliably detect effects smaller than $\eta^2 = 0.015$ [71]. The relationships between variables in the patient group were assessed with Pearson's r. Confirmatory factor analysis (CFA) and structural equation modelling (SEM) were conducted. Measurement error was decreased and power was increased by forming latent variables [72]: psychopathological symptoms (represented by two measured indices: negative symptoms from PANSS and disorganization symptoms from PANSS [67]), processing speed and cognitive flexibility (composited of two measured indices: completion time from CTT 1 and from CTT 2 [63]), semantic fluency (animal fluency: total words; fruit fluency: total words), and phonemic fluency (letter k: total words; letter f: total words [16, 17, 19]. SEM models were built following the criteria for mediation of Baron and Kenny [73]. The requirements for mediation were tested in correlation analysis; therefore we used only indices of dependent variables (types of verbal fluency) that were significantly correlated with independent variables (psychopathological symptoms) and the mediator (processing speed and cognitive flexibility). The mediator contained only one aspect of executive functions (cognitive flexibility) due to the lack of significant correlations of psychopathological symptoms, verbal fluency, and BCST scores measuring other dimensions of executive functioning, such as concept formation and problem-solving. Point estimates for the model parameters were obtained by maximum likelihood estimations. The following fit indices were used: the chi-square statistic, root mean square error of approximation (RMSEA) < 0.07, standardized root mean square residual (SRMR) < 0.08, goodness of fit index (GFI), and the comparative fit index (CFI) > 0.95 [74]. Total, direct, and indirect effects were tested with bias-corrected 10,000 bootstrap samples and 95% confidence intervals for the indices [75]. Standardized regression weights (β) were used as path coefficients. The alpha criterion was 0.05 for all statistical analyses. All tests were two-tailed.

Results

Participant characteristics

Demographic and clinical characteristics for participants are presented in Table 1. There were 50 females and 58 males in the SZ group and 53 females and 55 males in the HC group. There were no significant differences between SZ and HC groups in sex, age, or education.

Differences in neurocognitive functioning

Table 2 shows three indices of semantic and phonemic fluency: total words, mean cluster size, and switches. For semantic fluency, all main effects of group

	SZ (n=108)	HC (<i>n</i> = 108)	t / χ ²	p	d
Age: M (SD)	32.98 (7.47)	31.31 (6.65)	1.74 ^a	0.083	0.24 ^c
Years of education: M (SD)	14.27 (2.86)	14.90 (2.40)	-1.75 ^a	0.081	0.24 ^c
Sex—female / male: n (%)	50 (46.3) / 58 (53.7)	53 (49.1) / 55 (50.9)	0.07 ^b	0.785	-
		Outcome range (min–m	ax):		
Duration of illness (years): M (SD)	8.93 (6.72)	0—26			
Psychotic episodes: M (SD)	4.96 (4.51)	1—25			
Psychopathological symptoms in PANSS:					
Positive: M (SD)	8.17 (4.31)	5—25			
Negative: M (SD)	14.39 (5.53)	7—30			
Disorganization: M (SD)	12.21 (4.35)	8—27			
Affect: M (SD)	8.66 (3.04)	5—20			
Resistance: M (SD)	5.31 (2.68)	4—19			
Total: M (SD)	50.77 (15.25)	31—109			

Table 1	Demographic and clinica	l characteristics of partic	ipants with schizop	hrenia (SZ) and health	y controls (HC)
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PANSS Positive and Negative Syndrome Scale, M Mean, SD Standard deviation

^a Student's *t*-test

^b Chi-squared test

^c Cohen's *d* effect size: small (0.20–0.49), medium (0.50–0.79), large (>0.80)

Table 2 Differences between participants with schizophrenia (SZ) and healthy controls (HC) in verbal fluency, cognitive strategies, executive functions, and processing speed

		SZ HC		Group	effect		Type of task effect			Interaction effect		
		(n = 108) M (SD)	(n = 108) M (SD)	F	p	η²	F	p	η²	F	p	η²
Comparison in ver	bal fluency and cognitive strat	egies										
Semantic fluency:												
Total words	Animal fluency	18.85 (6.30)	23.77 (7.43)	28.11	< 0.001	0.12	254.55	< 0.001	0.54	12.55	< 0.001	0.06
	Fruit fluency	13.95 (4.18)	16.07 (4.06)									
Mean cluster size	Animal fluency	0.13 (0.02)	0.11 (0.02)	30.14	< 0.001	0.12	168.53	< 0.001	0.44	1.98	0.161	0.01
	Fruit fluency	0.15 (0.02)	0.14 (0.02)									
Total switches	Animal fluency	0.43 (0.14)	0.44 (0.13)	10.07	0.002	0.05	16.10	< 0.001	0.07	5.46	0.020	0.03
	Fruit fluency	0.45 (0.14)	0.52 (0.13)									
Phonemic fluency	:											
Total words	Letter k	14.20 (4.75)	16.09 (5.23)	2.88	0.091	0.01	287.57	< 0.001	0.57	11.27	< 0.001	0.05
	Letter f	10.53 (4.56)	10.60 (4.15)									
Mean cluster size	Letter k	0.13 (0.03)	0.12 (0.03)	0.53	0.468	0.01	42.87	< 0.001	0.17	3.49	0.063	0.02
	Letter f	0.14 (0.03)	0.14 (0.03)									
Total switches	Letter k	0.65 (0.20)	0.69 (0.16)	3.85	0.051	0.02	3.62	0.059	0.02	0.00	0.969	0.00
	Letter f	0.62 (0.21)	0.66 (0.16)									
Comparison in exe	ecutive functions and processir	ng speed										
Concept formation	n and problem-solving:											
BCST	% Perseverative errors	2.96 (0.56)	2.81 (0.38)	21.18	< 0.001	0.09	1.67	0.197	0.01	0.97	0.325	0.01
	% Non-perseverative errors	3.08 (0.59)	2.83 (0.49)									
Processing speed a	and cognitive flexibility:											
CTT	CTT 1: Completion time	3.97 (0.36)	3.60 (0.28)	105.31	< 0.001	0.33	1615.33	<0.001	0.88	6.70	0.010	0.03
	CTT 2: Completion time	4.68 (0.36)	4.22 (0.28)									

BCST Berg Card Sorting Test, CTT Color Trails Test, F Two-way mixed analysis of variance (ANOVA) in scheme 2 (groups) \times 2 (type of tasks), η^2 Eta squared effect size: small (0.01–0.059), medium (0.06–0.139), large (0.14–1.00), M Mean, SD Standard deviation

	Total effect	ect			Direct effect	ffect			Indirect effect	t effect		
	ш	SE	95% CI	þ	ш	SE	SE 95% CI	d	ш	SE	95% CI	d
Model 1: Standardized effects for mediation												
Variables: Psychopathological symptoms to animal fluency: total words	-0.335	0.124	0.124 -0.531:-0.053 0.017 -0.214 0.135 -0.437.0073 0.154 -0.121 0.062 -0.285:-0.028	0.017	-0.214	0.135	-0.437:0.073	0.154	-0.121	0.062	-0.285:-0.028	0.003
Variables: Psychopathological symptoms to animal fluency: mean cluster size	0.358	0.122	0.108:0.576	0.004	0.279	0.127	0.127 0.030:0.517	0.027	0.027 0.079	0.045	0.009:0.197	0.026
Model 2: Standardized effects for mediation												
Variables: Negative symptoms to semantic fluency	-0.334	0.112	-0.529:-0.092 0.009 -0.209 0.112 -0.417:0.023 0.073 -0.125 0.056	0.009	-0.209	0.112	-0.417:0.023	0.073	-0.125	0.056	-0.265:-0.038	0.003
Variables: Negative symptoms to phonemic fluency	-0.340	0.090	-0.511:-0.156 0.001 -0.220 0.093 -0.407:-0.036 0.021 -0.119 0.055	0.001	-0.220	0.093	-0.407:-0.036	0.021	-0.119	0.055	-0.252:-0.033	0.003
Model 3: Standardized effects for mediation												
Variables: Disorganization symptoms to semantic fluency	-0.302	0.107	-0.499:-0.080	0.010	-0.155	0.111	-0.357:0.074	0.174	-0.147	0.062	0.107 -0.499:-0.080 0.010 -0.155 0.111 -0.357:0.074 0.174 -0.147 0.062 -0.294:-0.045 <0.001	<0.001
Confidence interval, E Estimate, SE Standard error												

Table 3 Standardized effects for three models of mediation between negative and disorganization symptoms, and verbal fluency via processing speed and cognitive flexibility in
participants with schizophrenia

(0.002 = p < 0.001) and type of task (p < 0.001) were significant. The interaction effect of group and type of task was significant only for total words (p < 0.001) and number of switches (p = 0.020). Pairwise comparisons showed that SZ participants produced fewer words for animal (p < 0.001) and fruit (p < 0.001) fluency, and had fewer switches for fruit fluency than HC (p < 0.001). Moreover, both groups produced more words for animal than fruit fluency (both: p < 0.001). HC had more switches for fruit than animal fluency (p < 0.001). However, for phonemic fluency, main effects of type of task were significant only for total words (p < 0.001) and for mean cluster size (p < 0.001), and the interaction effect of group and type of task only for total words (p < 0.001). Pairwise comparisons showed that the SZ group produced fewer words for letter k fluency (p = 0.006) than HC and both groups produced more words for letter k than letter f fluency (both: p < 0.001). For concept formation and problem-solving (from BCST) and processing speed and cognitive flexibility (from CTT), the main effects of group were significant (for both: p < 0.001). Moreover, for processing speed and cognitive flexibility, there was a significant main effect of type of task (p < 0.001) and interaction effect between group and type of task (p=0.010). Pairwise comparisons showed that SZ participants had longer completion times on the first and second parts of the CTT (for both: p < 0.001), and all participants had longer completion times for the second than the first part of the CTT (both: p < 0.001).

Mediation analyses

For SZ, correlations between negative and disorganization symptoms, verbal fluency and strategies used, executive functions, and processing speed are presented in the Supplementary Materials (Tables S1-S7). Three mediation models were built. Table 3 and Figs. 1, 2 and 3 present standardized effects, and Table 4 presents model fit indices for all mediation models and standardized regression weights for latent variables. In the first model, the impact of processing speed and cognitive flexibility (mediator) on the relation between psychopathological symptoms (treated as a latent variable) and verbal fluency was tested. The next two mediation models focused separately on analyzing the significance of negative or disorganization symptoms (the second and third models, respectively) for different types of verbal fluency.

Firstly, we tested a model with two latent variables (psychopathological symptoms; processing speed and cognitive flexibility; Fig. 1). This model had significant total effects from psychopathological symptoms to total words for animal fluency (β =-0.335; *p*=0.017) and to mean cluster size for animal fluency (β =0.358; *p*=0.004); for the first path, the direct effect was non-significant

 $(\beta = -0.214; p = 0.154)$ but for the second path it was significant ($\beta = 0.279; p = 0.027$). These results suggest that the relationship between psychopathological symptoms and total words for animal fluency was fully mediated by processing speed and cognitive flexibility; the results also suggest that the relationship between psychopathological symptoms and mean cluster size was partly mediated by processing speed and cognitive flexibility. Together, the variables in model 1 predicted 19% of the variance for animal fluency and 16% for cluster size.

Secondly, we tested a model that includes three latent variables (processing speed and cognitive flexibility; semantic fluency; phonemic fluency; Fig. 2). For this model, there were significant total effects from negative symptoms to semantic fluency ($\beta = -0.334$; p = 0.009) and to phonemic fluency ($\beta = -0.340$; p = 0.001); the direct effect was non-significant for the first path ($\beta = -0.209$; p=0.073) but it was significant for the second path $(\beta = -0.220; p = 0.021)$. These results suggest that the relationship between negative symptoms and semantic fluency was fully mediated by processing speed and cognitive flexibility; the results also suggest that the relationship between negative symptoms and phonemic fluency was partially mediated by processing speed and cognitive flexibility. Together, the variables in model 2 predicted 34% of the variance for semantic fluency and 33% for phonemic fluency.

Thirdly, we tested a model with two latent variables (processing speed and cognitive flexibility; semantic fluency; Fig. 3). For this model, there were significant total effects from disorganization symptoms to semantic fluency (β =-0.302; *p*=0.010) and a non-significant direct effect (β =-0.155; *p*=0.174). These results suggest that the relationship between disorganization symptoms and semantic fluency was fully mediated by processing speed and cognitive flexibility. Together, the variables in model 3 predicted 32% of the variance for semantic fluency.

Discussion

The preliminary aim of our study was to compare verbal fluency including clustering and switching as cognitive strategies, executive functions, and processing speed between participants with schizophrenia and healthy controls. The results showed that the SZ group produced fewer words in both semantic tasks (animal and fruit fluency) and in one phonemic task (letter k fluency). Furthermore, individuals with schizophrenia manifested larger cluster size and fewer switches for semantic fluency. These results suggest difficulties with both semantic and phonemic fluency as well as disturbances in the switching strategy used in semantic fluency. Extended cluster size and lower switches in this group were consistent with the higher percent of perseverative errors in the

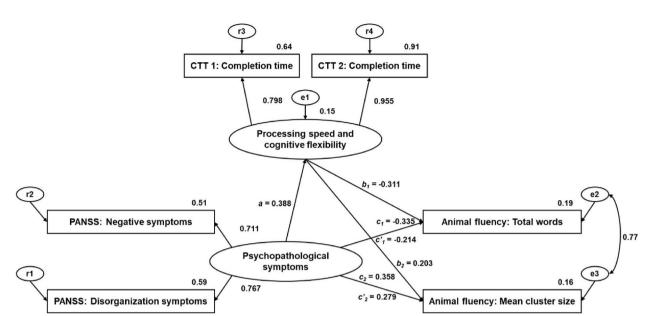


Fig. 1 The first mediation model showing processing speed and cognitive flexibility as a mediator of the relationships between psychopathological symptoms and animal fluency. Note. *a* path—Psychopathological symptoms predicting processing speed and cognitive flexibility. b_1 path, b_2 path—Processing speed and cognitive flexibility predicting animal fluency. c_1 path, c_2 path—Total effects. c'_1 path, c'_2 path—Direct effects. CTT—Color Trails Test. e—Residual error variance. PANSS—Positive and Negative Syndrome Scale. r—Item error variance

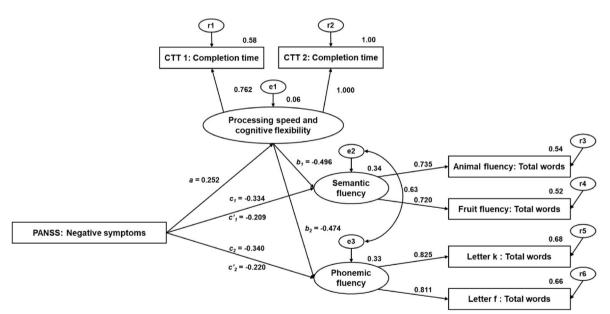


Fig. 2 The second mediation model showing processing speed and cognitive flexibility as a mediator of the relationships between negative symptoms and semantic and phonemic fluency. Note. *a* path—Negative symptoms predicting processing speed and cognitive flexibility. b_1 path, b_2 path—Processing speed and cognitive flexibility predicting semantic and phonemic fluency. c_1 path, c_2 path—Total effects. c'_1 path, c'_2 path—Direct effects. CTT—Color Trails Test. e—Residual error variance. PANSS—Positive and Negative Syndrome Scale. r—Item error variance

BCST, indicating a fixation on the current rule or semantic category that impairs performance. These results showed the specific pattern of using clustering and switching in semantic fluency in schizophrenia patients. The use of cognitive strategies for verbal fluency is the subject of ongoing discussion in the field [20-25, 30, 31], and the need for a detailed exploration of this issue has been highlighted in several meta-analyses [5-7, 13]. The current study revealed that individuals with schizophrenia and healthy controls produced more words for animal

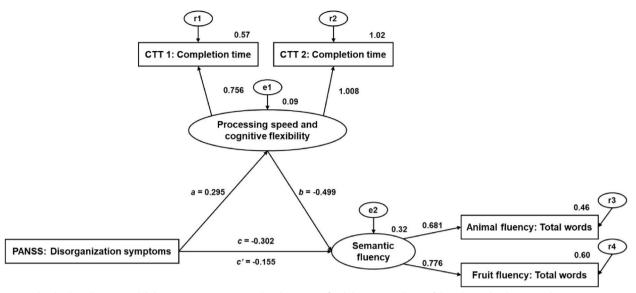


Fig. 3 The third mediation model showing processing speed and cognitive flexibility as a mediator of the relationship between disorganization symptoms and semantic fluency. Note. *a* path—Disorganization symptoms predicting processing speed and cognitive flexibility. *b* path—Processing speed and cognitive flexibility predicting semantic fluency. *c* path—Total effect; *c'* path—Direct effect. CTT—Color Trails Test. e—Residual error variance. PANSS—Positive and Negative Syndrome Scale. r—Item error variance

than fruit fluency, and in letter k than letter f fluency. This may be partially explained by the frequency of using items in each semantic/phonemic category in Polish [19].

Remarkably, the SZ group obtained larger cluster size even though they had reduced productivity in semantic fluency compared to controls. These results are only partially in line with previous studies, where no differences in clustering strategy between individuals with schizophrenia and controls were observed [24, 26, 29–31]. The findings of this study suggest the absence of disturbances in semantic memory and mental lexicon. However, these results may be explained by impairments in the effectiveness and organization of searching among different semantic subcategories in schizophrenia. Effective performance of semantic verbal fluency tasks demands cognitive control and searching not only among wellknown and automatically evoked semantic subcategories, but also across less common ones [14]. This means that, as shown in the current study, larger clusters may not support the efficacy of semantic fluency performance in individuals with schizophrenia, especially in relation to fewer switches. According to earlier studies, persons with schizophrenia have longer search time and make fewer switches in semantic fluency due to disorganization and slowed search through semantic networks [29, 76]. Therefore, a plausible explanation of our results could be that SZ participants become stuck on a few subcategories, which keeps them from producing more words from other categories [76]. It is difficult for them to switch to different semantic networks, so they stay longer within one subcategory or return to a previously generated one. Using automatic semantic links they try to search for and add new representatives within a subcategory that can more easily emerge from noise. However, this seems an ineffective strategy, especially when the task demands highly controlled processing to provide adaptive responses.

Difficulties in performing verbal fluency tasks may be deepened by poorer processing speed and cognitive flexibility in the SZ group in comparison to controls. Furthermore, individuals with schizophrenia had difficulties with formulating appropriate concepts and problem-solving. Executive function impairments may affect an individual's functioning in a variety of ways, such as difficulties with planning or proper selection between alternative courses of action to achieve a given goal [56]. Previous studies indicated that processing speed, cognitive flexibility, and reasoning or problem solving are among the cognitive domains that are often disrupted in schizophrenia [5, 11, 37–39].

The main aim of our study was to analyze models of the relationships between negative and disorganization symptoms in schizophrenia and verbal fluency (including clustering and switching as cognitive strategies) mediated via cognitive flexibility and processing speed. In individuals with schizophrenia, both of these processes are significantly reduced compared to controls. The first model suggests that slow processing speed and cognitive flexibility impairment may be a potential neuropsychological mechanism by which greater psychopathological Table 4 Model fit indices for three mediation models and standardized regression weights for latent variables loading

Model fit	indices											
	X ²	df	р	RMSEA (90% CI)			р		SRMR	GFI		CFI
Model 1	4.159	5	0.527	0.000 (0.000-0.122)			0.663		0.021	0.988		1.00
Model 2	5.141	9	0.822	0.000 (0.000-0.067)			0.912		0.019	0.987		1.000
Model 3	2.503	3	0.475	0.000 (0.000-0.152)			0.584		0.018	0.991		1.000
Standardiz	zed regres	sion w	eights for	latent variables								
					β	Lower 95% Cl		Upper 95% Cl			р	
Model 1												
Latent var	iable labe	lled as	psychopa	athological symptoms:								
PANSS: Ne	gative syr	nptom	าร		0.711	0.369		1.091			< 0.001	
PANSS: Dis	sorganizat	ion syı	mptoms		0.767	0.445		1.206			< 0.001	
Latent var flexibility:	iable labe	lled as	processir	ng speed and cognitive								
CTT 1: Cor	mpletion t	ime			0.798	0.600		0.931			< 0.001	
CTT 2: Cor	mpletion t	ime			0.955	0.808		1.209			< 0.001	
Model 2												
Latent var flexibility:	iable labe	lled as	processir	ng speed and cognitive								
CTT 1: Cor	mpletion t	ime			0.762	0.600		0.878			< 0.001	
CTT 2: Cor	mpletion t	ime			1.000	0.874		1.185			< 0.001	
Latent var	iable labe	lled as	semantic	fluency:								
Animal flu	ency: Tota	al word	ds		0.735	0.566		0.871			< 0.001	
Fruit fluen	cy: Total v	vords			0.720	0.541		0.872			< 0.001	
Latent var	iable labe	lled as	phonemi	c fluency:								
Letter k: To	otal words				0.825	0.685		0.940			< 0.001	
Letter f: To	tal words				0.811	0.698		0.906			< 0.001	
Model 3												
Latent var flexibility:	iable labe	lled as	processir	ig speed and cognitive								
CTT 1: Cor	mpletion t	ime			0.756	0.559		0.881			< 0.001	
CTT 2: Cor	mpletion t	ime			1.008	0.868		1.274			< 0.001	
Latent var	iable labe	lled as	semantic	fluency:								
Animal flu	ency: Tota	al word	ds		0.681	0.439		0.881			< 0.001	
Fruit fluen	cy: Total v	vords			0.776	0.565		1.067			< 0.001	

β Standardised regression weight estimate, CFI Comparative fit index, CI Confidence interval, CTT Color Trails Test, df Degrees of freedom, GFI Goodness of fit index, PANSS Positive and Negative Syndrome Scale, RMSEA Root mean square error of approximation, SRMR Standardized root mean square residua, χ² Chi-square statistic

symptoms result in decreased productivity and extended cluster size in semantic fluency in schizophrenia. The second model implies that this neuropsychological mechanism influences the relationships between negative symptoms of schizophrenia and productivity in semantic and phonemic fluency. The third model suggests that slow processing speed and cognitive flexibility impairment impact the relationship between disorganization symptoms and productivity only in semantic fluency in schizophrenia. When processing speed and cognitive flexibility were included in the mediation models, the previously statistically significant relationships between psychopathological symptoms and verbal fluency task performance became non-significant (for productivity in semantic fluency) or significant but weaker than before (for semantic clustering and productivity in phonemic fluency). Specifically, we found that decreased processing speed and cognitive flexibility was a more significant predictor for productivity in semantic fluency than psychopathological symptoms. However, for semantic clustering and productivity in phonemic fluency, both the neuropsychological mechanism and psychopathological symptoms were important predictors. This provides evidence that the postulated mechanism plays an important explanatory role in deficits revealed in various types of verbal fluency in schizophrenia.

It seems that slow processing and disturbed cognitive flexibility in schizophrenia, understood as attentional set shifting-that is, the ability to switch between different aspects of the task under strictly defined criteria (reactive flexibility [77, 78])-may constitute the underlying mechanism or some of the basic abilities for the implementation of tasks carried out in more open conditions. Verbal fluency pertains to rather open tasks, where searching for appropriate names and subcategories is realized in the context of broad activation of semantic networks. The activity of competitive networks that do not meet the defined criteria should be eliminated. These less-constrained tasks seem to demand greater self-monitoring and managing of cognitive activity than the highly structured methods imposing clearly defined signals and conditions. Verbal fluency tasks also demand spontaneous flexibility, including original ideation and divergent thinking [79, 80]. On the grounds of the already-dedifferentiated network, individuals with schizophrenia manifesting disorganization and negative symptoms cannot adapt to the increase in total noise, inhibit distractors, and select appropriate new subcategories of semantic clusters [20, 30]. Additionally, negative symptoms related to cognitive rigidity disturb the search of semantic networks, which may be deepened by the deficient cognitive flexibility and processing speed observed in schizophrenia. This is partially congruent with previous findings that negative symptoms predispose one towards a less flexible strategy [54, 57].

The obtained findings are related to several meta-analyses that confirmed a simple relationship between negative or disorganization symptoms, problems in verbal fluency, and executive dysfunctions in schizophrenia [13, 53]. In the previous literature, there is little research examining negative and disorganization symptoms in schizophrenia, verbal fluency, and executive functions, especially taking into account various indices and types of verbal fluency. Therefore, our discussion of the tested pathways makes reference solely to research examining only single relationships between these variables. Although some previous studies have confirmed the association between negative or disorganization symptoms and clustering strategy in semantic fluency [25, 30], other studies have not [23, 26, 31]. The results of our mediating models are partially consistent with the results of Brébion et al. [59], who revealed that processing speed mediates the relationship between negative symptoms and productivity in verbal fluency in schizophrenia. In the current study, cognitive flexibility was included as a mediator along with processing speed, which is a novel aspect compared to previous studies. These functions treated together appeared to be important to the relationships between psychopathological symptoms and productivity and clustering strategy in semantic fluency. Referring only to negative symptoms, the neuropsychological mechanism modifies their relationships with productivity in phonemic fluency as well. The relationships between psychopathological symptoms and neurocognitive functioning in schizophrenia are very complex and it should be assumed that there are many directions of dependence [81].

Verbal fluency, executive functions, and psychopathological symptoms in schizophrenia, as well as the reciprocal relations between them, are still not fully understood. There are some discrepancies in the results of previous studies, which may be caused by a number of factors, including the clinical condition of individuals with SZ, the versions of the verbal fluency tasks used, and the methodologies used to calculate switching and clustering strategies. The present study has innovative aspects, as it attempts to fill the gap in the literature regarding the complexity and character of various types of verbal fluency performance as well as the relationships between psychopathological symptoms and cognitive impairments. Our research contributes to the still debatable issue of which factors play primary roles in determining verbal fluency in schizophrenia and provides valuable insights by highlighting the mediating effect of processing speed and cognitive flexibility on the relations between psychopathological symptoms of schizophrenia and productivity in semantic or phonemic fluency, and semantic clustering. This is relevant to effective treatment outcomes in individuals with schizophrenia. Taking into account the obtained results, it is worth considering the therapeutic use of specialized training for executive functions, especially regarding cognitive flexibility and processing speed. Improving these aspects may enhance the quality of functioning in patients with schizophrenia and increase their activity in social life. Verbal fluency is an open task that provides insight into how to organize information and search for it in the mental lexicon [77]. This type of cognitive activity is required in everyday challenges where the patient must discriminate important stimuli from distractors. For this reason, in cognitive remediation it is worth making training situations more similar to everyday ones using methods with ecological validity to develop flexibility and processing speed [82]. In the present study, these processes turned out to be deficient in individuals with schizophrenia and have an important role in modifying other functional connections.

Several limitations of our study need to be addressed. First, we did not measure other aspects of processing speed (e.g., motor speed [83]) that could be related to semantic and phonemic fluency [59]. Second, we did not measure IQ, which is impaired in schizophrenia [84] and can be related to verbal fluency [85]. Third, we did not control psychotic medications and did not measure chlorpromazine equivalent, which can be a predictor of neurocognition in schizophrenia [86, 87]. Consequently, it is difficult to distinguish the relative specific impact of schizophrenia and antipsychotic medications on cognitive functioning. The mentioned weaknesses of our study may constitute a potential obstacle to generalising the results.

Conclusions

The current study found that individuals with schizophrenia are characterized by a specific pattern of performance on semantic fluency tasks: they demonstrated few switches and poor productivity with extended cluster size. However, in terms of phonemic fluency, different capacities were observed for different versions of the test. Participants with schizophrenia demonstrated weakened processing speed and cognitive flexibility as well as diminished problem-solving and ability to formulate appropriate concepts. Processing speed and cognitive flexibility are a probable neuropsychological mechanism modifying the relationships between psychopathological symptoms of schizophrenia and various types of verbal fluency. The exacerbation of psychopathological symptoms as well as disturbed cognitive flexibility and slow processing explain in an essential way difficulties in semantic clustering and productivity in phonemic fluency. However, only flexibility and processing speed, not psychopathological symptoms, had a significant impact on productivity in semantic fluency. Based on our results, interventions that target the enhancement of flexibility and processing speed could prove effective in cognitive remediation among patients with schizophrenia.

Supplementary Information

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Supplementary Material 1.
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Authors' contributions

Conceptualization, E.M.T; funding acquisition, E.M.T. and J.S.; investigation, E.M.T., P.P., and K.W.; methodology, E.M.T.; project administration, E.M.T., A.B., and K.W.; supervision, J.K-M., J.S., L.S., B.M., M.H., A.J., and M.M.; writing-original draft, E.M.T.; writing-review and editing, E.Z., A.B., E.K., P.P., J.S., A.M., L.S., A.J., S.T.M., M.H., B.M., K.L., K.W., J.K-M., A.R., and M.M. All authors have read and agreed to the published version of the manuscript.

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Data availability

The data of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of Pomeranian Medical University (KB-0012/49/17 from 27 March 2017) and Ethics Committee of the Institute of Psychology at University of Szczecin (KB-8/2015 from 21 May 2015).

Consent for publication Not applicable in this section.

Competing interests

The authors declare no competing interests.

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