Semantic fluency reveals reduced functional connectivity between subcategorical co-hyponyms in recent-onset inpatients with first-episode psychosis

Gabrić, Petar; Vandek, Mija

Source / Izvornik: Clinical Linguistics & Phonetics, 2021

Journal article, Submitted version Rad u časopisu, Rukopis poslan na recenzijski postupak (preprint)

Permanent link / Trajna poveznica: https://urn.nsk.hr/urn:nbn:hr:131:679137

Rights / Prava: Attribution 4.0 International/Imenovanje 4.0 međunarodna

Download date / Datum preuzimanja: 2024-09-27

ersity of Zagreb

ulty of Humanities



Repository / Repozitorij:

ODRAZ - open repository of the University of Zagreb Faculty of Humanities and Social Sciences





Semantic fluency reveals reduced functional connectivity between subcategorical cohyponyms in recent-onset inpatients with first-episode psychosis

Petar GABRIĆ^{a, b}, Mija VANDEK^a

^a Department of Linguistics, University of Zagreb, Croatia

^b Institute for German Linguistics, Philipps University of Marburg, Germany

<u>Corresponding author</u>: Petar Gabrić, Institute for German Linguistics, Philipps University of Marburg, Pilgrimstein 16, 35032 Marburg an der Lahn, Germany; email: <u>petar.gabric@uni-marburg.de</u>, <u>petar.gabric1@gmail.com</u>

Petar Gabrić ORCiD 0000-0003-2644-194X

Mija Vandek ORCiD 0000-0003-3398-7350

Abstract

Data on clustering and switching during semantic fluency (SF) in patients with first-episode psychosis (PwFEP) are scant. We aimed to investigate (1) clustering and switching on SF in PwFEP using more detailed clustering analyses and (2) the possibility of disproportionate clustering deficits across different SF tasks in PwFEP and healthy subjects (HS), with the latter being suggested by the current literature on patients with schizophrenia. We recruited 22 Croatianspeaking PwFEP with schizophrenia features or symptoms and 22 HS matched in age, sex distribution, and handedness. All patients were medicated and had a mean illness duration of 1 month. The categories animals, trees, vegetables, fruits, and musical instruments were administered for SF. PwFEP produced significantly fewer correct words in the aggregate score, as well as across all categories. The switching rate was significantly higher in PwFEP, but no post hoc comparisons were significant. PwFEP also produced significantly smaller clusters, yet the post hoc comparisons for the tree and fruit task were not significant. A higher switching rate and smaller clusters indicate less efficient functional connectivity within subcategories of the given categories, but not necessarily between the subcategories. Although both less likely to produce a cluster once a switch has been uttered and less likely to produce clusters larger than two words compared to HS, the latter deficit was more pronounced. Our results further suggest that PwFEP might show normal clustering performance on some SF tasks. We discuss the results in the context of the hypothesis of semantic hyperactivation in psychoses.

Keywords: semantic fluency; schizophrenia; first-episode psychosis; clustering; hypernymy; cohyponymy Word count: 6874 (inclusive of references, tables, and figures)

1. Background

1.1. Clustering and switching on semantic fluency

In a semantic fluency (SF) task, the subject is to name as many members of a given semantic category (e.g. *animals*) within a time limit. Despite its frequent use, the cognitive and specific linguistic correlates of SF remain mostly unclear. Although the presumed working memory and executive functioning components of both SF and letter fluency are often emphasized (Amunts et al., 2020), studies suggest that both general cognitive and specific linguistic processing subserve performance on verbal fluency (Fong et al., 2020; Stielow & Stenneken, 2017). Nonetheless, which linguistic (or lexical) processes subserve verbal fluency remains likewise unclear. Functional imaging, cortical modulation, and lesion studies suggest that performance on SF is mediated by the metabolic activity and structural integrity of the bilateral inferior frontal gyri and left temporal cortex (Biesbroek et al., 2016; Nagels et al., 2012).

Performance on SF is often interpreted using only the raw number of correct words. However, it has been observed that subjects engaged in a verbal fluency task employ two specific cognitive mechanisms for optimal performance: clustering and switching (Troyer et al., 1997). Clustering relates to the tendency of subjects to successively produce words denoting concepts belonging to the same subcategory (i.e. subcategorical co-hyponyms; e.g. *reptiles*) of the given semantic

category (e.g. animals). Switching stands for the change of the semantic subcategory of the given category.For example, if a subject starts the animal task with the output *dog–cat–kangaroo–whale–shark*, we will count three accessed categories (*pets, kangaroo, and marine animals*), two clusters (*pets and marine animals*), two switches (*pets–kangaroo and kangaroo–marine animals*), and four clustered words (*dog, cat, whale, and shark*). Described as such, clustering and switching reflect the functional connectivity both within semantic subcategories (clustering) and between semantic subcategories (switching) of the given category in the mental lexicon. Clustering and switching have been described as relatively automatic and controlled processes, respectively (Troyer & Moscovitch, 2006). Recent research shows that clustering and switching on SF are correlated with matrix reasoning and processing speed (Fong et al., 2020). Nonetheless, Vandek et al. (2018) and Gabrić and Vandek (2020) found that clustering and switching on the tree, but not the animal task was associated with cognitive flexibility, indicating the existence of category specificities in clustering and switching.

1.2. Prior studies in patients with schizophrenia

Patients with schizophrenia regularly perform significantly poorer on SF compared to healthy subjects (Chen et al., 2020; Gourovitch et al., 1996; Joyce et al., 1996; Lemieux & Macoir, 2017; Neill et al., 2014; Phillips et al., 2004; Rosenkranz et al., 2019; Rossell et al., 1999; Tyburski et al., 2015; van Beilen et al., 2004). Because studies suggest that patients with schizophrenia exhibit abnormally broad semantic spreading activation on semantic tasks compared to healthy subjects (Kuperberg et al., 2018; Spitzer, 1997), a plausible hypothesis would be that patients with schizophrenia with sc

healthy subjects, reflecting their presumed diminished capacity for localized semantic spreading activation (or greater capacity for broader semantic spreading activation). However, results regarding clustering and switching have been mixed and difficult to interpret, presumably due to methodological differences across studies and deficiencies in the quality of the statistical procedures in some studies. Several studies compared the raw values of clusters, clustered words (CW), and switches (SW) without controlling for total output, thus failing to capture the specific contributions of clustering and switching in the SF deficits in their samples (Batty et al., 2015; Elvevåg et al., 2002; Kosmidis et al., 2005; Moore et al., 2006; Rinaldi et al., 2013; Robert et al., 1998; Veleva et al., 2019). Studies that analyzed either CW or SW while controlling for total output yielded no significant differences between groups (SW: Berberian et al., 2016; Landrø & Ueland, 2008, Okruszek et al., 2013; both CW and SW: Bozikas et al., 2005), significantly fewer clustered words in the patient group (Allen et al., 1993; Berberian et al., 2016), or significantly higher switching in patients with hallucinations but not without hallucinations (Popescu & Micluția, 2006). Thus, (1) there is no evidence that patients with schizophrenia switch either significantly more or significantly less than healthy subjects (when controlling for the total output), and (2) the results regarding cluster magnitude are mixed. Notably, regarding clustering on 60-second SF tasks, Berberian et al. (2016) used only the animal task, while Bozikas et al. (2005) analyzed the aggregate score for the categories animals, fruits, and objects, pointing to possible categoryspecific effects on cluster magnitude on SF in patients with schizophrenia.

Another approach has been to calculate the so-called 'cluster size'. Most studies have employed the calculation for cluster size as proposed by Troyer et al. (1997): [= ($N_{clustered words}$ - $N_{clusters}$)/ $N_{switches}$]. However, this method yields a variable that simultaneously gives information on (1) the relative frequency of clustering events compared to switching events (i.e. the likelihood

of building a cluster once a switch has been produced) and (2) the number of words listed within a cluster once a cluster has been produced (e.g. the likelihood that a cluster will continue after two words have been clustered before switching again). Studies that calculated cluster size as proposed by Troyer et al. (1997) found no significant differences between patients with schizophrenia and healthy subjects (Elvevåg et al., 2002; Landrø & Ueland, 2008; Moore et al., 2006; Okruszek et al., 2013). Additionally, studies using semantic space modelling of the SF output report that the output of patients with schizophrenia is semantically disorganized compared to healthy controls, indicating dysfunctional connectivity between concepts in the mental lexicon (Aloia et al., 1996; Berto & Galaverna, 2016; Paulsen et al., 1996; Popescu & Micluția, 2006; Sumiyoshi et al., 2009; Sung et al., 2012).

1.3. Prior studies in patients with first-episode psychosis

Similarly to chronic patients, patients with first-episode psychosis (PwFEP) produce significantly fewer correct words than healthy subjects on SF tasks (Blessing et al., 2009; Giovannetti et al., 2003; Nuyen et al., 2005). Giovannetti et al. (2003) is the only study we encountered that analyzed clustering and switching. They found no significant differences between groups in cluster size on animal fluency. However, contrary to Troyer et al. (1997), they employed an arbitrary formal semantic-feature-based system for clustering in which two successive words could be classified as clusters if they shared features (e.g. *small, herbivore*) in at least four out of six feature categories (e.g. *size, diet*). Problematically, (1) studies using computational approaches have not suggested that organization of the output on animal fluency can be classified according to all these features (Aloia et al., 1996; Paulsen et al., 1996; Popescu & Micluția, 2006), (2) there appears to be

convergence across some feature categories (e.g. geographical location and habitat, zoological class and biological order, etc.), while (3) the higher number of categorization decisions needed to be made by the experimenter for every word (instead of one categorization decision for two successive words) arguably increases the risk of error.

The aims of the present study were (1) to investigate clustering and switching on SF in PwFEP, as previous research has been scant, (2) to investigate possible category-specific deficits in cluster magnitude on SF in PwFEP, as they are a possible reason for the currently disproportionate results across the few studies conducted, and (3) to separately examine the switching rate and cluster magnitude in PwFEP. To disentangle these two components of 'cluster size', we calculated (1) the switching rate $[= (N_{switches}+1-N_{clusters})/(N_{switches}+1)]^1$ (as also used in e.g. Popescu & Micluția 2006) and (2) cluster magnitude (=N_{clustered words}/N_{clusters}) (as also used in e.g. Batty et al. 2015; Giovanetti et al. 2003). Calculated as such, the switching rate can range from 0 to 1, with a value of 0 possible only if the subject produced a cluster with the first subcategory they accessed and did not switch to another subcategory (due to continuous production within the first subcategory, silence, or alternations between the two), while a value of 1 implies the subject built absolutely no clusters. Cluster magnitude can range from 1 (if the subject built no clusters) or 2 (the minimum size of a cluster, as per its definition), while the maximum cluster magnitude is unknown and restricted by human physiology, subject's vocabulary size, and the task time limit. Presumably, this approach allows us an inspection of the efficiency of the connectivity between the more abstract and schematized co-hyponymic subcategories of a given category (switching rate; e.g. co-hyponyms *birds–reptiles–farm animals* of the category *animals*), as well as within the subcategories where

¹ 1 is added because the subcategory which is accessed first can never be a switch (because there is no preceding subcategory), but it can be a cluster.

more concrete concepts are situated (cluster magnitude; e.g. co-hyponyms *elephant–lion– crocodile* of the subcategory *African animals*) in the mental lexicon of PwFEP.

2. Materials and methods

2.1. Subjects

22 Croatian-speaking inpatients diagnosed with an acute and transient psychotic disorder (F23) according to ICD-10 criteria (WHO, 1993) were recruited from the University Psychiatric Hospital 'Vrapče' of the University of Zagreb. Descriptive data are available in Table 1. All patients were in the young adult range. Nineteen patients were diagnosed with an acute schizophrenia-like psychotic disorder (F23.2), and three patients were diagnosed with an acute polymorphic psychotic disorder with symptoms of schizophrenia (F23.1). All patients experienced only one psychotic episode in their lifetime, and their first psychotic episode was the reason for their current hospitalization (cf. Folnegović et al. 1994). Thirteen patients were assessed within one month of the first psychotic episode, while others were tested after either one (N = 3), two (N = 2), three (N = 2), four (N = 1), or five months (N = 1).

All patients were receiving antipsychotics. The daily dosages of different antipsychotics were transformed into chlorpromazine equivalents (CPZE) (Danivas & Venkatasubramanian, 2020). Nine patients were receiving intermediate (400–799 mg), while 13 patients were receiving low daily antipsychotic dosages (0–399 mg; Dudley et al., 2017). Fourteen patients were receiving two antipsychotics. Of these, eight were receiving a combination of a typical and an atypical

antipsychotic, while six were receiving two atypical antipsychotics. The eight patients receiving monoantipsychotic therapy were all receiving atypical antipsychotics. Sixteen patients were receiving concomitant psychopharmacological treatment. All patients receiving concomitant treatment were receiving benzodiazepines. Six patients were receiving anticholinergics. Two patients each were receiving mood stabilizers, antidepressants, and hypnotics.

	Healthy subjects	Patients
Age (years)	23.000 (4.220) R 17–33	23.045 (4.226) R 17–33
Males ratio	14/22	14/22
Handedness (self-report)	D 21, L 1	D 21, L 1
Illness duration (months)		1.000 (1.512) R 0–5
Daily antipsychotic dosage (CPZE; mg)		422.348 (195.474) R 100–800
Concomitant psychopharmacological therapy		16/22

Table 1. Sociodemographic and clinical data.

Note: For age, illness duration, and the daily antipsychotic dosage, mean values are reported, alongside the standard deviations in parentheses and ranges in the second row of the cells. Median values for age, illness duration, and the daily antipsychotic dosage were 22, 0, and 400, respectively.

22 Croatian-speaking healthy subjects (HS) were recruited for the comparison group. HS were matched with PwFEP in age, the distribution of sexes, and handedness. All HS denied having histories of psychiatric and neurological disorders. Ethical approval for the study was obtained by the Ethical Committee of the University Psychiatric Hospital 'Vrapče' (no. 23-305/8-18). All subjects signed an informed consent form.

2.2. Semantic fluency

Semantic fluency was administered using five semantic categories as cues: *animals*, *trees*, *vegetables*, *fruits*, and *musical instruments*. Subjects were told to name as many members of the given category as they could. Cues were given aurally and verbally by an experimenter. The time limit was set at 60 seconds. The subjects' outputs were audio-recorded and subsequently transcribed for analyses.

The following dependent variables were used: (1) the raw number of correct words, (2) perseveration rate, (3) intrusion rate, (4) switching rate, and (5) cluster magnitude. We calculated both the total scores across the five subtasks and individual scores for the five subtasks. Incorrect words included errors (perseverations and intrusions) and hypernyms. Hypernyms were, by their definition, only classified as such if the subject named both the hypernym (e.g. *bird*) and its hyponym (e.g. *ostrich*), but not if they produced, e.g. the word *bird*, but no hyponymic instances of the concept BIRD. Sex variations of animal names (e.g. *cow-bull*) were classified as correct. Perseverations included repetitions of words (regardless of their position), while intrusions encompassed words that denoted non-members of the given category (e.g. *apple* in the vegetable subtask). The perseveration and intrusion rates were calculated by dividing the raw number of perseverations and intrusions, respectively, by the total output.

Clusters were defined as groups of at least two successive words belonging to the same semantic subcategory of the given category. Switches included words that denoted a concept belonging to a different semantic subcategory of the given category compared to the preceding word (Troyer et al., 1997). The switching rate was calculated by dividing the raw number of non-clustered switches by the raw number of times a new subcategory was accessed (i.e. raw number of switches plus one

for the first subcategory, which can never be a switch). Cluster magnitude was calculated by dividing the raw number of clustered words by the raw number of clusters.

2.3. Statistics

Statistical analyses were conducted in JASP (JASP Team, 2020). Because a considerable part of the data across the five SF subtasks was non-normal in distribution and highly skewed, non-parametric tests were applied. The total scores across the five SF subtasks were compared between groups using the Mann-Whitney U test with the significance level set at .05. Subsequently, the Kruskal-Wallis test was conducted with the independent variable *group* (HS vs. PwFEP). Post hoc comparisons were conducted using the Mann-Whitney U test. A Bonferroni correction was applied by dividing the alpha value by the number of group comparisons for each dependent variable, with the significance level thus set at 0.01 (0.05/5). The effect size for the Mann-Whitney U test is given by the matched rank biserial correlation. Because no HS produced intrusions on the animal subtask, the post hoc comparison between groups for this variable was conducted using the one-sample Wilcoxon signed-rank test with the test value set at 0 ± 1 . Associations between age, the clinical variables, and the SF variables were analyzed using Spearman correlation coefficients.

3. Results

3.1. Sociodemographic data

There were no significant correlations between age and the two clinical variables (both p > 0.100). There were no significant correlations between age and the SF total scores and no significant differences between sexes in the total SF scores neither in the two groups combined nor in the individual groups (all p > 0.100).

3.2. Clinical data

Illness duration and daily antipsychotic dosage were significantly negatively correlated ($\rho = -0.564$, p = 0.006). There were no significant correlations between the two clinical variables and the total SF scores (all p > 0.100). There were no significant differences in the total SF scores between patients tested within the first month after the episode and those tested in the period afterwards, between patients differing in the level of the daily antipsychotic dosage, the number of antipsychotics, and type of antipsychotics, as well as between patients receiving and not receiving concomitant psychopharmacological therapy (all p > 0.100).

3.3. Semantic fluency

Comparisons of the total SF scores across the five categories between PwFEP and HS are shown in Table 2. All between-group differences were significant. PwFEP produced both perseverations and intrusions at significantly higher rates, indicating poorer performance monitoring and looseness of the semantic categories' boundaries, respectively. PwFEP further switched at significantly higher rates and built significantly smaller clusters than HS, indicating dysfunctional connectivity between co-hyponymic concepts in the given semantic categories. The effect size was larger for cluster magnitude compared to switching rate, possibly indicating that clustering ability at higher rates (> 2 words) might be particularly impaired within the clustering deficit (i.e. switching surplus) as a whole in PwFEP.

Results of the Kruskal-Wallis test testing the effect of group on SF performance are shown in Table 3. The effect of group was significant for all SF variables. Post hoc comparisons revealed that PwFEP produced significantly less correct words on all subtasks (animals: U = 65.5, p < 0.001, $r_b = 0.729$; musical instruments: U = 72.0, p < 0.001, $r_b = 0.702$; fruits: U = 73.5, p < 0.001, $r_b = 0.696$; trees: U = 117.0, p = 0.003, $r_b = 0.517$; vegetables: U = 117.5, p = 0.003, $r_b = 0.514$), with the effect sizes somewhat higher for the animal, musical instrument, and fruit compared to the tree and vegetable subtasks.

Although PwFEP and HS differed in the total perseveration and intrusion rates in the aggregate score and the effects of group on both variables were significant, there were no significant differences between the two groups in these variables in the post hoc comparisons after the Bonferroni correction. The highest effect sizes were found for the perseveration rate on the animal subtask (U = 316.5, p = 0.027, $r_b = 0.308$) and the intrusion rate on the tree subtask (U = 312.5, p = 0.042, $r_b = 0.291$).

PwFEP displayed a significantly higher total switching rate, yet none of the post hoc comparisons reached significance after Bonferroni correction. The comparison of performances in the vegetable subtask turned insignificant after the Bonferroni correction (U = 328.0, p = 0.045, $r_b = 0.355$). Descriptive data showed that PwFEP tended to switch at higher rates compared to HS on all subtasks. However, the mean difference between groups for the tree (0.7 %) subtask was trivial, as well as lower compared to the mean differences for the vegetable (12.7), musical instrument (8.7), animal (8.4), and fruit subtasks (4.7).

PwFEP had significantly smaller cluster magnitudes compared to HS in the animal (U = 94.5, p < 0.001, $r_b = 0.610$), musical instrument (U = 94.5, p < 0.001, $r_b = 0.610$), and vegetable subtasks (U = 106.5, p < 0.001, $r_b = 0.560$). The comparison of performances in the fruit subtask turned insignificant after the Bonferroni correction (U = 153.5, p = 0.036, $r_b = 0.366$). Additionally, similarly to the analyses of the total SF scores, the effect of group was stronger for cluster magnitude compared to the switching rate, again possibly indicating that clustering at higher rates might be more impaired than the clustering ability as a whole. Data for cluster magnitude are visually summarized in Figures 1 and 2.

Table 2. Comparisons between groups in the aggregate scores across the five SF categories.

	Patients	Healthy subjects	Mann-Whitney U test			
Correct words (raw)	61.136 (13.410) R 39–88	87.500 (17.468) R 54–136	$U = 48.0, p < 0.001, r_b = 0.802$			
Perseveration rate (%)	4.5 (3.9) R 0.0–15.1	1.7 (2.3) R 0.0–9.8	$U = 367.0, p = 0.003, r_b = 0.517$			
Intrusion rate (%)	3.0 (3.4) R 0.0–10.9	0.7 (0.9) R 0.0–3.0	$U = 351.0, p = 0.008, r_b = 0.450$			
Switching rate (%)	60.3 (7.8) R 40.0–72.7	53.1 (10.4) R 34.2–68.9	$U = 336.5, p = 0.027, r_b = 0.390$			
Cluster magnitude	2.547 (2.500) R 2.118–3.130	3.020 (2.920) R 2.308–4.133	$U=81.0,p<0.001,r_b=0.665$			

Note: Mean values are reported, alongside the standard deviations in parentheses and ranges in the second row of the cells.

	Animals		Trees		Vegetables		Fruits		M. instruments		11	
	PwFEP	HS	PwFEP	HS	PwFEP	HS	PwFEP	HS	PwFEP	HS	- H ₍₁₎	Р
Correct words (raw)	17.227 (5.218)	24.591 (4.626)	9.409 (4.261)	13.455 (4.091)	10.864 (3.932)	14.273 (4.014)	12.818 (3.142)	17.455 (3.320)	10.818 (4.019)	17.727 (6.663)	43.391	< 0.001
Perseveration rate (%)	4.0 (5.5)	0.7 (1.8)	4.2 (8.4)	1.1 (3.6)	3.9 (5.6)	1.5 (2.8)	4.7 (7.6)	2.9 (4.2)	5.2 (7.4)	2.4 (4.8)	7.201	0.007
Intrusion rate (%)	1.5 (4.5)	0.0 (0.0)	4.5 (9.8)	1.5 (3.0)	7.3 (11.4)	1.2 (2.8)	1.4 (3.1)	1.2 (2.6)	1.4 (4.1)	0.5 (1.6)	3.931	0.047
Switching rate (%)	44.2 (13.9)	35.8 (19.5)	41.9 (19.9)	41.2 (22.9)	65.9 (16.4)	53.2 (22.6)	55.8 (13.7)	54.1 (16.3)	54.2 (21.9)	45.5 (17.6)	5.027	0.025
Cluster magnitude	2.809 (0.497)	3.593 (0.906)	2.433 (0.741)	2.711 (0.613)	1.968 (0.459)	2.413 (0.385)	2.447 (0.616)	2.818 (0.713)	2.394 (0.747)	3.492 (1.093)	46.511	< 0.001

Table 3. Descriptive data for the five SF subtasks and results of the Kruskal-Wallis test testing the effect of group on SF performance.

Note: Results of the post hoc comparisons are reported in the main text. Mean values are reported. Standard deviations appear in parentheses.

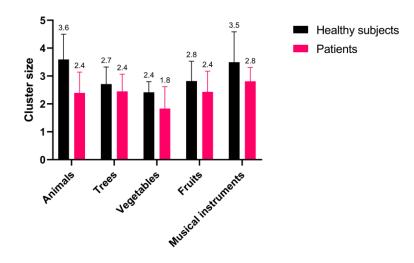


Figure 1. A visual summary of the cluster magnitude data in the two groups and across the five SF subtasks.

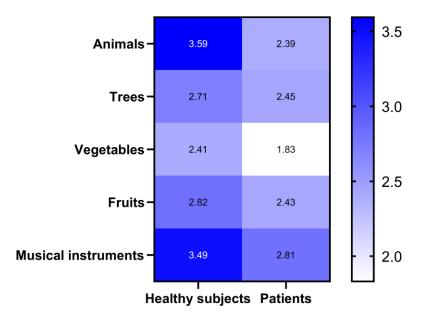


Figure 2. Heat map of cluster magnitude showing group on the x-axis and the subtask on the y-axis. The dark blue areas indicate relatively larger clusters, while the white and light blue areas indicate relatively smaller clusters.

4. Discussion

As anticipated, PwFEP produced significantly less correct words both in the aggregate score and across the five subtasks and on the individual subtasks, as shown by the post hoc comparisons. This result is in line with the current evidence suggesting that both chronic and first-episode patients display cognitive deficits (Mesholam-Gately et al., 2009) and with previous studies reporting deficits in productivity on SF (Blessing et al., 2009; Chou et al., 2015). Furthermore, PwFEP had significantly higher perseveration rates, indicating a diminished capacity for performance monitoring and possible impairments in working memory, as well as significantly higher intrusion rates, indicating that the boundaries of semantic categories are looser compared to HS. The latter result agrees with studies demonstrating abnormally broad semantic spreading activation on semantic tasks in patients with schizophrenia (Assaf et al., 2006; Spitzer, 1997). Nevertheless, none of the post hoc comparisons for the two error variables was significant after the Bonferroni correction.

Regarding switching and clustering, PwFEP had a significantly higher switching rate compared to HS in the aggregate score across the five subtasks. Still, no significant differences were found in the post hoc comparisons. Moreover, PwFEP produced significantly smaller clusters in the aggregate score. The post hoc comparisons between-group differences were significant for the animal, musical instrument, and vegetable, but not the tree and fruit subtasks. Although none of the post hoc comparisons in the switching rate achieved significance, the mean difference between groups on the tree task was trivial (0.7) and smaller compared to other subtasks, suggesting that both the switching rate and cluster magnitude on the tree subtask might be relatively normal in

PwFEP. Importantly, in both the analyses of the aggregate scores and the Kruskal-Wallis test, the effect of group was greater for cluster magnitude than for the switching rate, suggesting greater impairments in cluster magnitude compared to the relative cluster frequency. Debatably, this might suggest a greater deficit in the processing of more concrete concepts and a less pronounced, albeit existent, deficit in the processing of more abstract concepts in PwFEP.

The smaller cluster magnitude indicates that PwFEP displayed less efficient connectivity between co-hyponymic concepts in an accessed subcategory of the given subtask category (e.g. cohyponyms elephant-lion-crocodile of the subcategory African animals). Consequences of this presumed less efficient connectivity are (1) higher risk of not building a cluster once a switch has been generated and (2) higher risk of switching after two clustered words have been uttered. It might be further suggested that the higher switching rate in PwFEP indicates relatively intact connectivity between co-hyponymic concepts on the category level (e.g. co-hyponyms birds*reptiles–farm animals* of the category *animals*). However, a higher intrusion rate and a deficit in the raw total number of switches (U = 144.5, p = 0.023, r_b = 0.403, not reported in the Results) indicate abnormalities in the cognitive dynamics between co-hyponymic subcategories of a given category in PwFEP as well. Further, although PwFEP also tended to produce less non-clustered switches (total score) compared to HS (mean difference: 3.954), there were no significant differences between groups in the total raw number of non-clustered switches (U = 144.5, p =0.121, $r_b = 0.275$). However, when we excluded the errors from the raw number of non-clustered switches, the difference between groups turned significant (mean difference: 6.454; U = 128.0, p = 0.008, $r_b = 0.471$), indicating that although switching may be more spared compared to cluster magnitude, there are clearly dysfunctions in the connectivity between co-hyponymic subcategories of a given semantic category as well.

Our results further show that there are possibly category-specific effects on the deficits in cluster magnitude in PwFEP. As reported in the Introduction, significantly smaller clusters in patients with schizophrenia during 60-second SF have been found on animal fluency tasks (Berberian et al., 2016), but not in a study analyzing the aggregate scores of the categories *animals*, *fruits*, and objects (Bozikas et al., 2005). Importantly, we found no significant differences in cluster magnitude on the tree and fruit subtasks, confirming the possibility that patients with schizophrenia (and FEP for that matter) might not show significantly smaller clusters when the category *fruits* is used. Since in our two previous unrelated studies we found that performance on the tree subtask, but not the animal is associated with cognitive flexibility in healthy subjects (Gabrić & Vandek, 2020; Vandek et al., 2018), and since PwFEP in our sample demonstrated no significant differences in cluster magnitude on the tree subtask, it is possible that patients with FEP (and, by extension, schizophrenia) display less pronounced or no clustering deficits on semantic fluency tasks which engage executive functioning rather than relatively automatic semantic processing. Notably, the mean difference between groups in the switching rate on the tree subtask was only 0.7, supporting the hypothesis of the tree subtask's specificity.

Regarding the hypothesis of abnormally broad semantic spreading activation in schizophrenia, although our results are in agreement with the hypothesis, they can be interpreted by other phenomena as well, such as selective degradation of the semantic memory. Be that as it may, if we assume that the deficits observed in our study were due to abnormally broad semantic spreading activation, our results suggest that (1) the broader co-activation is not drastically broad, i.e. it relatively infrequently (but still significantly more often than in HS) surpasses the category's boundaries (indicated by the rates of intrusions; cf. Erdeljac et al., 2019) and that (2) its degree on SF tasks is category-dependent. Furthermore, because most studies with chronic patients with

schizophrenia failed to find significant differences in clustering and switching strategies compared to healthy subjects (Bozikas et al., 2005; Okruszek et al., 2013), it is possible that this kind of phenomenon in the context of SF performance is not necessarily associated with the diagnosis of schizophrenia or the presence of positive symptoms but perhaps with other clinical factors such as a recent history of a psychotic episode or recent illness onset (< one month). A previous study on SF in schizophrenia found that the SF output is disorganized in patients with an earlier age of illness onset (< 45; Paulsen et al., 1996). Unfortunately, we collected no follow-up data to identify patients who subsequently met ICD-10 criteria for schizophrenia so it remains unclear whether the eventual abnormally broad semantic spreading activation might be associated with an earlier onset of schizophrenia.

5. Limitations

Firstly, the sample size was small. Secondly, we did not investigate the possible influence of psychotic and other symptoms on performance. Thirdly, we focused on natural semantic categories, failing to systematically investigate eventual differences in the processing of semantic categories differing in the level of concreteness, naturalness, animacy, etc.

6. Conclusion

Patients with first-episode psychosis (PwFEP) produced significantly fewer correct words in the aggregate score, as well as across all categories. The switching rate was significantly higher in PwFEP, but no post hoc comparisons were significant. PwFEP also produced significantly smaller

clusters, yet the post hoc comparisons for the tree and fruit task were not significant. A higher switching rate and smaller clusters indicate less efficient functional connectivity within a subcategory of the given category, but not necessarily between subcategories of the given category. Although both less likely to produce a cluster once a switch has been uttered and to produce clusters larger than two words compared to healthy subjects, the latter deficit was more pronounced. Possibly, PwFEP might have greater difficulty in processing more concrete compared to more abstract concepts. Finally, our results also suggest that there are category-specific effects on the clustering deficit in PwFEP, possibly demonstrating that PwFEP might show normal performance on executively more demanding semantic fluency subtasks.

Acknowledgements

We thank Ninoslav Mimica and Aleksandar Savić from the University Psychiatric Hospital 'Vrapče' of the University of Zagreb for making this research possible, allowing us to work with patients at the Hospital, as well as their generous insight. We further thank them for their assistance in data collection, data analyses, and interpretations relating to psychiatric practice. We also thank Vlasta Erdeljac and Martina Sekulić Sović from the Department of Linguistics of the University of Zagreb for inviting us and encouraging us to work on these data.

Funding

This work was supported by the Faculty of Humanities and Social Sciences of the University of Zagreb under Grant 11-831-1006.

Declaration of interest statement

The authors report no conflict of interest.

References

- Allen, H. A., Liddle, P. F., & Frith, C. D. (1993). Negative features, retrieval processes and verbal fluency in schizophrenia. *British Journal of Psychiatry*, 163(6), 769–775. <u>https://doi.org/10.1192/bjp.163.6.769</u>
- Aloia, M. S., Gourovitch, M. L., Weinberger, D. R., & Goldberg, T. E. (1996). An investigation of semantic space in patients with schizophrenia. *Journal of the International Neuropsychological Society*, 2(4), 267–273. <u>https://doi.org/10.1017/S1355617700001272</u>
- Amunts, J., Camilleri, J. A., Eickhoff, S. B., Heim, S., & Weis, S. (2020). Executive functions predict verbal fluency scores in healthy participants. *Scientific Reports*, 10, 11141. https://doi.org/10.1038/s41598-020-65525-9
- Batty, R., Francis, A., Thomas, N., Hopwood, M., Ponsford, J., Johnston, L., & Rossell, S. (2015). Verbal fluency, clustering, and switching in patients with psychosis following traumatic brain injury (PFTBI). *Psychiatry Research*, 227(2–3), 152–159. https://doi.org/10.1016/j.psychres.2015.03.040
- Berberian, A. A., Moraes, G. V., Gadelha, A., Brietzke, E., Fonseca, A. O., Scarpato, B. S., Vicente, M. O., Seabra, A. G., Bressan, R. A., & Lacerda, A. L. (2016). Is semantic verbal fluency impairment explained by executive function deficits in schizophrenia?.

Brazilian Journal of Psychiatry, 38, 121–126. <u>https://doi.org/10.1590/1516-4446-2015-</u> 1663

- Berto, G., & Galaverna, F. S. (2016). Semantic memory organization on verbal fluency test "Human Body Parts" in patients with chronic schizophrenia diagnosis and healthy controls. *European Journal of Psychiatry*, 30(2), 97–108. http://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S0213-61632016000200001
- Biesbroek, J. M., van Zandvoort, M. J. E., Kapelle, L. J., Velthius, B. K., Biessels, G. J., & Postma, A. (2016). Shared and distinct anatomical correlates of semantic and phonemic fluency revealed by lesion-symptom mapping in patients with ischemic stroke. *Brain Structure and Function*, 221, 2123–34. <u>https://doi.org/10.1007/s00429-015-1033-8</u>
- Blessing, A., Wangelin, B., Regehr, H., & Rudolph, N. (2009). Verbal fluency tasks in first-episode psychosis. *Clinical Neuropsychiatry*, 6(1), 21–28. <u>https://psycnet.apa.org/record/2009-06871-003</u>
- Bozikas, V. P., Kosmidis, M. H., & Karavatos, A. (2005). Disproportionate impairment in semantic verbal fluency in schizophrenia: differential deficit in clustering. *Schizophrenia Research*, 74, 51–59. https://doi.org/10.1016/j.schres.2004.05.001
- Chen, R. Y. L., Chen, E. Y. H., Chan, C. K. Y., Lam, L. C. W., & Lieh-Mak, F. (2000).
 Verbal fluency in schizophrenia: reduction in semantic store. *Australian and New Zealand Journal of Psychiatry*, 34, 43–48. <u>https://doi.org/10.1046/j.1440-1614.2000.00647.x</u>
- Danivas, V., & Venkatasubramanian, G. (2020). Current perspectives on chlorpromazine equivalents: comparing apples and oranges!. *Indian Journal of Psychiatry*, 55(2), 207–208. <u>https://doi.org/10.4103/0019-5545.111475</u>

- Dudley, K., Liu, X., & De Haan, S. (2017). Chlorpromazine dose for people with schizophrenia. *Cochrane Database of Systematic Reviews*, 4(4), CD007778. <u>https://doi.org/10.1002/14651858.CD007778.pub2</u>
- Elvevåg, B., Fisher, J. E., Gurd, J. M., & Goldberg, T. E. (2002). Semantic clustering in verbal fluency: schizophrenic patients *versus* control participants. *Psychological Medicine*, 32(5), 909–917. <u>https://doi.org/10.1017/S0033291702005597</u>
- 14. Erdeljac, V., Kužina, I., Vandek, M., Sekulić Sović, M., Mimica, N., Ostojić, D., & Savić, A. (2019). Semantic and pragmatic relations in categorization in early course psychosis.
 In: V. Erdeljac & M. Sekulić Sović (eds.), *Interdisciplinary Linguistics and Psychiatric Research on Language Disorders* (pp. 55–67). FF Press. https://doi.org/10.17234/9789531758314.05
- Folnegović, Z., Hrabak-Zerjavić, V., Šmalc-Folnegović, & Mimica, N. (1994). Hospital incidence of schizophrenia in Croatia over a 25-year period. *Schizophrenia Research*, 11(2), 99–100. <u>https://www.sciencedirect.com/science/article/pii/0920996494902488</u>
- 16. Fong, M. C. M., Hui, N. Y., Fung, E. S. W., Ma, M. K. H., Law, T. S. T., Wang, X., & Wang, S. W. (2020). Which cognitive functions subserve clustering and switching in category fluency? Generalisations from an extended set of semantic categories using linear mixed-effects modelling. *Quarterly Journal of Experimental Psychology*, 73(12), 2132–2147. <u>https://doi.org/10.1177/1747021820957135</u>
- 17. Gabrić, P., & Vandek, M. (2020, October 21–24). Quantitative and qualitative differences in performance within the semantic and letter fluency tasks [Poster presentation]. 12th Annual Meeting of the Society for the Neurobiology of Language, Online, US. https://doi.org/10.17605/osf.io/te52u

- Giovannetti, T., Goldstein, R. Z., Schullery, M., Barr, W. B., Bilder, R. M. (2003).
 Category fluency in first-episode schizophrenia. *Journal of the International Neuropsychological Society*, 9, 384–393. <u>https://doi.org/10.10170S1355617703930049</u>
- Gourovitch, M. L., Goldberg, T. E., & Weinberger, D. R. (1996). Verbal fluency deficits in patients with schizophrenia: semantic fluency is differentially impaired as compared with phonologic fluency. *Neuropsychology*, 10(4), 573–577. <u>https://doi.org/10.1037/0894-4105.10.4.573</u>
- 20. JASP Team (2020). JASP (Version 0.13.1) [Computer software]. https://jasp-stats.org/
- Joyce, E. M., Collinson, S. L., & Crichton, P. (1996). Verbal fluency in schizophrenia: relationship with executive function, semantic memory and clinical alogia. *Psychological Medicine*, 26, 39–49. <u>https://doi.org/10.1017/S0033291700033705</u>
- 22. Kosmidis, M. H., Bozikas, V. P., Vlahou, C. H., Kiosseoglou, G., Giaglis, G., & Karavatos, A. (2005). Verbal fluency in institutionalized patients with schizophrenia: Age-related performance decline. *Psychiatry Research*, 134(3), 233–240. https://doi.org/10.1016/j.psychres.2005.02.003
- Kuperberg, G. R., Delaney-Busch, N., Fanucci, K., & Blackford, T. (2018). Priming production: neural evidence for enhanced automatic semantic activity preceding language production in schizophrenia. *NeuroImage: Clinical*, 18, 74–85. <u>https://doi.org/10.1016/j.nicl.2017.12.026</u>
- 24. Landrø, N. I., & Ueland, T. (2008). Verbal memory and verbal fluency in adolescents with schizophrenia spectrum disorders. *Psychiatry and Clinical Neurosciences*, 62(6), 653–661. <u>https://doi.org/10.1111/j.1440-1819.2008.01864.x</u>

- 25. Lemieux, P., & Macoir, J. (2017). Fonctions cognitives sous-jacentes aux déficits de fluence verbale dans la schizophrénie: revue de la littérature. Annales Médico-psychologiques, revue psychiatrique, 175(2), 127–139. https://doi.org/10.1016/j.amp.2016.06.002
- Mesholam-Gately, R. I., Giuliano, A. J., Goff, K. P., Faraone, S. V., & Seidman, L. J. (2009). Neurocognition in first-episode schizophrenia: a meta-analytic review. *Neuropsychology*, 23(3), 315–336. <u>https://doi.org/10.1037/a0014708</u>
- 27. Moore, D. J., Savla, G. N., Woods, S. P., Jeste, D. V., & Palmer, B. W. (2006). Verbal fluency impairments among middle-aged and older outpatients with schizophrenia are characterized by deficient switching. *Schizophrenia Research*, 87(1–3), 254–260. https://doi.org/10.1016/j.schres.2006.06.005
- 28. Nagels, A., Kircher, T., Dietsche, B., Backes, H., Marquetand, J., & Krug, A. (2012). Neural processing of overt word generation in healthy individuals: the effect of age and word knowledge. *NeuroImage*, 61, 832–840. <u>https://doi.org/10.1016/j.neuroimage.2012.04.019</u>
- Neill, E., Gurvich, C., & Rossell, S. L. (2014). Category fluency in schizophrenia research: is it an executive or semantic measure?. *Cognitive Neuropsychiatry*, 19(1), 81–95. <u>https://doi.org/10.1080/13546805.2013.807233</u>
- 30. Nuyen, J., Sitskoorn, M. M., Cahn, W., & Kahn, R. S. (2005). Verbal memory in firstepisode schizophrenia: heterogeneity in performance?. *Journal of the International Neuropsychological Society*, 11, 152–162. <u>https://doi.org/10.1017/s1355617705050162</u>
- 31. Okruszek, Ł., Rutkowska, A., & Wilińska, J. (2013). Clustering and switching strategies during the semantic fluency task in men with frontal lobe lesions and in men with

schizophrenia. *Psychology of Language and Communication*, 17(1), 93–100. https://doi.org/10.2478/plc-2013-0006

- 32. Paulsen, J. S., Romero, R., Chan, A., Davis, A. V., Heaton, R. K., & Jeste, D. V. (1996). Impairment of the semantic network in schizophrenia. *Psychiatry Research*, 63(2–3), 109– 121. <u>https://doi.org/10.1016/0165-1781(96)02901-0</u>
- 33. Phillips, T. J., James, A. C. D., Crow, T. J., & Collinson, S. L. (2004). Semantic fluency is impaired but phonemic and design fluency are preserved in early-onset schizophrenia. *Schizophrenia Research*, 70, 215–222. <u>https://doi.org/10.1016/j.schres.2003.10.003</u>
- 34. Popescu, C. A., & Micluția, I. V. (2006). Semantic fluency in schizophrenia. Journal of Evidence-Based Psychotherapies, 6(2), 105–118. http://jebp.psychotherapy.ro/vol6no2/semantic-fluency-in-schizophrenia/
- 35. Rinaldi, R., Lefebvre, L., & Trappeniers, J. (2014). Language, executive functioning and symptomatology—Is fluency a transversal tool in schizophrenia?. *Open Journal of Psychiatry*, 3(4), 358–369. https://doi.org/10.4236/ojpsych.2013.34038
- 36. Robert, P. H., Lafont, V., Medecin, I., Berthet, L., Thauby, S., Baudu, C., & Darcourt, G. (1998). Clustering and switching strategies in verbal fluency tasks: comparison between schizophrenics and healthy adults. *Journal of the International Neuropsychological Society*, 4(6), 539–546. <u>https://doi.org/10.1017/S1355617798466025</u>
- 37. Rosenkranz, A., Kircher, T., & Nagels, A. (2019). Neuropsychological correlates underlying verbal fluency deficits in schizophrenia: the role of attention and executive function. In: V. Erdeljac & M. Sekulić Sović (eds.), *Interdisciplinary Linguistics and Psychiatric Research on Language Disorders* (pp. 45–54). FF Press. <u>https://doi.org/10.17234/9789531758314.04</u>

- 38. Rossell, S. L., Rabe-Hesketh, S., Shapleske, J., & David, A. S. (1999). Is semantic fluency differentially impaired in schizophrenic patients with delusions?. *Journal of Clinical and Experimental Neuropsychology*, 21(5), 629–642. https://doi.org/10.1076/jcen.21.5.629.865
- Spitzer, M. (1997). A cognitive neuroscience view of schizophrenic thought disorder. Schizophrenia Bulletin, 23(1), 29–50. <u>https://doi.org/10.1093/schbul/23.1.29</u>
- 40. Stielow, A., & Stenneken, P. (2017). Der Beitrag exekutiver und sprachlicher Teilleistungen in semantischen und formal-lexikalischen Wortflüssigkeitsaufgaben. *Sprache · Stimme · Gehör*, 41, 197–203. <u>https://doi.org/10.1055/s-0043-117202</u>
- 41. Sumiyoshi, C., Ertugrul, A., Yagcioglu, A. E. A., & Sumiyoshi, T. (2009). Semantic memory deficits based on category fluency performance in schizophrenia: similar impairment patterns of semantic organization across Turkish and Japanese patients. *Psychiatry Research*, 167(1–2), 47–57. <u>https://doi.org/10.1016/j.psychres.2007.12.009</u>
- 42. Sung, K., Gordon, B., Vannorsdall, T. D., Ledoux, K., Pickett, E. J., Pearlson, G. D., & Schretlen, D. J. (2012). Semantic clustering of category fluency in schizophrenia examined with singular value decomposition. *Journal of the International Neuropsychological Society*, 18, 565–575. <u>https://doi.org/10.1017/S1355617712000136</u>
- 43. Troyer, A. K., & Moscovitch, M. (2006). Cognitive processes of verbal fluency tasks. In:
 A. M. Poreh (Ed.), *Studies on Neuropsychology, Neurology and Cognition: The Quantified Process Approach to Neuropsychological Assessment* (pp. 143–160). Taylor & Francis. https://psycnet.apa.org/record/2007-16443-009

- 44. Troyer, A. K., Moscovitch, M., & Winocur, G. (1997). Clustering and switching as two components of verbal fluency: evidence from younger and older healthy adults. *Neuropsychology*, 11(1), 138–146. <u>https://doi.org/10.1037//0894-4105.11.1.138</u>
- 45. Tyburski, E., Sokołowski, A., Chęć, M., Pełka-Wysiecka, J., & Samochowiec, A. (2015).
 Neuropsychological characteristics of verbal and non-verbal fluency in schizophrenia patients. *Archives of Psychiatric Nursing*, 29, 33–38.
 https://doi.org/10.1016/j.apnu.2014.09.009
- 46. van Beilen, M., Pijnenborg, M., van Zomeren, E. H., van den Bosch, R. J., Withaar, F. K.,
 & Bouma, A. (2004). What is measured by verbal fluency tests in schizophrenia?. *Schizophrenia Research*, 69, 267–276. <u>https://doi.org/10.1016/j.schres.2003.09.007</u>
- 47. Vandek, M., Gabrić, P., Kužina, I., Erdeljac, V., & Sekulić Sović, M. (2018, July 2–4).
 Verbal fluency and working memory interaction [Poster presentation]. 10th International
 Workshop on Language Production, Nijmegen, the Netherlands.
 <u>https://doi.org/10.17605/osf.io/au6vd</u>
- 48. Veleva, I. I., Stoimenova, M. J., & Valkova, M. P. (2019). A comparative study of verbal fluency in patients with paranoid schizophrenia, first grade relatives and healthy controls. *Archives of the Balkan Medical Union*, 54(2), 325–329. https://doi.org/10.31688/ABMU.2019.54.2.16
- 49. WHO (World Health Organization) (1993). The ICD-10 Classification of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines. World Health Organization. <u>https://www.who.int/classifications/icd/en/bluebook.pdf</u>