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Preliminary Evidence for Impaired Rapid Verb Generation in Schizophrenia

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Abstract

It has been hypothesized that nouns and verbs are processed within relatively separable semantic memory networks. Although abnormal semantic processing is a common feature of schizophrenia-spectrum disorders, no prior studies have specifically examined the comparability of noun and verb generation deficits in schizophrenia. In the current study, verb (action), noun (animal), and letter (f) fluency performance was evaluated in 22 inpatients with schizophrenia and 27 healthy comparison subjects. On average, individuals with schizophrenia performed approximately one standard deviation below the healthy comparison subjects on action, animal, and letter fluency. Action fluency – but not letter or animal fluency – was moderately correlated with tests of working memory, response inhibition, semantic memory, and cognitive flexibility. Findings suggest that verb- and noun-based fluency deficits are of comparable severity in schizophrenia, but that the impairment in verb generation may be driven by different underlying cognitive mechanisms. Further, hypothesis-driven research on the nature and extent of verb network disruption in schizophrenia appears warranted.

Keywords

Schizophrenia; Neuropsychology; Cognitive processes; Verbal fluency; Verbs

Abnormalities within frontotemporal systems are hypothesized to play an important role in the etiology and expression of schizophrenia-spectrum disorders (SCZ). For example, in addition to ventriculomegaly, neuroimaging studies reveal altered structure and function of the thalamus, medial temporal lobes, and prefrontal cortex in individuals with SCZ (Davidson & Henrichs, 2003; Shenton, Dickey, Frumin, & McCarley, 2001). SCZ is also associated with impairments in many aspects of cognition, most notably episodic memory, language, attention, working memory, and executive functions (e.g., Fioravanti, Carlone, Vitale, Cinti, & Clare, 2005). Another common feature of SCZ is impairment in semantic memory, which is an aspect of declarative memory in which information related to facts, symbols, and concepts are

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processed (e.g., McKay, McKenna, Bentham, Mortimer, Holbery, & Hodges, 1996). It has been argued that the thought disorder evident in some individuals with SCZ, which is often expressed as disorganized speech (e.g., loose associations), may arise from abnormal semantic processing (e.g., Goldberg, Aloia, Gourovitch, Missar, Pickar, & Weinberger, 1998). In other words, SCZ-associated thought disorder may reflect inefficiencies navigating semantic networks, perhaps secondary to disorganization, degradation, and/or developmental abnormalities within the semantic memory systems (e.g., Goldberg et al., 1998).

One traditional measure of the integrity of semantic networks, verbal fluency, is reliably impaired in persons with SCZ (Bokat & Goldberg, 2003). Verbal fluency tests tax the speeded, strategic aspects of word search and retrieval from semantic memory stores by requiring examinees to orally generate as many words as possible that belong to a particular semantic category (e.g., animals) or begin with a specific letter of the alphabet within a predetermined time limit (often 60 sec). Category fluency tasks are conventionally thought to reflect the integrity of temporolimbic neural systems and semantic memory stores, whereas letter fluency is more commonly linked to frontal systems, executive functions and lexico-semantic networks. Although large effect sizes are evident on both letter- and category-based fluency tasks in SCZ, a recent meta-analysis revealed a disproportionate deficit in category fluency (Bokat & Goldberg, 2003). It was hypothesized that the differential category fluency impairment may signal particular compromise of semantic networks. To this end, prior investigations suggest that the semantic fluency deficits in SCZ are driven by impaired access to (Joyce, Collinson, & Crichton, 1996), disorganization within, and/or degradation of semantic memory stores (Bozikas, Kosmidis, & Karavatos, 2005; Henry, Crawford, & Phillips, 2005), rather than problems with strategic search and retrieval (Elvevåg, Weinstock, Akil, Kleinman, & Goldberg 2001).

Importantly, a considerable body of research now indicates that neuroanatomical dissociations exist between certain semantic memory systems (Goodglass, Klein, Carey, & Jones, 1966), which raises a series of interesting conceptual questions regarding the category fluency deficits evident in SCZ. For instance, is SCZ associated with differential deficits in the rapid generation of words from major semantic networks, such as nouns and verbs? Damasio and Tranel (1993) proposed a double dissociation between the neural networks that support the processing of nouns and verbs. Although aspects of these word and concept retrieval systems likely overlap (Damasio, Tranel, Grabowski, Adolphs, & Damasio, 2004), noun generation is closely linked to dominant temporoparietal neural networks (e.g., Cappa, Binetti, Pezzini, Padovani, Rozzini & Trabucchi, 1998; Tranel, Adolphs, Damasio, & Damasio, 2001), while verb generation is more dependent upon frontal systems (e.g., Cappa & Perani, 2003).

We are aware of only one prior article published on verb-based semantic memory processing in SCZ. Marvel and colleagues (Marvel, Schwartz, & Isaacs, 2004) presented a series of nouns to 46 individuals with SCZ and 46 demographically similar nonpsychiatric controls who were asked to respond with a semantically-related action word (e.g., tree – climb). Relative to the comparison sample, the SCZ group committed more verb generation errors, which were negatively correlated with performance on a measure of working memory. The verb generation deficit observed in the SCZ cohort was particularly pronounced in a high word selection condition (i.e., when noun words with many possible verb responses were presented). Findings were interpreted to suggest that word search deficits, perhaps related to frontal systems dysfunction, may underlie the verb generation impairment in SCZ. Thus, one logical extension of these interesting findings would be to examine verb (and noun) generation in SCZ using tasks with increased self-initiated word search and retrieval demands, such as clinical tests of verbal fluency.

To our knowledge, however, no studies have yet examined spontaneous rapid verb generation (i.e., action fluency) in SCZ. Action (verb) fluency was developed by Piatt and colleagues (Piatt, Fields, Paolo, Koller, & Tröster, 1999a) to provide a valid measurement of rapid verb generation from semantic memory. In this task participants are asked to rapidly generate as many verbs (i.e., “things that people do”) as possible within a 60 second time limit. The reliability and psychometric properties of this test is supported in healthy controls (Woods, Carey, Tröster, Grant, & The HNRC Group 2005a). The construct validity of action fluency has also been consistently supported. For example, action fluency is sensitive to the frontostriatal dysfunction associated with HIV infection (Woods, Scott, Sires, Grant, Heaton, Tröster & The HNRC Group 2005b) and Parkinson’s disease (Piatt et al., 1999a; Piatt, Fields, Paolo, & Tröster, 1999b). Moreover, action fluency was more strongly associated with tests of executive functions (e.g., divided attention), working memory, and motor skills than noun fluency (Woods et al., 2005b). Evidence of divergent validity is provided by the lack of correlations between action fluency and tests of noun naming, praxis, or verbal episodic memory, which are cognitive functions mediated by more posterior neocortical regions (Piatt et al., 1999a; Woods et al., 2005a,b).

The primary aim of the present study was to evaluate the nature, extent, and cognitive substrates of verb (action) and noun (animal) verbal fluency in SCZ. Given evidence of prominent semantic memory impairment in SCZ and involvement of both frontal and temporal brain systems in its neuropathophysiology, it was hypothesized that patients with SCZ would demonstrate impaired performance on both verb and noun fluency relative to demographically similar nonSCZ comparison subjects. Based on prior literature (e.g., Woods et al., 2005a), it was also hypothesized that action and letter fluency would correlate more strongly with standard measures of executive functions (e.g., Wisconsin Card Sorting Test) and working memory (e.g., backward digit span) within the SCZ sample than noun fluency. In contrast, it was expected that noun, but not verb or letter fluency would be associated with a measure of episodic memory (delayed recall).

Materials and Method

Participants

Participants consisted of 22 inpatients at a large, mid-Atlantic state psychiatric hospital who met Diagnostic and Statistical Manual (4th ed.; *DSM-IV*; American Psychiatric Association, 1994) criteria for SCZ and 27 nonpsychiatric comparison subjects (nonSCZ). Exclusion criteria for both groups included a history of neurological or severe psychiatric disease (other than schizophrenia-spectrum disorders in the SCZ group), mental retardation, HIV infection, or a history of head injury with a loss of consciousness greater than 30 min. Participants were also excluded if they met *DSM-IV* criteria for any substance related disorder (e.g., cocaine dependence) within one year of evaluation. As shown in Table 1, there were no statistically significant between-groups differences in age, years of education, sex, or handedness (all $ps > .10$). Although the SCZ sample contained a larger proportion of non-Caucasian participants ($p = .04$), the groups did not differ in demographically-estimated premorbid verbal IQ as measured by the Wechsler Test of Adult Reading (Psychological Corporation, 2001). On average, participants in the SCZ group evidenced mild-to-moderate psychiatric symptoms (see Table 1) at the time of evaluation as measured by Brief Psychiatric Rating Scale (BPRS; Overall & Gorham, 1962).

Procedure

This retrospective neuropsychological study was approved by the human research protections committees at the sponsoring institutions. The nonSCZ group was administered the action (Piatt et al., 1999a), animal (Benton, Hamsher & Sivan, 1983), and letter (Benton et al.,

1983) fluency tests as part of their participation as seronegative controls in a University research project on neuroAIDS. Action, animal, and letter verbal fluency data in the SCZ group were obtained from retrospective chart reviews of neuropsychological evaluations that were performed as part of routine clinical care at the above-mentioned inpatient psychiatric facility. Several other neuropsychological tests were chosen for analysis in the SCZ group and were specifically selected on the basis of their relevance to verb generation, demonstrated construct validity, and available sample size. The specific tests selected for inclusion were: 1) Wisconsin Card Sorting Test (64-card version; $n = 21$; Kongs, Thompson, Iverson, & Heaton, 2000); 2) Trailmaking Test, Parts A and B ($n = 20$; Reitan & Wolfson, 1985); 3) Stroop Color-Word Test ($n = 18$; Trennery, Crosson, DeBoe, & Leber 1989); 4) the Information ($n = 14$) and Digits Backward ($n = 22$) subtests from the Wechsler Adult Intelligence Scale (3rd ed; WAIS-III, Psychological Corporation, 1997); and 5) Repeatable Battery for the Assessment of Neuropsychological Status (RBANS; $n = 15$; Randolph, 1998).

Standardized, published instructions were used for all of the verbal fluency tests. The action fluency task required participants to generate “as many things as (they) can think of that people do” in 60 seconds (Piatt et al., 1999a). Verb responses that are not plausibly performed by humans (e.g., photosynthesize) and questionable noun-verb homonyms (e.g., comb) were queried and, if indicated, were coded as intrusions (Woods et al., 2005). On the animal fluency task, participants were asked to generate as many different animal names as possible in 60 seconds. Similarly, the letter fluency test required the participants to generate as many words as possible beginning with the letter “f” over a 60 second period. For all fluency tasks, participants were instructed not to respond with proper names or to generate a previously spoken word with a different suffix. Published normative standards were used to derive demographically-adjusted T-scores ($M = 50$, $SD = 10$) for action (Woods et al., 2005b), animal (Tombaugh, Kozak, & Rees, 1998), and letter (Tombaugh et al., 1998) fluency total scores.

Results

Due to concerns regarding limited power (Type II error) resultant from the relatively small number of participants in this study, the critical alpha level was set at $p < .05$ for all analyses and effect sizes (e.g., unbiased Cohen’s d values) are used for interpretation whenever possible. Comprehensive descriptive statistics from all three verbal fluency measures are displayed by group in Table 2. A repeated-measures multiple analyses of variance was conducted with SCZ as the between-subjects factor and fluency raw scores (action, animal, and letter) as the within-subjects factor. Results showed significant main effects for SCZ ($F(1, 45) = 23.8$, $p < .0001$) and verbal fluency ($F(2, 44) = 27.0$, $p < .0001$), but no significant group by fluency interaction ($F(2, 44) = 1.5$, $p = .23$). Univariate tests revealed persons with SCZ scored significantly below the nonSCZ group on action fluency ($t(47) = 3.43$, $p = .001$, $d = -0.97$, 95% confidence interval (CI) = -1.55 , -0.36). The SCZ and nonSCZ groups also differed on animal fluency ($t(47) = 3.88$, $p = .0003$, $d = -1.09$, $CI = -1.69$, -0.47) and letter fluency ($t(47) = 5.72$, $p < .0001$, $d = -1.61$, $CI = -2.24$, -0.93) in the expected directions. No group differences were present on action fluency intrusions or perseverations (all $ps > .10$).

Figure 1 shows that 64% of the SCZ sample was impaired on action fluency (i.e., T-score < 40) when demographically-adjusted normative standards were applied (Woods et al., 2005b), whereas just 22% of the nonSCZ sample was similarly impaired ($\chi^2(1, 48) = 8.6$, $p = .003$). Consistent with the raw score analyses, there were no between-group differences in normatively derived impairment rates on action fluency intrusions or perseverations (all $ps > .10$). Only 33% of SCZ participants and 4% of controls were impaired on animal fluency (Fisher’s Exact test $p = .02$), which was a significantly smaller proportion than was impaired on action fluency (Fisher’s Exact test $p = .04$). Follow-up analyses showed that 32% of the SCZ group were impaired on action, but not animal fluency (no participant evidenced the

inverse profile of deficits). Similar to action fluency, 62% of the SCZ sample and 13% of the comparison samples were impaired on letter fluency (Fisher's Exact test $p < .0001$). Thirty-six percent of the SCZ group was impaired only on either letter (18%) or action (18%) fluency, whereas 41% were impaired on both tasks.

Correlational analyses between all three fluency measures and clinical tests of working memory, executive functions, episodic memory, and semantic memory in the SCZ sample are presented in Table 3. Action fluency was significantly correlated with performance on WAIS-III Digits Backward and Information subtests ($ps = .05$), Stroop Color-Word Test errors ($p = .006$), TMT B-A ($p = .03$), and letter fluency ($p = .04$). Neither animal nor letter fluency demonstrated strong relationships with these clinical tests, with the exception of a modest correlation between TMT B-A and animal fluency ($p = .04$). By way of comparison, there was a significant correlation between the RBANS Delayed Memory Index and animal fluency ($p = .02$), but not action ($p = .38$) or letter ($p = .63$) fluency.

Finally, a series of *post hoc* analyses were undertaken to determine whether the action fluency findings could be attributed to the confounding effects of ethnicity, psychiatric symptom severity, or medications. Across groups, results revealed no main effect of ethnicity in predicting action fluency, nor any interaction between ethnicity and SCZ (all $ps > .10$). Within the SCZ group, there was not a significant correlation between the BPRS Brief and action fluency (Spearman's $\rho = -.15$, $p > .10$). Finally, no significant differences were observed between participants on and off typical antipsychotics, atypical antipsychotics, or mood stabilizing agents (all $ps > .10$).

Discussion

Results from the current study reveal preliminary, but nonetheless strong evidence of rapid verb generation deficits in a sample of inpatients with SCZ. On average, persons with SCZ performed approximately one standard deviation below nonSCZ healthy comparison subjects ($d = -0.97$) on a test of action (verb) fluency, which required participants to quickly generate verbs from semantic memory. These findings are consistent with those of Marvel et al. (2004), who were the first to report verb generation deficits in SCZ, which were particularly evident when word search demands were increased. The present study extends the original work of Marvel and colleagues by using timed verbal fluency tasks with greater self-initiated word search and retrieval demands, as well as by including a complementary measure of noun generation (i.e., animal fluency) with similar administration procedures and task demands to the verb generation test.

The effect size associated with the action fluency deficit was broadly commensurate to those observed for letter and animal fluency in this study sample, as well as in recent meta-analyses of verbal fluency in SCZ (e.g., Bokatz & Goldberg, 2003). Thus the impairments in verb- and noun-based fluency appear to be of similar overall severity, indicating that normal information processing functions are disrupted in both noun and verb networks in SCZ. One possible interpretation of these data is that SCZ-associated verbal fluency deficits simply reflect the effects of generalized central nervous system dysfunction. Thus, word generation impairment in SCZ is evident regardless of the particular semantic category that is used to guide the word search and retrieval process. This interpretation is consistent with literature indicating that individuals with SCZ often evidence generalized impairment across multiple cognitive domains (Fioravanti et al., 2005).

Although the overall *severity* of impairment was similar across fluency tasks, results from this study nevertheless raise the possibility that the cognitive substrates of noun and verb generation impairment in SCZ differ from one another. For example, only a small (and nonsignificant)

correlation was observed between action and animal fluency, which was somewhat attenuated relative to prior data from large normative samples (Woods et al., 2005b). In fact, a larger proportion of SCZ participants were impaired on action versus animal fluency (indeed, 32% of the SCZ group were impaired on action, but not animal fluency). Moreover, action fluency – but not other fluency tasks – was moderately correlated with working memory, response inhibition, cognitive flexibility, and semantic memory in SCZ, despite the fact that all three fluency tests have comparable administration protocols and putative cognitive demands (i.e., all require rapid search and retrieval from semantic memory). In turn, animal, but not action fluency correlated with a measure of delayed memory, which parallels construct validity data on action fluency from healthy adults and individuals with HIV infection (Woods et al., 2005a,b). Action fluency may place relatively greater burdens on executive control of speeded verb-based semantic network search and retrieval strategies in SCZ than animal fluency. This notion is consistent with a prior study showing that nonspeeded verb generation deficits in SCZ were particularly pronounced when search difficulty was increased (Marvel et al., 2004).

It may also be that the verb generation deficits evident in SCZ stem from problems engaging motor representations while retrieving action words (Cappa & Perani, 2003). This interpretation is consistent with a recent conceptual model proposed by Damasio and colleagues (2004), which suggests that word and concept retrieval are highly dependent on sensory imagery. Supporting this hypothesis, individuals with SCZ have shown to be inaccurate in generating internal images of motor movements (Danckert, Rossetti, d'Amato, Dalery, & Saoud, 2002). In addition, neuromotor abnormalities are common in SCZ, even in first episode individuals who are neuroleptic naïve (Cortese, Caligiuri, Malla, Manchanda, Takhar, & Haricharan, 2005.). Moreover, prior research shows that action fluency correlates with measures of motor speed and coordination (Woods et al., 2005b). Although it is important to note that motoric activities represent only one subcategory of verbs (Kemmerer & Tranel, 2000), further investigation of the association between language-based motor representations and verb generation deficits in SCZ is warranted.

The current study also extends the research of Marvel et al. (2004) by demonstrating the potential clinical implications of verb generation deficits in SCZ. Not only did the SCZ cohort generate fewer verbs than healthy controls at the group level, but a substantial proportion were classified as impaired per demographically-adjusted normative standards. Such findings are important because, while group differences in the normal range may be of conceptual interest, differences indicative of actual impairment may be clinically meaningful. For example, a deficit in action fluency may signify an increased risk of problems independently performing instrumental activities of daily living (IADL; e.g., employment, financial management, medication adherence). A recent study reported that impaired action fluency performance was associated with a fivefold increase in risk of IADL dependence among persons infected with HIV (Woods, Morgan, Dawson, Scott, Grant, & The HNRC Group, in press). In fact, relative to traditional letter and animal fluency tasks, action fluency may provide incremental ecological validity in this regard (Woods et al., in press).

The action fluency deficits observed in this study are not better explained by secondary disease characteristics or demographic factors. *Post hoc* analyses revealed no associations between action fluency performance and psychiatric symptom severity or psychotropic drug use. In addition, the SCZ and nonSCZ samples did not differ in age, education, sex, handedness, and estimated premorbid verbal IQ. Although there was a smaller proportion of Caucasians in the SCZ group, there was no evidence of a main effect of ethnicity on action fluency, nor any interaction between ethnicity and SCZ (all p s > .10). Nevertheless, it is important to highlight several limitations to the internal and external validity of this study. The study samples were relatively small, which, although less of a concern in light of our significant main effects, may have nevertheless limited our power to detect interactions associated with small-to-medium

effect sizes. In addition, the SCZ cohort was comprised exclusively of inpatients, thereby calling into question the generalizability of our findings to community-dwelling individuals with SCZ who may evidence milder cognitive deficits. Furthermore, our SCZ sample was not sufficiently large to examine possible differences in rapid verb generation between various subtypes of SCZ. Similarly, no specific measures of positive and negative symptoms (e.g., Scale for the Assessment of Positive and Negative Symptoms; Andreasen & Olsen, 1982) were available to more carefully delineate associations between verb generation and SCZ symptom severity. Given prior research linking negative symptoms to cognitive deficits in SCZ, this will be an important area for future research.

In summary, this study provides preliminary evidence for impaired rapid verb generation in persons with SCZ and, together with the findings of Marvel et al. (2004), indicates that further exploration of the nature and extent of the verb processing deficits in SCZ is warranted. Larger and more representative cohorts are needed to conduct more sophisticated multivariate analyses that may clarify the cognitive mechanisms of SCZ-associated deficits in verb generation and the extent to which they are distinguishable from noun generation. Future studies will also need to employ a broader, multimodal assessment of noun and verb processing. For example, the inclusion of both oral and written verb generation tasks might provide insights into the contributions of phonological versus orthographic processing to the verb-based semantic memory deficit in SCZ (e.g., Hillis, Oh, & Ken, 2004b). Similarly, the use of action and object naming (e.g., Kemmerer & Tranel, 2000) and concept recognition (Damasio et al., 2004) tests that are matched on item frequency and difficulty level are needed to determine the relative contributions of word search, retrieval and/or conceptual knowledge to the observed verb generation deficit in SCZ. Finally, studies are needed to determine the relationships between rapid verb generation deficits and biological markers of central nervous system dysfunction in SCZ (e.g., neocortical atrophy).

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Figure 1.

Bar graph displaying the proportion of SCZ ($n = 22$) and nonSCZ ($n = 27$) participants who were impaired on action, animal, and letter fluency according to demographically-adjusted normative standards. Intr = intrusions. Pers = perseverations. * $p < .01$. ** $p < .001$

Table 1
Demographic Characteristics of the SCZ and nonSCZ Study Groups.

Variable	nonSCZ (<i>n</i> = 27)	SCZ (<i>n</i> = 22)
Age (years)	45.7 (10.5)	40.9 (12.2)
Education (years)	11.5 (2.2)	10.5 (3.0)
WTAR Estimated Verbal IQ	100.0 (6.2)	97.9 (7.1)
Proportion men (%)	70	91
Proportion Caucasian (%) *	74	45
Proportion right-handed (%)	89	82
Proportion on typical antipsychotics (%)	----	45
Proportion on atypical antipsychotics (%)	----	86
Proportion on mood stabilizers (%)	----	50
Brief Psychiatric Rating Scale (total)	----	37.4 (7.0)

Note. SCZ = schizophrenia; WTAR = Wechsler Adult Test of Reading.

*
p < .05.

Table 2
Action, Letter, and Animal Fluency Scores in the SCZ and nonSCZ Groups.

Verbal Fluency Variable	nonSCZ (<i>n</i> = 27)	SCZ (<i>n</i> = 22)
Action Fluency ***		
Total Correct	15.8 (5.4)	10.8 (4.8)
Intrusions ^a	0.0 (1.0)	0.0 (1.3)
Perseverations ^a	2.0 (3.0)	1.0 (2.0)
Animal Fluency ***	20.7 (6.1)	14.6 (4.8)
Letter Fluency (F) ***	15.8 (4.8)	8.6 (4.0)

Note. SCZ = schizophrenia.

^aData represent medians with the interquartile range in parentheses.

p < .001.

Table 3

Correlations Between Action, Animal and Letter Fluency and Measures of Working Memory, Semantic Memory, Episodic Memory, and Executive Functions in SCZ.

Test Variable	Verbal Fluency		
	Actions	Animals	Letter (F)
Animal Fluency	0.30	----	-0.18
Letter Fluency (F)	0.46 [*]	----	----
WAIS-III Digits Backward	0.42 [*]	0.24	0.21
WCST-64 Categories	0.32	0.01	0.07
Stroop Color-Word Errors	-0.62 ^{**}	-0.16	-0.06
TMT B-A	-0.50 [*]	-0.40 [*]	-0.25
RBANS Delayed Memory	0.25	0.64 [*]	0.14
WAIS-III Information	0.53 [*]	-0.10	0.29

Note. RBANS = Repeatable Battery for the Assessment of Neuropsychological Status; TMT = Trail Making Test; WAIS-III = Wechsler Adult Intelligence Scale (3rd ed.); WCST-64 = Wisconsin Card Sorting Test, 64 Card Version.

*
p < 0.05.

**
p < 0.01.