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Is there disproportionate impairment in semantic or phonemic fluency in schizophrenia?

WILLIAM S. KREMEN,[1] LARRY J. SEIDMAN,[2] STEPHEN V. FARAONE,[2] AND MING T. TSUANG[2]

[1]Department of Psychiatry, University of California, Davis School of Medicine, 2230 Stockton Blvd., Sacramento, CA, and UC Davis–Napa Psychiatric Research Center, Napa State Hospital, Napa, CA
[2]Harvard Medical School Department of Psychiatry at Massachusetts Mental Health Center, Brockton-West Roxbury VA Medical Center and Massachusetts General Hospital, and Harvard Institute of Psychiatric Epidemiology and Genetics, 74 Fenwood Road, Boston, MA

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Abstract

Phonemic and semantic fluency involve the capacity to generate words beginning with particular letters or belonging to particular categories, respectively. The former has been associated with frontal lobe function and the latter with temporoparietal function, but neuroimaging studies indicate overlap of underlying neural networks. Schizophrenia patients may experience disproportionate semantic fluency impairment owing to abnormal semantic organization; however, executive dysfunction in schizophrenia suggests possible disproportionate phonemic fluency impairment. Moreover, little is known about the diagnostic specificity of either verbal fluency deficit to schizophrenia or their stability over time. We examined 83 schizophrenia patients, 15 bipolar disorder patients, and 83 normal controls. Both fluency types were impaired in schizophrenia patients. Schizophrenia patients as a whole manifested disproportionate semantic fluency impairment relative to bipolar disorder patients, but only a subset of schizophrenia patients manifested disproportionate semantic fluency impairment relative to controls. Few characteristics, except to some extent paranoid-nonparanoid subtype, meaningfully differentiated schizophrenia patients with and without this disproportionate impairment. Verbal fluency measures were moderately stable over a 4-year period in schizophrenia patients and controls ($.48 < rs < .79$). These results mirror a literature that overall suggests a small degree of disproportionate semantic fluency impairment in schizophrenia, but also some heterogeneity in fluency deficits. (*JINS*, 2003, *9*, 79–88.)

Keywords: Verbal fluency, Semantic memory, Frontal cortex, Temporoparietal cortex, Schizophrenia

INTRODUCTION

Verbal fluency is often impaired in schizophrenia (Heinrichs & Zakzanis, 1998), but the status of semantic (category) *versus* phonemic (letter) fluency performance is still not well understood. Retrieval of object categories relies to a greater extent on the inherent organization of semantic knowledge, whereas retrieval based on letter cues necessitates the formation of less frequently utilized and more novel categories. Phonemic fluency may, thus, require greater effort and more active strategic searching than semantic fluency because the former is less congruent with the way in which the semantic memory store is organized (Martin et al., 1994; Rosen, 1980).

Reprint requests to: William S. Kremen, Ph.D., Department of Psychiatry, University of California, Davis School of Medicine, 2230 Stockton Boulevard, Sacramento, CA 95817. E-mail: wskremen@ucdavis.edu

Both frontal and temporoparietal function have been linked to verbal fluency. Traditionally, impaired phonemic fluency has been associated with frontal lobe dysfunction (Benton, 1968; Milner, 1964), whereas posterior cortical dysfunction has been more strongly associated with impairment in semantic fluency (Newcombe, 1969). This distinction is far from a clear dichotomy, with several studies failing to show the same pattern of phonemic-semantic fluency differences for patients with frontal lobe *versus* posterior cortical lesions (Troyer et al., 1998). One reason for the inconsistencies may be differences in location of lesion (particularly left *vs.* right hemisphere), given the verbal nature of these tasks.

Few neuroimaging studies have examined phonemic and semantic fluency in the same individuals. In those that have, the most consistent finding is that both tasks are associated with left frontal lobe activation, but there is a greater extent of left (predominantly inferior) frontal lobe activations in

phonemic than in semantic fluency (Gourovitch et al., 2000; Mummery et al., 1996; Paulesu et al., 1997; Pujol et al., 1996). In studies that also examined non-frontal regions, semantic fluency was associated with greater activation than phonemic fluency primarily in left temporal neocortex and medial temporal cortex (Gourovitch et al., 2000; Mummery et al., 1996). Greater activations during semantic than phonemic fluency were also observed in left posterior cingulate and retrosplenial cortex (Gourovitch et al., 2000; Paulesu et al., 1997), perhaps reflecting the involvement of context or episodic retrieval processing (Maddock, 1999). Taken together, these neuroimaging studies suggest a good deal of overlap in neural networks underlying phonemic and semantic fluency, with small relative differences in the extent of frontal and posterior cortical activation, respectively.

Comparisons of patients with dementia of the Alzheimer's type and Huntington's disease provide support for this relative dissociation in that the former tend to manifest differential impairment in semantic fluency, whereas the latter tend to be equally impaired on phonemic and semantic fluency (Butters et al., 1987; Martin & Fedio, 1983; Monsch et al., 1994). It has been proposed that the deficit in Alzheimer's disease is associated with a breakdown in the structure of semantic knowledge (Martin & Fedio, 1983), whereas impairment in Huntington's disease may be associated with executive dysfunction caused by abnormalities in frontal-striatal connections (Butters et al., 1987). Paralleling the lack of difference in Huntington's disease, Baldo and Shimamura (1998) reported an absence of differential impairment on the fluency tasks in patients with frontal lobe lesions. Studies of normal participants are consistent with a relative dissociation in that secondary tasks that are thought to primarily activate either frontal or temporal-hippocampal brain regions, disproportionately interfere with performance on phonemic and semantic fluency, respectively (Martin et al., 1994; Moscovitch, 1992; 1994).

There is evidence of both prefrontal and temporal lobe system pathology in schizophrenia, including extensive connections with subcortical and posterior brain regions such as thalamus, basal ganglia, cerebellum, and parietal cortex (Andreasen et al., 1998; Heckers, 1997; Lawrie & Abukmeil, 1998; McCarley et al., 1999; Seidman, 1983). Thus, understanding the relative severity of semantic and phonemic fluency deficits has implications for understanding frontal and temporal lobe abnormalities in schizophrenia.

What then is the pattern of verbal fluency performance in schizophrenia? The majority of studies utilizing non-written fluency tasks have shown that both schizophrenia patients and controls generate more words in response to semantic cues than to phonemic cues (Arango et al., 1999; Beatty et al., 1993; Elvevåg et al., 2001; Feinstein et al., 1998; Goldberg et al., 1998; Joyce et al., 1996; Laurent et al., 2000). In contrast, while finding the same pattern in controls, Gourovitch et al. (1996) found the opposite pattern in schizophrenia patients. Schizophrenia patients displayed the opposite pattern in two other studies (Gruzelier et al., 1988; Roxborough et al., 1993), but their controls did as well (1996). Goldberg and colleagues (Feinstein et al., 1998; Goldberg et al., 1998; Gourovitch et al., 1996) have argued that semantic fluency is disproportionately impaired, but the aforementioned studies provide mixed support for this hypothesis.

Goldberg and colleagues have suggested that abnormalities in the semantic store above and beyond executive dysfunction related to search and retrieval cause disproportionate semantic fluency impairment in schizophrenia. This conclusion was, in part, based on the fact that schizophrenia patients benefitted from cueing in semantic fluency, but not more than controls did; they concluded that deficient performance was not due primarily to inefficient access (i.e., retrieval), implying additional abnormality of the semantic store (Feinstein et al., 1998). Paulsen et al. (1996) found direct evidence of semantic network disorganization in schizophrenia patients with onset before age 45 based on the proximity of animal names generated along two dimensions (small-large, domestic-wild). Because schizophrenia patients improved their semantic fluency performance with cueing, Joyce et al. (1996) argued that inefficient access to, rather than abnormalities of, the semantic store accounts for the impairment in schizophrenia. The logic of the former groups would be more consistent with semantic fluency deficits reflecting temporoparietal abnormalities in schizophrenia, whereas Joyce et al.'s reasoning more strongly implicates prefrontal cortex.

In utilizing verbal fluency measures, our initial hypothesis was that, given strong evidence of executive and prefrontal cortical dysfunction in schizophrenia (Seidman et al., 1992; Weinberger et al., 1994), phonemic fluency was likely to be disproportionately impaired relative to semantic fluency. Given the mixed findings and the proposition of disproportionate semantic fluency impairment by some authors, further study of this issue is warranted. Moreover, most studies examining both fluency types have had relatively small sample sizes.

For understanding any neurocognitive deficit in schizophrenia, it is also important to examine its clinical correlates, its diagnostic specificity, and whether or not it reflects a trait-like phenomenon. Thought disorder is perhaps most compelling as a clinical correlate that may be associated with semantic fluency because it would be consistent with abnormal facilitation, inhibition, or organization within the semantic network (Maher et al., 1983; Spitzer et al., 1993). Goldberg et al. (1998), for example, found disproportionate semantic fluency impairment in a subset of schizophrenia patients with moderate/severe thought disorder. Elvevåg et al. (2001) reported that covarying IQ reduced schizophrenia-control differences in phonemic much more than in semantic fluency; their findings would suggest that general intellectual impairment accounts for a fair amount of phonemic, but not semantic, fluency deficits in schizophrenia.

It is of further interest whether the pattern of verbal fluency deficits is diagnostically specific to schizophrenia as opposed to being a manifestation of major psychiatric ill-

ness or psychosis in general. Feinstein et al. (1998) suggested specificity of disproportionate fluency impairment relative to affective (primarily unipolar) disorder patients. Bipolar disorder provides a more conservative comparison in that it can be more similar to schizophrenia, as evidenced by the sometimes difficult differential diagnosis between the two. In addition, state-dependent factors such as symptom exacerbations or medication changes may affect cognitive function. Similar correlations in patients and controls over time would suggest that fluency measures are relatively trait-like, whereas lower correlations in patients would be consistent with a greater influence of state-dependent factors.

Having included both phonemic and semantic fluency as part of a larger neuropsychological battery in previous work, we examined these issues in a sample that was considerably larger than most previous studies. We sought to determine whether schizophrenia patients displayed disproportionate impairment in either semantic or phonemic fluency, and whether their semantic fluency deficits were associated with thought disorder or other clinical correlates. Having tested a small group of bipolar disorder patients with psychotic features, we wished to further examine the question of diagnostic specificity. In addition, we assessed verbal fluency in a subset of schizophrenia patients and controls in a 4-year follow-up study, thus enabling us to measure how stable performance was in patients relative to controls.

METHOD

Research Participants

Participants gave informed consent and were paid to participate. Details of the inclusion/exclusion criteria have been presented elsewhere (Faraone et al., 1995; Kremen et al., 1995). All patients had diagnoses of DSM-III-R (American Psychiatric Association, 1987) schizophrenia or bipolar disorder based on the Schedule for Affective Disorders and Schizophrenia (Endicott & Spitzer, 1978), medical record reviews, and consultation with clinicians. They had English as their primary language, and at least eight years of formal education. They were excluded if they had neurologic disease or damage; current substance abuse (within the past 6 months); history of head injury with loss of consciousness greater than five minutes; mental retardation; or medical illnesses associated with neurocognitive impairment.

Controls were recruited from nonprofessional hospital staff and advertisements in the community. Except for psychopathology or family history of psychosis, selection criteria were the same as for patients. Controls were screened for current psychopathology with a short form of the Minnesota Multiphasic Personality Inventory (Vincent et al., 1984), and excluded if any clinical or validity scale, except Masculinity-Femininity, was above 70.

The present analyses include 83 schizophrenia patients (24 paranoid, 59 nonparanoid), 15 patients with bipolar disorder with psychotic features (14 manic, 1 mixed type), and 83 controls with data on both fluency measures. (See Table 1 for demographics.) Comparisons among the bipolar disorder patients, controls, and these schizophrenia patients on a large number of neuropsychological variables appear elsewhere (Seidman et al., 2002), but data on these verbal fluency measures have not been published previously.

Procedures and Instruments

To minimize state-dependent effects, patients were tested when they were judged to be relatively stable clinically

Table 1. Characteristics of schizophrenia (SZ), bipolar disorder (BP), and normal control (NC) groups

	Schizophrenia (n = 83)		Bipolar (n = 15)		Control (n = 83)			
Variable	M	(SD)	M	(SD)	M	(SD)	Test	p
Age (years)	43.6	(11.9)	40.7	(13.1)	41.1	(15.4)	F	.48
Education (years)	12.0	(2.3)	13.9	(2.7)	13.69	(2.5)	F	.0001[a]
WRAT–R Reading	99.7	(16.9)	101.2	(13.3)	100.9	(13.3)	F	.87
WAIS–R IQ[b]	90.68	(10.64)	—		104.59	(12.55)	t	.0001
WAIS–R Vocabulary	10.0	(3.3)	11.7	(3.2)	11.4	(3.3)	F	.02
Age at 1st Hospitalization[c]	24.3	(6.4)	28.1	(10.3)	—		t	.26
Length of Illness (years)[c]	19.9	(11.1)	12.6	(7.1)	—		t	.04
Antipsychotic Medications (mg)[d]	644.4	(374.7)	337.3	(576.5)	—		K-W χ^2	.03
	%		%		%			
Sex (% female)	22.9		53.3		59.2		χ^2	.0001[e]
Ethnicity (% Caucasian)[f]	83.1		71.4		89.3		χ^2	.19

Note: WRAT–R = Wide Range Achievement Test–Revised (standard score); WAIS–R = Wechsler Adult Intelligence Scale–Revised (age-scaled score); K-W = Kruskal-Wallis.
[a]SZ < BP = N based on Newman-Keuls test. [b]Based on four WAIS–R subtests; see Kremen et al. (2001) for details. This IQ estimate was not available for bipolar disorder participants. [c]n = 82 for SZ; n = 11 for BP. [d]In chlorpromazine equivalents; n = 81 for SZ; n = 11 for BP. [e]SZ < BP = NC. [f]n = 80 for SZ; n = 10 for BP.

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(i.e., at their "baseline") by clinical staff who were familiar with them.

Test measures

Relevant portions of the test battery were as follows: 1) current IQ was based on four Wechsler Adult Intelligence Scale–Revised (WAIS–R; Wechsler, 1981) age-scaled subtest scores–Vocabulary, Digit Span, Block Design, Digit Symbol (For details see Kremen et al., 2001); 2) The Wide Range Achievement Test–Revised (WRAT–R; Jastak & Wilkinson, 1984) Reading subscale served as an index of expected/premorbid intellectual ability (cf. Dalby & Williams, 1986; Kremen et al., 1996); 3) The FAS test (Benton, 1967, 1968) was used to measure verbal fluency. First, phonemic fluency was assessed by asking participants to generate as many words as possible beginning with the letters F, A, and S for a period of 1 minute each. The score used was the average for the three letters. Next, semantic fluency was assessed by asking participants to generate as many words as possible belonging to the category "animals" for a period of 1 minute.

Symptom ratings

Symptoms were rated according to the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1983) and the Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984). Analyses for this study were based on the reality distortion (delusions, hallucinations), poverty (negative symptoms), and disorganization (bizarre behavior, positive formal thought disorder) dimensions as well as the global thought disorder rating alone (cf. Toomey et al., 1997).

Data Analysis

First, we used a 3 (Diagnosis: schizophrenia, bipolar, control) × 2 (Fluency Type: phonemic, semantic) repeated measures multivariate analysis of variance (MANOVA) in order to test for group differences and a Diagnosis × Fluency Type interaction. A significant interaction would be consistent with disproportionate impairment in either phonemic or semantic fluency in at least one of the groups.[1] Pairwise comparisons for each fluency type were tested with Student Newman-Keuls tests. We also report effect sizes on the basis of Cohen's (1988) *d* to make it easier to directly compare between-group differences where sample sizes vary. Relationships between fluency measures and clinical/demographic variables were examined by means of correlational (including point-biserial) and χ^2 analyses, analysis of covariance, and MANOVA. Correlation and multiple regression were used to measure stability of fluency performance over time. All tests were two-tailed.

[1]Because the bipolar disorder group was substantially different in size from the other two groups, it is important to note that MANOVAs/ANOVAs were performed by means of general linear models for unbalanced designs in which adjusted (least squares) means are tested so as to account for the artifactual effect that cell size differences may have on group means (Freund et al., 1986).

RESULTS

Initial Assessment

Group differences

Fluency scores are shown in Table 2. The MANOVA comparing all three groups revealed significant main effects for diagnostic group [$F(4,354) = 12.44$, $p < .0001$] and fluency type [$F(1,178) = 139.63$, $p < .0001$]. Newman-Keuls tests showed that the schizophrenia group performed significantly worse than either controls or bipolar disorder patients. Controls and bipolar disorder patients were not significantly different from one another. All groups produced more words during semantic than phonemic fluency.

There was also a significant Diagnosis × Fluency Type interaction [$F(2,178) = 3.53$, $p < .04$]. To elucidate the interaction effect, we performed MANOVAs between pairs of groups. There was a nearly significant interaction in the schizophrenia-control comparison [$F(1,164) = 3.85$, $p < .052$], suggesting a larger difference in semantic than in phonemic fluency. However, it seems unlikely that this interaction reflects clinically meaningful differences for the two types of fluency tasks in that there were quite similar effect sizes for each (*d*s = 1.02 and .91). The interaction was not significant in the bipolar-control comparison [$F(1,96) = 1.30$, $p = .26$], but it was significant in the schizophrenia-bipolar comparison [$F(1,96) = 5.35$, $p < .03$]. In contrast to the schizophrenia-control comparison, the effect size for the semantic fluency difference in the schizophrenia-bipolar comparison was meaningfully larger than it was for the phonemic fluency difference (*d*s = 1.00 and .54).

Demographic/clinical factors

SANS and SAPS data were available for 64 schizophrenia patients; 20 were in the follow-up and 44 were not. Scores at time 1 were as follows: formal thought disorder [$M = 2.09$, $SD = 1.58$]; poverty [$M = 1.87$, $SD = 1.16$]; reality distortion [$M = 2.17$, $SD = 1.48$]; disorganization [$M = 1.31$, $SD = 1.04$]. Correlations with global formal thought disorder were −.09 and −.13 for semantic and phonemic fluency, respectively [*df*s = 62, *p*s > .30]. Correlations with the three symptom dimensions were also nonsignificant [$-.19 \leq r\text{s} \leq -.07$, *df*s = 62, *p*s > .13].

As seen in Table 1, the schizophrenia group had a lower proportion of women than the bipolar or control groups. However, there were no significant sex differences or interactions with sex. Correlations in schizophrenia patients were nonsignificant for age, age of first psychiatric hospitalization, length of illness, sex, and ethnicity, but were significant for education, WRAT–R Reading, and current IQ. The correlations with phonemic and semantic fluency scores

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Table 2. Phonemic and semantic fluency scores in schizophrenia (SZ), bipolar disorder (BP), and normal control (NC) groups

Time 1 assessment for entire sample									
	Schizophrenia (n = 83)		Bipolar (n = 15)		Control (n = 83)				
Variable	M	(SD)	M	(SD)	M	(SD)	$F(2,178)$	p	*SNK*
Phonemic fluency (average of F, A, S)	10.1	(4.2)	12.3	(4.6)	13.5	(3.5)	16.54	.0001	SZ < BP = NC
F	10.1	(4.9)	12.9	(4.6)	13.9	(4.1)	15.45	.0001	SZ < BP = NC
A	9.0	(4.2)	10.7	(4.2)	11.6	(3.9)	8.55	.0003	SZ = BP < NC
S	11.0	(4.7)	13.3	(5.7)	15.0	(4.4)	15.54	.0001	SZ < BP = NC
Semantic fluency (animals)	14.0	(4.8)	19.2	(7.1)	18.9	(4.8)	21.84	.0001	SZ < NC = BP
Time 1 assessment for those who participated in follow-up[a]									
	Schizophrenia (n = 28)				Control (n = 45)				
Variable	M	(SD)	—		M	(SD)	$F(1,71)$	p	—
Phonemic fluency (average of F, A, S)	10.5	(4.4)	—		13.5	(3.5)	10.54	.002	—
Semantic fluency (animals)	13.2	(4.4)	—		19.3	(5.0)	27.82	.0001	—
Time 2 assessment for those who participated in follow-up[a]									
Phonemic fluency (average of F, A, S)	10.6	(4.6)	—		14.3	(3.5)	14.98	.0002	—
Semantic fluency (animals)	13.4	(5.8)	—		19.8	(4.9)	27.78	.0001	—

Note: ANOVA = Analysis of Variance; SNK = Student Newman-Keuls test.
[a]There was no follow-up of bipolar disorder patients.

were extremely similar for these measures, suggesting that there was no differential relationship to either fluency type.

Given the study of Elvevåg et al. (2001) in which covarying IQ was thought to have a greater effect on schizophrenia-control differences in phonemic than in semantic fluency plus the fact that schizophrenia patients in the present study had lower IQs than controls, we also performed the MANOVA for schizophrenia patients and controls while controlling for IQ. After covarying for IQ, p-values for phonemic and semantic fluency were .051 and .0021, respectively; the Diagnosis × Fluency Type interaction went from $p < .052$ to $p = .13$.[2] Although covarying IQ did reduce significance, we do not think it had a substantially greater impact on phonemic fluency. The F-value after controlling for IQ was somewhat lower for phonemic than for semantic fluency (3.88 vs. 9.77), but it was similarly lower before controlling for IQ (33.95 vs. 43.30). Covarying each of the four WAIS–R subtests separately, we found that the effect of covarying IQ was almost entirely accounted for by Digit Symbol. Moreover, when we examined correlations between individual WAIS–R subtests and each fluency type in schizophrenia, Digit Symbol showed the largest discrepancy [$r(79) = .41$, $p < .0002$ with semantic fluency; $r(79) = .27$, $p < .02$].

[2]These analyses included 81 schizophrenia patients because two patients did not have scores on all of the four WAIS-R subtests used to generate IQs.

We also looked at paranoid and nonparanoid schizophrenia. Interactions for nonparanoids *versus* either controls or paranoids were nonsignificant, but there was a nearly significant Diagnosis × Fluency Type interaction in the comparison of controls and paranoid subtype patients [$F(1,105) = 3.90$, $p < .051$]. In this case, effect sizes were .71 and .39 for semantic and phonemic fluency, respectively. As would be expected, paranoid patients had more education [$M = 13.25$, $SD = 2.07$ *vs.* $M = 11.49$, $SD = 2.14$; $t(81) = 3.42$, $p < .001$], and higher WRAT–R Reading [$M = 107.75$, $SD = 13.82$ *vs.* $M = 96.37$, $SD = 17.08$; $t(79) = 2.89$, $p < .005$] and IQ [$M = 97.76$, $SD = 10.05$ *vs.* $M = 87.69$, $SD = 9.46$; $t(79) = 4.29$, $p < .0001$] than nonparanoid patients, but they did not differ on other demographic/clinical variables.

Comparison of Initial and Follow-Up Assessments (See Table 3)

Stability over time

Forty-five controls and 28 schizophrenia patients completed the verbal fluency tasks at an average 4-year follow-up. Correlations between scores at time 1 and time 2 showed moderate stability that was similar in both groups: phonemic fluency ($r(43) = .67$, $p < .0001$ for controls, and $r(26) = .79$, $p < .0001$ for patients); semantic fluency ($r(43) = .53$, $p < .0002$ for controls, and $r(26) = .48$, $p < .009$ for pa-

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Table 3. Characteristics of schizophrenia (SZ) and normal control (NC) groups who participated in follow-up study

	Schizophrenia (n = 28)		Control (n = 45)			
Variable	M	(SD)	M	(SD)	Test	p
Age (years)	39.9	(10.3)	38.1	(12.4)	t	.52
Education (years)	11.6	(1.9)	14.4	(2.3)	t	.0001
WRAT–R Reading	99.8	(16.8)	100.9	(13.6)	t	.75
IQ[a]	91.3	(12.0)	105.7	(12.4)	t	.0001
WAIS–R Vocabulary	10.0	(4.1)	11.5	(3.1)	t	.15
Age at 1st Hospitalization	22.4	(6.3)	—			
Length of Illness (years)	18.8	(11.6)	—			
Antipsychotic Medications (mg)[b]	683.1	(504.6)	—			
	%		%			
Sex (% female)	17.9		60.0		χ^2	.0004
Ethnicity (% Caucasian)[c]	95.4		78.6		χ^2	.03

Note: WRAT–R = Wide Range Achievement Test–Revised (standard score); WAIS–R = Wechsler Adult Intelligence Scale–Revised (age-scaled score); K-W = Kruskal-Wallis.
[a]Based on four WAIS–R subtests; see Kremen et al. (2001) for details. [b]n = 26. [c]In chlorpromazine equivalents; n = 26.

tients). To test for the possibility that the ability to predict time 2 scores from time 1 scores might be accounted for by differences in time to follow-up, we performed multiple regression analyses with time 2 score as the dependent variable and time 1 score, time to follow-up, and the time 1 score × time to follow-up interaction as the independent variables. A significant interaction would show that the ability of time 1 scores to predict time 2 scores varies with time to follow-up. None of the interaction terms was significant whether looking at patients and controls combined or separately (ps > .31).

Group differences

At time 2, there was a significant Diagnosis × Fluency Type interaction [$F(1,71) = 5.39$, $p < .03$] such that the patients demonstrated disproportionate impairment in semantic fluency. Effect sizes for semantic and phonemic fluency differences were 1.22 and .93, respectively. We re-examined the time 1 scores of the 45 controls and 28 schizophrenia patients who also had time 2 scores. This analysis resulted in a highly significant Diagnosis × Fluency Type interaction for these participants at time 1 [$F(1,71) = 7.21$, $p < .009$]. Effect sizes for semantic and phonemic fluency differences were now 1.27 and .78, respectively. Group mean scores for each test were very similar at time 1 and time 2. Thus, the disproportionate impairment of this subgroup at time 2 does not seem to be accounted for by change in scores over time.

Demographic/clinical factors

Tables 1 and 3 show that those who participated in the follow-up tended to be younger than their counterparts who did not [Controls $M = 44.71$, $SD = 17.71$ *vs.* $M = 38.11$, $SD = 12.44$); $t(64.8) = 1.93$, $p < .058$; Patients $M = 45.40$, $SD = 12.33$ *vs.* $M = 39.93$, $SD = 10.29$; $t(81) = 2.02$, $p < .05$]; however, there were no age differences for patients *versus* controls. Controls who participated in the follow-up were significantly more educated than controls who did not [$M = 12.63$, $SD = 2.42$ *vs.* $M = 14.40$, $SD = 2.33$; $t(81) = -3.38$, $p < .002$], but patients did not differ in education. Despite the education difference, fluency performances were quite similar for controls regardless of participation in the follow-up. There was a trend for patients who were in the follow-up to have earlier age at first hospitalization than those who were not [$M = 22.43$, $SD = 6.26$ *vs.* $M = 25.24$, $SD = 6.29$; $t(80) = 1.92$, $p < .059$]. Unlike the entire sample, there was a significantly greater proportion of ethnic minorities in schizophrenia patients compared with controls who participated in the follow-up. However, the Diagnosis × Fluency Type interactions remained significant even after all minority participants were removed from the analysis.

DISCUSSION

Heterogeneity of Verbal Fluency Differences

Consistent with previous studies, schizophrenia patients in this study were significantly impaired in both phonemic and semantic fluency, and both patients and controls generated more words for semantic than for phonemic cues. Evidence in support of disproportionate impairment in semantic fluency in schizophrenia patients relative to controls was mixed. A look at our study plus several others that have examined both fluency types in schizophrenia patients

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and controls (Arango et al., 1999; Beatty et al., 1993; Feinstein et al., 1998; Gourovitch et al., 1996; Gruzelier et al., 1988; Joyce et al., 1996; Laurent et al., 2000; Roxborough et al., 1993) indicates that the average effect sizes, weighted by number of participants, were 1.24 and .92 for semantic and phonemic fluency, respectively. These numbers suggest modestly disproportionate semantic fluency impairment in schizophrenia. They provide only a rough estimate, however, because stimulus cues differed across studies. The studies also demonstrate heterogeneity in that only about half suggest any disproportionate impairment.

Interestingly, although our initial study did not suggest disproportionate impairment, follow-up results revealed disproportionate semantic fluency impairment in a subset of schizophrenia patients at both time 1 and time 2. Schizophrenia patients who did not participate in our follow-up still had slightly, although not significantly, more impaired phonemic than semantic fluency. The means for either fluency type were not significantly different between schizophrenia patients who did or did not participate in the follow-up. Thus, although the interaction was significant for those who participated in the follow-up, differences between them and schizophrenia patients who did not participate in the follow-up were apparently fairly subtle.

Comparison of paranoid patients *versus* controls suggested disproportionate semantic fluency impairment in this schizophrenia subtype. Although the absolute effect sizes were smaller for paranoid patient-control comparisons, the difference in effect sizes for semantic and phonemic fluency was about the same as the weighted average of the different studies noted. Absolute level of performance was significantly better in paranoid than in nonparanoid subtype patients for phonemic fluency [$p < .003$], and was better at a trend level for semantic fluency [$p < .08$], but there was no Diagnosis $\times$ Fluency Type interaction for comparisons of paranoid and nonparanoid patients. Thus, paranoid patients in our sample displayed better overall verbal fluency than nonparanoid patients but appeared to have a deficit in semantic fluency relative to their own phonemic fluency performance. In the study of Paulsen et al. (1996), nonparanoid patients had more semantic network disorganization than paranoid patients, but they did not differ in quantity of output (paranoid patients averaged about one word less). Paulsen et al. did not assess phonemic fluency, so it is difficult to fully compare results.

Demographic/Clinical Factors

Overall, few characteristics distinguished schizophrenia subgroups who did or did not participate in our follow-up study, and those that did appear unlikely to explain the verbal fluency patterns. There was a trend toward younger age at first hospitalization in the subset with disproportionate semantic fluency impairment. Given that early onset has been associated with delayed language development in schizophrenia (DeLisi et al., 1991), one possibility is that earlier onset of schizophrenia tends to be associated with greater abnormalities of the semantic store. Paulsen et al. (1996) did not find differences in word output, but earlier onset patients in their study did have had more disorganized semantic networks than later onset patients. It should be noted, however, that all patients in the present study would be in their early onset group (age of onset ≤ 45). On the other hand, paranoid patients in our study appeared to have greater relative semantic fluency impairment, but had nonsignificantly later onset than nonparanoid patients.

Given the interaction for paranoid patients and controls, it could be that the disproportionate semantic fluency in schizophrenia patients who participated in the follow-up was accounted for by more paranoid subtypes in that subgroup. However, the proportion of paranoid subtypes did not differ for patients who did [36%] or did not [25%] participate in the follow-up [$\chi^2(1) = .95$, $p = .33$]. Paranoid patients had higher general intellectual ability than nonparanoid patients, but this seems unlikely to explain the results because controlling for IQ had virtually no effect on analyses comparing paranoid or nonparanoid patients to controls.

For the entire schizophrenia sample, covarying IQ reduced schizophrenia-control differences, but it did not affect phonemic more than semantic fluency. Elvevåg et al. (2001) concluded that there was a differential impact, but the pattern of results in their study was actually similar to that of the present study. Thus, we conclude that covarying general intellectual ability does not appear to have preferential impact on either fluency type. Although we expected the effect of covarying IQ to be primarily a function of verbal ability, we found that its effect was almost entirely accounted for by Digit Symbol. Rather than suggesting the influence of general intellectual function, our results point to perceptual-motor, or processing speed as an important factor underlying verbal fluency in schizophrenia. Previous work suggests that processing speed partially accounts for episodic memory deficits in encoding, recall, and recognition in schizophrenia (Brébion et al., 1998). The present study suggests that processing speed may also be important in semantic memory in schizophrenia, although this conclusion must be considered tentative given the *post hoc* nature of this analysis.

In contrast to previous work by Goldberg et al. (1998), disproportionate semantic fluency was not associated with thought disorder in the present study. We analyzed thought disorder as a continuous variable, but the results did not change when we dichotomized it as in the Goldberg et al. study. On the other hand, Goldberg et al. (1998) used a more comprehensive measure of thought disorder than we had in the present study, a factor that could account for the different relationships observed.

It seems unlikely that antipsychotic medication effects accounted for the schizophrenia patient deficits. It is problematic to equate groups for medication because of potential confounds with severity and type of illness. However, bipolar disorder patients were receiving antipsychotic medications and they had slightly better semantic fluency performance than did controls. Anticholinergic medication may

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impair episodic memory, but its impact on semantic memory is less clear. Interestingly, schizophrenia patients who were receiving anticholinergics ($n = 48$) had better phonemic fluency performance than those who were not [$n = 32$; $t(78) = -2.27$, $p < .03$]. Paulsen et al. (1996) did not find quantitative fluency differences in schizophrenia subgroups, but subgroups with greater semantic network disorganization did have a significantly lower proportion of patients who were receiving anticholinergics. Potential effects of anticholinergic medication on verbal fluency may thus warrant further investigation.

Specificity

Our results do suggest some diagnostic specificity of verbal fluency deficits in that patients with psychotic bipolar disorder were unimpaired. Indeed, these chronic bipolar disorder patients had nonsignificantly better semantic fluency than did controls. Lack of a significant phonemic fluency difference was not due to lack of power with the small bipolar sample ($d = .33$); we would have needed 100 bipolar disorder patients for this difference to have been significant. These results extend those of Feinstein et al. (1998), who found no deficits in a group of mostly unipolar depressed patients. Nevertheless, confidence in the bipolar patient results is somewhat reduced given the small sample size.

Stability

The follow-up assessment showed moderate stability in verbal fluency performance over a 4-year period ($.48 < rs < .79$). Correlations for phonemic and semantic fluency were similar in controls and schizophrenia patients. Even with a much longer time interval, our data indicate similar stability to that of other samples. Phonemic fluency correlations were .71 in an elderly sample after one year, and .88 in an adult sample after 19–42 days (Lezak, 1995); we are not aware of stability coefficients for semantic (animal) fluency. These results support the notion that verbal fluency in schizophrenia is a reasonably trait-like cognitive measure.

Limitations

A conclusion of mildly disproportionate semantic fluency impairment in schizophrenia may be subject to misinterpretation if measures do not have equivalent psychometric discriminating power (Chapman & Chapman, 1978). Normal control data across studies indicate that with the cues used, phonemic fluency is usually more difficult than semantic fluency. As such, we cannot definitively rule out the pattern of results being due to generalized deficit, but this possibility seems unlikely for three reasons. First, the average tendency across studies was in the direction of slightly greater relative impairment in patients on the easier task. Second, patient-control differences were larger for semantic fluency in the study of Roxborough et al. (1993), even though phonemic and semantic fluency were of equal difficulty in controls. Third, Gourovitch et al. (1996) found a double dissociation in phonemic and semantic fluency performance in schizophrenia—a result that cannot be explained by a generalized deficit.

We measured only quantitative verbal fluency output. As shown by Paulsen et al. (1996), for example, abnormalities in the organization of the semantic network in some schizophrenia patients may still be present even when patient subgroups do not differ in productivity.

Summary

Verbal fluency measures were moderately stable in schizophrenia patients and controls over a 4-year period. In the present study, both patient groups and controls generated more words during semantic than phonemic fluency. Although not significant in the schizophrenia group as a whole, there was evidence of disproportionate semantic fluency impairment in two partially overlapping subsets of schizophrenia patients: patients who participated in the follow-up study and paranoid subtype patients. We were unable to identify clear distinguishing characteristics of the former subgroup or reasons why the latter subgroup would manifest this pattern.

Combining the results of different studies suggests small disproportionate semantic fluency impairment in schizophrenia. Our original expectation that schizophrenia patients would display disproportionate phonemic fluency impairment was not supported. Taken together, these results might be viewed as supporting the notion that an additional breakdown of semantic knowledge or semantic information processing is responsible for semantic fluency deficits in some patients with schizophrenia. However, the lack of any relationship between fluency and thought disorder in the present study, and the fact that paranoid subtype patients tend to have milder thought disorder than other subtypes may weaken such a conclusion.

Evidence for heterogeneity in fluency performance (cf. Goldberg et al., 1998; Paulsen et al., 1996) suggests that summary results may mask underlying heterogeneity within studies. Our sample size was larger than most previous studies, a factor that is likely to have increased our ability to detect heterogeneity.

The present study also supports the specificity of verbal fluency deficits to schizophrenia *versus* bipolar disorder, extending previous results with primarily unipolar depressed patients (Feinstein et al., 1998). Interestingly, whereas the present study indicated disproportionate semantic fluency impairment in only a subset of schizophrenia patients relative to controls, it did so for the entire schizophrenia group relative to bipolar disorder patients.

Some neuroimaging studies of verbal fluency have suggested abnormal frontal-temporal connectivity (Friston et al., 1996; Frith et al., 1995) or abnormal connectivity within frontal regions in schizophrenia (Spence et al., 2000). Neuroimaging of schizophrenia subgroups that do or do not man-

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ifest disproportionate semantic fluency impairment could shed new light on the neural substrates of these different patterns. Limitations of neuroimaging paradigms often necessitate experimental control of the pace of word generation; however, the present results suggest that it may be important to examine neural correlates of processing speed in relation to verbal fluency.

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