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Frequency of normative word associations in the speech of individuals at familial high-risk for schizophrenia

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Abstract

The intrusion of associations into speech in schizophrenia disrupts coherence and comprehensibility, a feature of formal thought disorder referred to as loosened associations. We have previously proposed that loosened associations may result from hyperactivity in semantic association networks, leading to an increased frequency of associated words appearing in speech. Using Computed Associations in Sequential Text (CAST) software to quantify the frequency of such associations in speech, we have reported more frequent normative associations in language samples from patients with schizophrenia and in individuals with schizotypal characteristics. The present study further examined this deviance in schizophrenia by studying normative associations in those who share genes with an individual with schizophrenia, (i.e. first-degree relatives of probands with schizophrenia; HR) but who do not have an illness. Familial high-risk participants (n = 22), and controls (n = 24) provided verbal responses to cards from the Thematic Apperception Test. CAST analysis revealed that HR used more associated words in their speech compared to controls. Furthermore, the frequency of normative word associations was positively correlated with dimensional and total scores of schizotypy derived from ratings of the Structured Interview for Schizotypy, which confirms past research showing a relationship between schizotypy and hyperassociations. Our results suggest that language disturbances in schizophrenia likely arise from an underlying psychopathological mechanism, hyperactivity of semantic associations.

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Conflict of Interest

We have no conflicts of interest to declare.

Contributors

Dr. Manschreck and A. Merrill oversaw and completed the processing of the language samples and statistical analysis, and wrote the first draft of the manuscript. Dr. Chun consulted on statistics and reviewed the manuscript. Dr. DeLisi and G. Jabbar recruited participants, completed participant interviews, and organized the transcription of the speech samples. Dr. DeLisi was responsible for the overall grant of which this study was a part and Dr. Manschreck was responsible for this sub-study. All authors contributed to and have approved the final manuscript.

Keywords

schizophrenia; familial high-risk; language; normative word associations; schizotypy; formal thought disorder

1. Introduction

Many individuals with schizophrenia exhibit disturbances in language and thought. For example, the intrusion of associated thoughts into speech in schizophrenia can alter coherence and comprehensibility, a feature of formal thought disorder traditionally referred to as loosened associations (Bleuler, 1911/1950). A theory of language disturbances in schizophrenia (Maher, 1972; 1983; 2003) proposes that loosened associations are the result of hyperactivity in associational networks. In organized speech, planning for an utterance activates related words in an associational network, but most of these associations are subsequently inhibited if they are not part of the intended communication. However, in deviant speech, due to heightened activation or diminished inhibition processes, activated associations are more likely to intrude into speech, resulting in a high rate of related words. To the listener, these associations may not be noticeable. As the relationship between the associated words is easily understood and it is merely the high frequency of the associated words that is distinctive, we refer to each of these pairs as a “normative word association.”

To explore hyperactivity of normative word associations using a laboratory based quantitative measure, Maher and Manschreck developed specialized software, Computed Associations in Sequential Text (CAST) (Maher et al., 2005). The CAST is a computerized method to count the number of normative word associations in a speech sample. The CAST draws from a dictionary that contains index words (primarily high frequency words in the English language), and words commonly associated to them. For example, for the index word *dog*, the normative associations are *cat*, *bark*, *animal* and *puppy*. Using this dictionary as a reference, the CAST is used to compare the rates of normative word associations between different samples of speech.

In the first study using the CAST, Maher et al. (2005) analyzed speech samples from patients with schizophrenia (without formal thought disorder) and healthy controls. As predicted, the speech from individuals with schizophrenia contained a higher frequency of normative word associations. Additionally, this study found that associations were related to strategic semantic priming processes. These results fit with Maher’s theory of hyperactivity of associated word networks and demonstrated the utility of the CAST as a technique to study associational networks and language.

However, this study could not distinguish between deviances that represent a core feature of schizophrenia and those that are illness-related features. One approach to disentangle such findings is to study individuals who have schizotypy traits, but not a clinical diagnosis of schizophrenia. These individuals show some features similar to schizophrenia and there is a high conversion rate of schizotypy to schizophrenia. Thus in a second CAST study, the same research group found that individuals who scored high on measures of schizotypy used an increased number of normative word associations in speech compared to controls (Lenzenweger et al., 2007).

Another approach to distinguish underlying mechanisms of schizophrenia from illness-related features is to study healthy individuals who have a relative with schizophrenia and are still within the age of risk for its development (i.e. thus at familial high-risk). For example, research has shown that healthy high-risk individuals perform worse than controls

socially (Glatt et al., 2006), neuropsychologically (Seidman et al., 2006), and in other aspects of functioning (Asarnow, 1988). These studies concluded that deficits shared by individuals with schizophrenia and their relatives may be related to a genetic liability for the illness.

First-degree relatives of schizophrenia probands also show deviances in both thought and language. Relatives show evidence of thought disorder on the Thought Disorder Index, scoring intermediate between controls and patients with schizophrenia (Hain et al., 1995). The speech of relatives of patients with schizophrenia may contain vague references, missing information references, ambiguous word meanings, and structural unclarity (Docherty et al., 1999; 2004). Research using Latent Semantic Analysis (Landauer et al., 1998), a computational modeling technique used to compare the semantic features of passages of text, has shown that features of communication can accurately distinguish between the speech of relatives, patients, and controls. However, another study examining the complexity of sentence structure in patients with schizophrenia, relatives, and controls found reduced complexity in patients, but not family members or controls (DeLisi, 2001).

Such research suggests the importance of studying language deviances in HR participants. Therefore, the primary goal of the current study was to extend work on normative word associations to HR. The familial high-risk approach provides us with (a) the ability to further examine the genetic vulnerability to schizophrenia and work towards developing biomarkers for the illness, and (b) a powerful foundation for understanding the nature of hyperactivity of association networks as a source of language deviance. Our primary hypothesis was that HR would show hyperassociations similar to that previously seen in individuals with schizophrenia and those with schizotypal features. Specifically, HR would have a greater number of normative word associations in a speech sample compared to controls as measured by the CAST.

The secondary goal of the present study was to examine the relationship between schizotypy traits and hyperassociations in this sample. In previous research, Lenzenweger et al. (2007) assessed schizotypy with the Schizotypy Personality Questionnaire (SPQ; Raine, 1991) and found a positive relationship between positive and disorganized features of schizotypy and increased normative word associations. For the present study, our sample was collected as part of a larger study that included the Structured Interview for Schizotypy (SIS). Because the SPQ and SIS are organized into different dimensions, it is difficult to use the findings from Lenzenweger et al. to support specific hypotheses regarding schizotypy as measured by the SIS. However, schizotypy was included in the present study to expand on previous work and gather more information about the characteristics related to hyperassociations. Therefore, we examined the following exploratory hypotheses.

We hypothesized that there would be a positive correlation between both global schizotypy and increased frequency of word associations, as well as specific schizotypy traits and frequency of word associations. Although it is difficult to apply the labels of positive, negative, and disorganized symptoms to the SIS, we predicted that the traits of schizotypy that reflect positive or disorganized symptoms of schizophrenia (i.e. magical thinking) would be positively correlated with frequency of normative word associations.

2. Methods and Procedures

2.1 Participants

Twenty-two HR and 24 controls (CT) were recruited from an ongoing study on genetic risk in schizophrenia carried out in the Boston area and volunteered to provide speech samples for this additional investigation. The study was approved by the human studies committees

of all recruitment sites and all participants gave written informed consent. Eligibility was determined using the Diagnostic Interview for Genetic Studies (DIGS) (Nurnberger et al., 1994). All participants were between the ages of 18 and 34 and had no Axis I psychotic disorders. Inclusion criteria for HR required having a first-degree relative with schizophrenia and an additional relative with psychosis, while CT had no family history of psychosis. To determine HR status, a family pedigree was obtained for both family sides from a reliable family informant. All known family branches and generations were recorded and detailed symptoms of the affected individuals were obtained to verify diagnosis. When available, any relative with schizophrenia was contacted to directly confirm their diagnosis.

2.2 Measures

2.2.1 Diagnostic Interview for Genetic Studies (DIGS)—All participants completed the DIGS (Nurnberger et al., 1994), a structured diagnostic interview widely used in family studies. The DIGS includes the modified SIS (Kendler et al., 1989), which measures features of schizotypal personality disorder along 14 dimensions.

2.2.2 Speech samples—Participants were shown five cards from the Thematic Apperception Test (TAT) (Morgan & Murray, 1935) and asked to describe the picture on each card¹. The cards were numbered 2, 3, 4, 5, 7, and corresponded to Morgan and Murray's (1935) numbered cards as follows: 2 = 18GF, 3 = 13B, 4 = 12M, 5 = 13MF, 7 = 12BG (Bellak & Abrams, 1997). Each participant was encouraged to speak for five minutes. Their responses were recorded, transcribed, and checked for accuracy with the recorded sample. The speech samples were then cut into 100 word segments of speech, a strategy we have employed in previous research on quantitative aspects of speech and that is consistent with limitations of the CAST software (Maher et al., 2005; Lenzenweger et al., 2007). Before all samples were cut, the total number of words in each sample was compared to ensure that the lengths did not differ between the groups. All speech samples contained at least 100 words.

2.2.3 CAST analyses—The CAST detects and records the presence of normative word associations in a transcribed speech sample. The CAST looks up each individual word from the sample (the index word) in a database of normative associations. The software then scans the text within a set word scan length to determine if a word associated to the index word is present. If it is, the association is counted. The word scan length can be adjusted, so that the program counts associations that occur within a range of 5, 10, 15, 20, 50, or 100 words from the index word. For example, when the scan length is set to 20 words, the program records any associated words that appear in the text 20 words before and after the index word. The program then moves on to the next word in the text (which is now the index word) and checks the surrounding 20 words for associations to the new index word. This process repeats until each word in the sample has been scanned as an index word. The final result of this process is a list of word pairs (an index word and each of its associations) that each represent a normative association. These pairs are counted, providing a frequency count of normative associations at each scan length for each sample.

2.2.4 Dictionary of normative associations—The CAST uses a dictionary of approximately 5,000 (index) words and their normative associations. Ever since the late 19th century, investigators in psychopathology have been attracted to speech characteristics in

¹In previous studies we had elicited speech samples in response to a Brueghel painting. This painting was selected as stimulus because of its ability to generate relatively spontaneous speech samples without verbal encouragement or interference from study staff. In the present study we were unable to collect samples using that stimulus. As the increased frequency of associations reflects greater hyperactivity, a provocative or highly active stimulus may be required.

normal and ill individuals (Bleuler 1911/1950; Jung & Riklin, 1906/1981). This interest led to attempts to generate word association norms to examine associations in psychiatric patients (Kent & Rosanoff, 1910). The source of the current index words was a combination of norms previously collected in our laboratory and norms published by the University of South Florida (Nelson et al., 1998). These norms were generated through procedures in which participants read individual words and responded with the first word that came to mind. The most common responses were tabulated into a rank order list and the top five associations for each index word were included in our dictionary, provided that more than three percent of the participants had given this response. These cut-offs ensured that the dictionary contained only normative responses.

2.3 Statistical analysis

Analysis of variance (ANOVAs) was used to test the hypothesis that HR and CT would differ in frequency of normative associations. For SIS scores, a non-parametric Mann-Whitney U was used to examine group differences and a standard Pearson correlation was used to examine the relationship between SIS and CAST scores. All analyses were completed with SPSS 17.0 and significance was set at the .05 level.

3. Results

3.1 Demographics

HR and CT groups were well-matched on demographics. There was no significant difference between the groups on age ($F(1,44) = 1.54, p = .22$) and education ($F(1,44) = .00, p = .97$). Intelligence data from the Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler, 1999) was available for all but 8 participants (3 CT; 5 HR), and was consistent with the education level comparison ($F(1,36) = .18, p = .68$). There was also no significant difference between the two groups on gender ($X^2 = .55, p = .46$). These results are presented in Table 1.

3.2 CAST

For the overall length of the speech samples, there was no difference in the mean number of words produced between HR and CT ($p > .05$). For both groups, there was a large range of lengths produced, with most samples between 200 and 500 words. We hypothesized that HR would have more normative word associations in their speech samples than CT. For each TAT card, the groups were compared on the frequency of normative word associations in the samples at each of the word scan ranges (i.e. 5, 10, 15, 20, 50, and 100). For all word scan ranges examined with card 5 responses, the speech of HR contained a significantly greater number of normative associations than the speech of CT. These results are presented in Table 2. For the speech samples generated from cards 2, 3, 4, and 7, there was no significant difference between the groups in terms of word associations at any of the word scan ranges (all $p > .05$). The images in these cards were less stimulating and may not have elicited the effects of hyperassociation activated by the arousing nature of card 5.

3.3 CAST and SIS

The word association frequencies generated from card 5 were used to examine the relationship to SIS responses. To examine the relationship between schizotypy and frequency of normative associations, we tested for a correlation between SIS scores and the number of word associations generated in the speech of the two groups. For this analysis, we used the association frequencies generated at word scan length 20, as this length produced the most robust group effect. In the combined sample, a two-tailed Pearson correlation

revealed that there was a significant positive correlation between the number of word associations and the global scores of schizotypy ($r = .33, p < .05$).

As exploratory analyses, we examined possible correlations between the word association frequency from word scan length 20 and specific dimensions of the SIS. In addition to the correlation with global SIS, word association frequencies were positively correlated with the traits of anger, social anxiety, restricted emotions, and magical thinking. These results are presented in Table 3. It is important to note that these exploratory analyses were not significant when a Bonferroni correction was applied due to the large number of variables.

4. Discussion

Our results indicate that individuals at familial high-risk for schizophrenia have significantly more normative associations in their speech than controls. These findings extend previous research that demonstrated this deviance in patients with schizophrenia and individuals with psychometrically assessed schizotypy traits. This study suggests that language disturbances in schizophrenia may arise from an underlying genetically influenced psychopathological mechanism, which we have identified as hyperactivity of associations. The mechanism behind hyperassociations is still being elaborated empirically and at present the underlying substrate is not yet understood. However, physiological studies using functional magnetic resonance imaging and N400 event-related potentials indicate that language deficits, including hyperassociations, may stem from dysfunctional brain network over inferior and prefrontal cortices (Kuperberg et al., 2007).

More generally, this study adds to a growing literature demonstrating deficits in HR in the absence of clinical symptoms. In HR, is the hyperactivity of associational networks related to the genetic predisposition to schizophrenia or is it possibly a precursor to the illness? Follow-up studies with high-risk individuals to determine who will develop the illness of schizophrenia would address this question. From our research, it seems likely that word associations provide clues to heightened vulnerability to schizophrenia. The hope is that measures such as this can be used to improve strategies for identifying the early stages of schizophrenia in young people.

The frequency of normative word associations was associated with global schizotypy and a number of schizotypy traits. Although these analyses were exploratory, these findings do confirm that some traits of schizotypy may be related to increased frequency of word associations. This study yielded some surprising results as restricted emotion, typically regarded as a negative symptom, was positively correlated with heightened frequency of associations. Also, magical thinking was associated with frequency of associations, a finding that confirms past research in which we (Lenzenweger et al., 2007) also found a correlation between word associations and magical thinking in a psychometrically defined schizotypal sample. These findings, along with the HR evidence, demonstrate that hyperassociations appear in the absence of clinical illness and may be most likely to occur in individuals with certain traits of schizotypy (or schizophrenia), with magical thinking as an example. We feel these findings are important to consider as we seek to determine what characteristics related to schizophrenia play a role in increased word associations and build a larger, more detailed, picture of the nature of hyperassociations.

These results provide further support for the CAST as an objective, quantitative measure of speech deviance when speech may or may not appear to be normal. One area to continue exploring with the CAST is the most appropriate word scan range to include in analyses. Similar to the original study with the CAST, this study used scan lengths ranging from 5 to 100 words and group differences were evident at all levels. However, from a theoretical

standpoint, an intrusion closely following an index word compared to one appearing nearly 100 words later may reflect different priming mechanisms. Past research has explored automatic versus strategic processing in semantic priming, and there is evidence that hyperassociations are more related to strategic processing, which implies a larger time span between the activation of a word and its intrusion into speech (Maher et al., 2005).

There are certain limitations to report. The sample was modest in size and should be increased in future investigations. Interestingly, the participants had an above average IQ, a reflection perhaps of the high frequency of college students among the participants. Furthermore, while significant group differences were found in the speech samples generated by card 5, there were no group differences with the other TAT cards. At this time we can only speculate why this card produced associational differences between the groups, but one factor may be the emotionally arousing nature of card 5, which is frequently viewed as disturbing or highly emotional. It is possible that HR react differently to this arousal, and this may contribute to a difference in the occurrence of associations in their speech. Interestingly, our earlier use of the Brueghel painting as stimulus for speech samples was predicated on multiple features of activity and interaction depicted in that work (Maher et al., 2005). As we continue to refine our methods, we should investigate the differences in stimuli used to provoke speech, and the emotional or cognitive reactions they elicit.

Nevertheless, the consistency of our findings with previous CAST research (Maher et al., 2005; Lenzenweger et al., 2007) suggests the value of the CAST and the prospect that increased frequencies of normative associations in speech may represent a biomarker for schizophrenia. For the latter possibility, longitudinal outcome studies are required to determine if this trait predicts the development of psychopathology.

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Table 1

Demographics

	HR	CT
Males	6	9
Females	16	15
Mean age (SD; range)	25.3 (3.2; 19–32)	24.2 (3.0; 18–32)
Years of education (SD; range)	15.5 (2.5; 9–22)	15.5 (1.6; 12–18)
WASI IQ (SD; range)	117.5 (12.1; 94–132)	115.5 (16.3; 77–141)

Table 2

CAST generated association counts in HR and CT speech samples

Word Scan Range	HR (SD)	CT (SD)	<i>F</i> (1,44)	<i>p</i>
Five	9.32 (3.15)	7.50 (3.12)	3.88	.055
Ten	17.86 (5.58)	13.83 (5.08)	6.57	.014
Fifteen	26.50 (7.73)	19.88 (6.73)	9.65	.003
Twenty	34.95 (9.62)	25.33 (8.12)	13.51	.001
Fifty	71.14 (19.08)	55.04 (16.37)	9.48	.004
Hundred	94.64 (25.81)	75.50 (23.51)	6.92	.012

Table 3

CAST 20 and SIS correlations

	CAST 20 N = 64
	<i>r</i>
GLOBAL SIS SCORE	.33 *
SCHIZOTYPAL DIMENSIONS [/]	
Social Isolation	.23
Introversion	.08
Sensitivity	.00
Anger	.39 **
Social Anxiety	.36 *
Schizotypal Social Anxiety	.14
Ideas of Reference	.13
Suspiciousness	.11
Pathological Jealousy	.09
Restricted Emotions	.33 *
Magical Thinking	.38 *
Illusions	.03
Sexual Anhedonia	.04

[/] There were no ratings in psychotic-like symptoms in either group.

* Significant at the 0.05 level

** Significant at the 0.01 level