Testing the Hypothesis That Formal Thought Disorders Are Severe Mood Disorders

Manuel J. Cuesta* and Victor Peralta
Psychiatric Unit B, Complejo Hospitalario de Navarra c/ Irunlarrea, 4 E-31008, Pamplona, Spain
*To whom correspondence should be addressed; tel: +34-848-422488, fax: +34-848-422488, e-mail: mcuestaz@cfnavarra.es

Background: It was recently hypothesized by Lake (Schizophrenia Bulletin 2008; 34: 109-117) that Formal Thought Disorder (FTD) can be accounted for by a single disorder that is currently diagnosed as bipolar disorder. Objectives: This study aimed to analyze the underlying dimensions of FTD and to examine to what extent FTD factors can be accounted for by clinical distractibility, attentional impairment, severity of mania, and familial liability of bipolar disorder and schizophrenia. Methods: Six hundred and sixty inpatients were assessed using a semistructured interview, and FTDs were assessed with the Thought, Language, and Communication scale. “Inattentiveness during Mental Status Testing” item of the Scale for the Assessment of Negative Symptoms scale and a composite mania score were used. The Family History-Research Diagnostic Criteria was used. Results: FTD is a multidimensional construct comprised at least 5 dimensions: disorganization, verbosity, poverty of speech, idiosyncratic thinking, and blocking. Clinical distractibility loadings split in 2 factors, disorganization and blocking, but it did not load on the mania-related (verbosity) factor. Attentional disturbance was significantly associated with each FTD factor except for idiosyncratic thinking, and these associations were largely independent from the severity of mania. The associations of FTDs with mania and attentional disturbances were independent from each other. FTD factors were not significantly associated with familial liability to bipolar or to schizophrenia. Conclusions: Disorganization was the main FTD component. Distractibility was a core feature of FTD factors but it was not specifically accounted for by mania-related attentional impairment. The hypothesis of mutual interdependence between mania and attentional disturbance leading to FTDs could not be confirmed.

Key words: thought disorders/formal thought disorders/psychosis/schizophrenia/attention/distractibility/familial liability

Introduction

Disturbed thinking was considered as a core symptom for “dementia praecox” in Kraepelin’s view尽管 although Bleuler went beyond and conferred full preeminence of Formal Thought Disorders (FTDs) over other symptoms in the diagnosis of schizophrenia.

Due to the inextricable links between thought, language, and speech, Andreasen, in her seminal article, focused on communicational issues as the primary vehicle through which FTDs are conveyed and eventually “incoherence” and “derailment” were established as true FTDs in Diagnostic and Statistical Manual for Mental Disorders (DSM) nosology. However, despite FTDs having long been considered as characteristic features of schizophrenia, both clinical experience and research contradict Bleulerian’s proposals because FTDs are neither necessary nor sufficient symptoms to be diagnosed with schizophrenia or psychosis in current diagnostic criteria. Furthermore, the prevalence of FTD varies in schizophrenia and other psychiatric disorders and almost all mania and schizophrenia patients (88% and 91%, respectively) showed at least one FTD symptom, but 53% of depressive patients showed it as well. Only 45% of schizophrenia patients showed severe degrees of FTDs.

Remarkable differences in the FTDs between patients with schizophrenia and those with mania have been reported, and adoption studies have demonstrated that the biological relatives of people with schizophrenia have elevated levels of trait FTD. However, recent research places a great deal of emphasis on the similarities of FTDs among schizophrenia and bipolar disorder patients, suggesting that these similarities are the expression of a more general overlap in sociodemographic and phenotypic characteristics and in pathophysiology treatment and genetic vulnerability. Thus, some authors conceptualize these diagnoses as disorders differing in quantitative terms that may well discard the kraepelinian dichotomy. In addition, the clinical spectra of affective and schizophrenic symptomatologies may occur...
FTDs are related to a complex dysfunction that involves disturbances in the rapid integration of content and phonemes to create reciprocal speech. Language organization requires that sublibraries of words (lexical neighborhoods) be rapidly accessed depending on proximate phonemes to allow real-time reciprocal verbal interaction. The neurobiological underpinnings of language disturbances in schizophrenia involve executive dysfunction, semantic memory abnormalities, and spreading activation in semantic memory. Therefore, dysfunction that involves the left temporal speech regions and includes abnormal functions of the anterior cingulate cortex and its integration with prefrontal brain regions may cause FTD or alterations in real-time speech production.

In a recent review article published in Schizophrenia Bulletin, Lake argues that psychotic symptoms, and more specifically FTD, are best accounted for by a mania state. Lake comes to the strong inference that “disordered thought and the functional psychoses can be accounted for by a single disorder, the disorder we currently diagnose as bipolar disorder.” According to Lake, in mania, the selective attention function deteriorates, thus allowing inappropriate and irrelevant stimuli to gain attention and focus, which is then clinically observed as distractibility. Increasing distractibility in mania leads to the disorganization of thought and behavior and to psychosis. Lake proposes a defective attentional filter/prioritizer mechanism of information processing that appears to be related to mania and would explain FTDs. A further assumption in Lake’s theory is that FTD is a unidimensional, quantitatively graded construct. However, these provoking and challenging proposals have not been empirically tested.

In this study, we examined Lake’s general hypothesis that FTDs are due to mania among a large sample of patients who were diagnosed with a functional psychotic disorder. More specifically, the hypotheses to be tested were as follows: (1) FTD is a unidimensional construct; (b) clinical distractibility is a core feature of FTD; (c) the severity of an FTD is accounted for by both the attentional impairment and the severity of mania, which in turn should be strongly correlated; and (d) while not explicitly formulated by Lake, his general hypothesis predicts that familial liability of bipolar disorder and FTD are correlated. We tested this hypothesis because it can be argued that within psychotic disorders, manic symptoms may be overlooked by more apparent and disruptive symptoms, such as delusions, hallucinations, and disorganization of thought and behavior. Thus, patients might be misdiagnosed particularly in the first episode of psychosis.

Hypotheses A and B were tested using a principal components analysis (PCA) of FTDs, including distractibility. It was expected that the PCA would yield either a single factor with high loading for distractibility or at least a main factor including distractibility. Hypothesis C was tested by examining the degree to which the severity of FTDs was accounted for by both the severity of attentional impairment and the mania. If a mania-related attentional impairment underlies FTDs, specific associations of mania with attentional impairment would be apparent, which in turn would be correlated with FTDs. Hypothesis D was tested by examining the degree to which the severity of FTDs accounted for familial liability of bipolar disorder.

Methods

Subjects

Participants were recruited through consecutive admissions to the Psychiatric ward of the Virgen del Camino Hospital (Pamplona, Spain) between 1988 and 1996. A predominantly urban geographic area of 250 000 inhabitants was the catchment area for the psychiatric admissions to this ward, and there were no other nearby facilities for psychiatric admissions. The main reasons for admission were illness exacerbation although a minority of patients was admitted due to treatment refractoriness or diagnostic clarification.

Inclusion criteria were as follows: (1) having at least one psychotic symptom as defined by the Diagnostic and Statistical Manual for Mental Disorders, Fourth Edition, (DSM-IV) criterion A for schizophrenia or severe negative symptoms and (2) a lack of severe drug abuse and/or demonstrable brain disease or mental retardation, confounding a diagnosis. The study was approved by the local ethical committee, and all subjects provided written informed consent to participate in the study.

At intake, patients underwent an extensive evaluation, including a semistructured interview (an expanded version of the Manual for the Assessment of Schizophrenia, MAS interview) and standardized clinical rating scales, as described elsewhere.

Diagnoses of specific psychotic disorders were performed using the DSM-IV. A diagnosis was based on a consensus best-estimate procedure with all available information sources including medical records and interviews with probands including at least a close relative.

Psychopathological dimensions were computed using the Comprehensive Assessment of Symptoms and History, which allows for the extraction of the “reality distortion,” “negative,” “disorganization,” “manic,” and “depression” symptom scores.

Premorbid functioning was evaluated using the Global Assessment Functioning-past year of DSM-III-R. Prognosis was evaluated through the total score on the Strauss-Carpenter scale. Response to treatment was assessed by the Guy’s Clinical Global Impression (CGI) scale efficacy index. Outcome measures, such as course, work activity, and social activity, were assessed by the MAS interview.

A family history of bipolar disorder and schizophrenia was ascertained using the Family History-Research
Table 1. Main Demographic and Clinical Characteristics of the Sample

<table>
<thead>
<tr>
<th></th>
<th>N (%)</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male)</td>
<td>384 (58.2)</td>
<td></td>
</tr>
<tr>
<td>Civil status (single)</td>
<td>484 (73.3)</td>
<td></td>
</tr>
<tr>
<td>DSM-IV diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>358 (54.2)</td>
<td></td>
</tr>
<tr>
<td>Schizoaffective disorder</td>
<td>61 (9.2)</td>
<td></td>
</tr>
<tr>
<td>Schizoaffective disorder</td>
<td>37 (5.6)</td>
<td></td>
</tr>
<tr>
<td>Major mood disorder</td>
<td>88 (13.3)</td>
<td></td>
</tr>
<tr>
<td>Delusional disorder</td>
<td>27 (4.1)</td>
<td></td>
</tr>
<tr>
<td>Brief psychotic disorder</td>
<td>57 (8.6)</td>
<td></td>
</tr>
<tr>
<td>Psychosis NOS</td>
<td>32 (4.8)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>36.1 (14.0)</td>
<td></td>
</tr>
<tr>
<td>Years of education</td>
<td>9.3 (3.2)</td>
<td></td>
</tr>
<tr>
<td>Age at illness onset</td>
<td>26.9 (10.6)</td>
<td></td>
</tr>
<tr>
<td>Number of previous hospitalizations</td>
<td>3.4 (4.3)</td>
<td></td>
</tr>
<tr>
<td>Global Assessment of Functioning, past year</td>
<td>61.7 (17.4)</td>
<td></td>
</tr>
</tbody>
</table>

Note: DSM-IV, Diagnostic and Statistical Manual for Mental Disorders, Fourth Edition

Diagnostic Criteria in first-degree relatives of the probands that were 15-years old or greater (n = 2987) as detailed elsewhere. A positive family history in first-degree relatives of schizophrenia and bipolar disorder, together with family size and age structure, served as elements to compute specific familial loading scores for both disorders, as devised by Pak Sham. These scores allowed for summarizing familiarity or accounting for the morbidity of schizophrenia and mood disorder morbidity in the family, by using a continuous measure of liability. The 600 patients were comprised 384 men (58%) and 276 women (42%), whose average education was 9.3 years (SD = 3.2). The mean age at index admission was 36.0 years (SD = 14.0), the mean age at onset was 26.9 years (SD = 10.6), and the average number of hospitalizations was 3.4 (SD = 4.3) (table 1).

The DSM-IV diagnostic breakdown of the patients was as follows: schizophrenia (n = 358, 54.2%), schizoaffective disorder (n = 61, 9.2%), bipolar disorder (n = 37, 5.6%), major mood disorder (n = 88, 9.6%), delusional disorder (n = 27, 4.1%), and psychosis NOS (n = 32, 4.8%). The DSM-IV diagnostic breakdown of the patients was as follows: deficit (n = 92, 13.9%) and nondeficit schizophrenia (n = 296, 44.8%), schizophreniform disorder (n = 61, 9.2%), bipolar disorder (n = 57, 8.6%), delusional disorder (n = 27, 4.1%), psychotic disorder not otherwise specified (n = 32, 4.8%), schizoaffective or bipolar, current manic (81, 12.2%), and schizoaffective or mood disorder, current depressive episode (n = 44, 6.6%) (table 1). Schizophrenia patients were divided into deficit and nondeficit syndrome schizophrenia subtypes using the Carpenter et al criteria for the deficit syndrome and a global severity score for the deficit syndrome was computed for each patient.

Assessment of FTD

Andreasen’s Thought, Language, and Communication (TLC) scale was used for the FTD assessments by the 2 authors. The TLC scale includes a broad range of speech behaviors than can be directly observed, and it has become the standard rating instrument to assess FTD because of its comprehensiveness and adequate psychometric characteristics. The TLC was scored using information from 2 clinical interviews that lasted at least 45 minutes conducted during the first 3 days of admission. The severity of FTD in the first 5 days of admission served to establish the scoring period in the TLC. Good to moderate interrater reliability, as measured by intra-class correlation coefficients, was achieved by the 2 raters in a subsample of 33 schizophrenic patients.

Assessment of Attentional Disturbance

Attentional impairment was measured using the “Inattentiveness during mental status testing” item included in the Scale for the Assessment of Negative Symptoms (SANS). This is a test of attention span during which participants are asked to spell “world” backwards and count down from 100 by serial 7s (at least a 10th grade education) or serial 3s (at least a 6th grade education) for a series of 5 subtractions. The item is rated from 0 (no attentional impairment), indicating no errors, to 5 (severe attentional impairment), indicating 4 or more errors.

The severity of mania was assessed by the Association for Methodology and Documentation in Psychiatry (AMDP) system. The psychopathology module from the AMDP comprises 100 symptoms and signs derived from German traditional descriptive psychopathology and are rated from 0 (absent) to 3 (severe) with specific anchor definitions. The AMDP covers all relevant manifestations of psychotic and mood disorders, the latter of which is represented by approximately 30 symptoms. We derived a mania scale by selecting 7 items typically relating to current definitions of mania: euphoria, irritability, increased self-confidence, hyperactivity, psychomotor agitation, excessive social contact, and hypersexuality. We specifically omitted FTDS to avoid confounding effects with FTDS. This 7-item scale had good internal consistency (Cronbach’s α = .77) and excellent discriminant ability against a DSM-IV diagnosis of a manic or schizomanic episode (receiver operating characteristic curve = 0.89).

Statistics

Individual TLC item raw scores were converted to z-scores relative to the overall baseline mean and SD to make the data better comply with the normality requirement. Thus,
Table 2. Descriptive and Correlational Statistics for the Outcome Variables

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
<th>Pearson’s Correlation Coefficients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>1. Mania score</td>
<td>2.5</td>
<td>3.4</td>
<td>0–18</td>
<td>—</td>
</tr>
<tr>
<td>2. FLS of bipolar disorder*</td>
<td>−0.1</td>
<td>0.3</td>
<td>−1.4–3.2</td>
<td>.20*</td>
</tr>
<tr>
<td>3. FLS of schizophrenia*</td>
<td>0.0</td>
<td>0.6</td>
<td>−1.3–6.5</td>
<td>.01</td>
</tr>
<tr>
<td>4. TLC scale, total score</td>
<td>9.4</td>
<td>8.5</td>
<td>0–48</td>
<td>.21*</td>
</tr>
<tr>
<td>5. Inattentiveness</td>
<td>2.0</td>
<td>1.7</td>
<td>0–5</td>
<td>.23*</td>
</tr>
</tbody>
</table>

Note: TLC, Thought, Language, and Communication; FLS, Familial Loading Score

*Log-transformed scores

*P < .001

The 18 TLC z-cores were subjected to exploratory PCA followed by a varimax rotation. Criteria for retaining the rotated factors were eigenvalues >1 and interpretability of the factors. Item loadings with absolute values >0.40 were used to describe the factors. Standardized factor scores were calculated and used in subsequent analyses.

We examined the distribution of factor scores across diagnostic breakdowns of patients, and group differences were computed using an ANOVA. The Sheffé post hoc test was used to isolate specific group differences when a statistically significant omnibus F test value was obtained.

To examine the association between the different components of thought disorder and attentional disturbance, the mania rating score and familial liability of bipolar disorder, we used linear regression analyses as appropriate. In these analyses, each illness feature was the dependent variable, the FTD domains were the independent variables, and age, gender, and years of illness duration were the confounding factors.

Results

Descriptive data of TLC scores and mania ratings for each diagnostic group are shown in online supplementary table 1. Globally, a great percentage of patients showed FTDs (TLC global rating score >0) (477, 72.7%) and abnormal mania ratings (mania score >0) (417, 63.1%).

Principal Components Analysis of TLC Items

Descriptive and correlational statistics for the outcome variables, TLC total score, familial liability score for bipolar disorder, mania rating scale, and inattentiveness score are shown in table 2. Mania score was positively and significantly related to familial liability of bipolar disorder, TLC total score, and Inattentiveness. However, mania score was not significantly related to familial liability of schizophrenia, which also did not show any significant associations with the other outcome variables mentioned above. Inattentiveness and TLC total scores were strongly associated.

The PCA showed that a 6-factor solution that explained 64% of the variance best accounted for the data (table 3). All of the items loaded (>0.40) in at least 1 factor and only 3 items (distractible speech, incoherence, and neologisms) loaded in more than 1 factor, resulting in a clear, unambiguous, and clinically interpretable factor structure. The Kaiser-Meyer-Olkin measure was 0.81, indicating good sampling adequacy. Factor 1 (disorganization, 19.2% of the explained variance) included distractible speech, tangentiality, derailment, incoherence, illogicality, circumstantiality, and loss of goal. This factor seemed to correspond to the classical concept of loss of associations. Factor 2 (verbosity, 11.9% of explained variance) included pressure of speech, incoherence, neologisms, clanging, and echolalia. Factor 3 (poverty of speech, 11.1% of the explained variance) included poverty of speech, poverty of content of speech, and perseveration. Factor 4 (idiomatic speech, 9.1% of the explained variance) included neologisms, word approximations, and stilted speech. Factor 5 (blocking, 8.6% of the explained variance) included distractible speech and blocking. Factor 6 only included the item of self-reference. Because this factor was difficult to interpret, it was not considered in subsequent analyses. A separate analysis of the TLC items among schizophrenia patients yielded the same factors with only minor differences in factor loadings.

The distribution of the TLC factor scores across diagnostic categories is shown in table 4. All factor scores significantly differed across the diagnostic categories (F > 6.5, df = 2, P < .001) with substantial significant differences in TLC factors among diagnostic groups. Briefly, while mania patients showed the highest scores in disorganization and verbosity factors, deficit schizophrenia did so in poverty of speech and idiosyncratic speech factors and schizophreniform disorder patients in blocking factor. In contrast, delusional disorder patients showed the lowest scores in disorganization, depressive in verbosity, mania in poverty of speech and idiosyncratic, and psychosis NOS in blocking factor (table 4). Moreover, we performed an ANCOVA analysis of FTDs factors as independent
variables, DSM diagnoses as dependent variable, and verbosity factor as covariate. After controlling for verbosity, there remained significant differences between diagnostic groups in poverty of speech factor ($F = 5.082, P < .025$) and idiosyncratic factor ($F = 3.715, P < .054$) but not in disorganization and blocking factors.

The contribution of the mania score, inattentiveness, and the familial loading score for schizophrenia and

Table 3. Severity, Prevalence, and Factor Structure of Individual Items From the Thought, Language, and Communication Rating Scale in 660 Psychotic Patients

<table>
<thead>
<tr>
<th></th>
<th>Mean (SD)</th>
<th>N (%)</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>V</th>
<th>VI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poverty of speech</td>
<td>0.73 (1.17)</td>
<td>236 (35.8)</td>
<td>-0.17</td>
<td>-0.07</td>
<td><strong>0.74</strong></td>
<td>-0.01</td>
<td>0.35</td>
<td>-0.08</td>
</tr>
<tr>
<td>Poverty of content of speech</td>
<td>0.95 (1.19)</td>
<td>317 (48.0)</td>
<td>0.16</td>
<td>-0.01</td>
<td><strong>0.84</strong></td>
<td>0.05</td>
<td>0.02</td>
<td>0.01</td>
</tr>
<tr>
<td>Pressure of speech</td>
<td>0.43 (0.90)</td>
<td>160 (24.2)</td>
<td>0.28</td>
<td><strong>0.67</strong></td>
<td>-0.21</td>
<td>-0.18</td>
<td>-0.08</td>
<td>0.17</td>
</tr>
<tr>
<td>Distractible speech</td>
<td>0.70 (1.13)</td>
<td>224 (33.9)</td>
<td><strong>0.55</strong></td>
<td>0.24</td>
<td>0.03</td>
<td>-0.08</td>
<td><strong>0.56</strong></td>
<td>0.10</td>
</tr>
<tr>
<td>Tangentility</td>
<td>0.89 (1.17)</td>
<td>290 (56.1)</td>
<td><strong>0.71</strong></td>
<td>0.01</td>
<td>0.08</td>
<td>0.23</td>
<td>-0.01</td>
<td>0.16</td>
</tr>
<tr>
<td>Derailment</td>
<td>1.01 (1.36)</td>
<td>279 (42.3)</td>
<td><strong>0.82</strong></td>
<td>0.34</td>
<td>-0.02</td>
<td>0.05</td>
<td>0.13</td>
<td>-0.04</td>
</tr>
<tr>
<td>Incoherence</td>
<td>0.59 (1.12)</td>
<td>175 (26.5)</td>
<td><strong>0.46</strong></td>
<td><strong>0.46</strong></td>
<td>0.11</td>
<td>0.28</td>
<td>0.27</td>
<td>-0.03</td>
</tr>
<tr>
<td>Illogicality</td>
<td>1.09 (1.29)</td>
<td>328 (49.7)</td>
<td><strong>0.64</strong></td>
<td>0.04</td>
<td>0.17</td>
<td>0.33</td>
<td>0.02</td>
<td>-0.25</td>
</tr>
<tr>
<td>Clangings</td>
<td>0.14 (0.53)</td>
<td>54 (8.2)</td>
<td>0.09</td>
<td><strong>0.80</strong></td>
<td>0.06</td>
<td>0.21</td>
<td>0.07</td>
<td>0.00</td>
</tr>
<tr>
<td>Neologisms</td>
<td>0.06 (0.33)</td>
<td>23 (3.5)</td>
<td>-0.01</td>
<td><strong>0.46</strong></td>
<td>0.10</td>
<td><strong>0.55</strong></td>
<td>0.08</td>
<td>-0.17</td>
</tr>
<tr>
<td>Word approximations</td>
<td>0.18 (0.58)</td>
<td>73 (11.1)</td>
<td>0.24</td>
<td>0.14</td>
<td>0.15</td>
<td><strong>0.66</strong></td>
<td>0.03</td>
<td>0.02</td>
</tr>
<tr>
<td>Circumstantiality</td>
<td>0.59 (0.96)</td>
<td>210 (38.6)</td>
<td><strong>0.65</strong></td>
<td>-0.12</td>
<td>0.15</td>
<td>0.16</td>
<td>-0.11</td>
<td>-0.27</td>
</tr>
<tr>
<td>Loss of goal</td>
<td>0.85 (1.17)</td>
<td>255 (39.6)</td>
<td><strong>0.79</strong></td>
<td>0.33</td>
<td>0.03</td>
<td>-0.04</td>
<td>0.15</td>
<td>-0.08</td>
</tr>
<tr>
<td>Perseveration</td>
<td>0.53 (0.97)</td>
<td>177 (26.8)</td>
<td>0.26</td>
<td>0.17</td>
<td><strong>0.65</strong></td>
<td>0.03</td>
<td>-0.10</td>
<td>0.16</td>
</tr>
<tr>
<td>Echolalia</td>
<td>0.09 (0.45)</td>
<td>32 (4.8)</td>
<td>0.09</td>
<td><strong>0.50</strong></td>
<td>0.35</td>
<td>0.05</td>
<td>0.05</td>
<td>0.34</td>
</tr>
<tr>
<td>Blocking</td>
<td>0.34 (0.84)</td>
<td>104 (15.8)</td>
<td>0.04</td>
<td>-0.01</td>
<td>0.11</td>
<td>0.11</td>
<td><strong>0.90</strong></td>
<td>0.07</td>
</tr>
<tr>
<td>Stilted speech</td>
<td>0.11 (0.44)</td>
<td>44 (6.9)</td>
<td>0.14</td>
<td>-0.08</td>
<td>-0.15</td>
<td><strong>0.66</strong></td>
<td>-0.02</td>
<td>0.24</td>
</tr>
<tr>
<td>Self-reference</td>
<td>0.13 (0.50)</td>
<td>47 (7.1)</td>
<td>0.02</td>
<td>0.11</td>
<td>0.05</td>
<td>0.09</td>
<td>0.09</td>
<td><strong>0.81</strong></td>
</tr>
</tbody>
</table>

Note: Factor loadings 0.40 are presented in bold.

Table 4. Means and SEs for Formal Thought Disorder’s Domains Across Psychotic Disorders

<table>
<thead>
<tr>
<th></th>
<th>DS (n = 92)</th>
<th>NDS (n = 296)</th>
<th>SF (n = 61)</th>
<th>BPD (n = 57)</th>
<th>DD (n = 27)</th>
<th>NOS (n = 32)</th>
<th>M (n = 81)</th>
<th>D (n = 44)</th>
<th>F (df = 6)*</th>
<th>Group Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disorganization</td>
<td>0.25 (0.10)</td>
<td>-0.06 (0.06)</td>
<td>-0.09 (0.12)</td>
<td>0.32 (0.13)</td>
<td>-0.67 (0.19)</td>
<td>-0.34 (0.17)</td>
<td>0.41 (0.10)</td>
<td>-0.53 (0.14)</td>
<td>8.36</td>
<td>M, BPD, DS &gt; DD, D, NOS, SF, NDS/NDS, SF &gt; D, DD</td>
</tr>
<tr>
<td>Verbosity</td>
<td>-0.17 (0.10)</td>
<td>-0.18 (0.06)</td>
<td>-0.10 (0.13)</td>
<td>-0.14 (0.13)</td>
<td>-0.14 (0.19)</td>
<td>0.52 (0.17)</td>
<td>0.72 (0.11)</td>
<td>-0.27 (0.14)</td>
<td>10.51</td>
<td>M, NOS &gt; D, NDS, DD, BPD/M &gt; SF/BPD &gt; D, NDS</td>
</tr>
<tr>
<td>Poverty of speech</td>
<td>1.04 (0.09)</td>
<td>-0.05 (0.05)</td>
<td>-0.07 (0.12)</td>
<td>-0.29 (0.12)</td>
<td>-0.50 (0.17)</td>
<td>-0.03 (0.16)</td>
<td>-0.63 (0.10)</td>
<td>0.10 (0.13)</td>
<td>25.77</td>
<td>DS &gt; M, DD, BPD, SF, NDS, D/D, NDS, SF, DD, NOS &gt; M</td>
</tr>
<tr>
<td>Idiosyncratic</td>
<td>0.24 (0.10)</td>
<td>0.13 (0.06)</td>
<td>0.21 (0.13)</td>
<td>-0.33 (0.13)</td>
<td>-0.08 (0.19)</td>
<td>-0.19 (0.17)</td>
<td>-0.48 (0.11)</td>
<td>-0.05 (0.15)</td>
<td>5.76</td>
<td>DS, SF, NDS &gt; M, BPD, NOS/D &gt; M</td>
</tr>
<tr>
<td>Blocking</td>
<td>-0.12 (0.10)</td>
<td>-0.04 (0.06)</td>
<td>0.54 (0.13)</td>
<td>0.26 (0.13)</td>
<td>-0.14 (0.19)</td>
<td>-0.29 (0.17)</td>
<td>-0.23 (0.11)</td>
<td>0.17 (0.15)</td>
<td>4.63</td>
<td>SF &gt; NOS, M, DD, DS, NDS, D/TPB &gt; NOS, M, NOS, DD</td>
</tr>
</tbody>
</table>

Note: DS, Deficit Schizophrenia; NDS, Nondeficit schizophrenia; SF, Schizophreniform Disorder; BPD, Brief Psychotic Disorder; DD, Delusional Disorder; NOS, Psychosis NOS; M, Schizoaffective or Bipolar Disorder, Current Manic Episode; D, Schizoaffective or Mood Disorder, and Current Depressive Episode.

*P < .001

Downloaded from https://academic.oup.com/schizophreniabulletin/article-abstract/37/6/1136/1894272 by guest on 23 January 2019
bipolar disorders were examined using stepwise regression analyses with thought factors as dependent variables (Table 5). The mania score entered in all regression equations and inattentiveness entered in all but the idiosyncratic speech regression model. Familial liability score of schizophrenia entered only the poverty of speech factor and FLS for bipolar disorder did not show any significant contributions. Similar results in regression procedures were obtained by selecting patients showing FTDs (TLC global ratings > 0).

Online supplementary table 2 shows that the direct associations between the FTD domains and familial liability for bipolar disorder, premorbid, clinical and psychopathological variables, attentional disturbances, and outcome variables. In addition, the same correlation coefficients were found even after controlling for confounding variables (age, gender, and number of years of evolution).

Familial liability of bipolar disorder was unrelated to any thought disorder domain. Mania was positively related to disorganization, particularly verbosity, and was inversely related to poverty of speech and blocking. Given that mania and attentional disturbance were significantly related, regression coefficients for mania were further adjusted for attentional disturbance, and the regression coefficients for attention were further adjusted for mania. After adjusting for attentional disturbance, all of the significant associations between mania and FTD domains remained statistically significant, indicating that the association pattern between FTD domains and mania are relatively independent of attentional disturbance. Attentional disturbance showed moderate to strong correlations with all of the thought domains except for the idiosyncratic one. Associations remained unchanged even after controlling for the mania rating, which indicates that the association pattern between FTD domains and attentional disturbance is independent from the rating of mania.

To further explore the specific contribution of mania to FTD across the different diagnostic groupings, we conducted linear regression analyses where those FTD domains that were positively related to mania (disorganization and verbosity) were the predictor variables, the mania rating was the criterion variable and age, gender, and illness duration were the confounding factors. The proportion of the variance explained ($R^2$) by disorganization and verbosity domains in patients with a diagnosis of schizoaffective or affective psychosis ($n = 125$), non(schizo)-affective psychoses ($n = 535$), and schizophrenia ($n = 358$) was .41, .20, and .18, respectively.

**Table 5. Stepwise Regression Analysis for Predicting Cognitive Domains Scores**

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>Step</th>
<th>Predictive Variables</th>
<th>$R^2$</th>
<th>$\Delta R^2$</th>
<th>$\beta$</th>
<th>Overall $F$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disorganization</td>
<td>1</td>
<td>Inattentiveness</td>
<td>.20</td>
<td>.43**</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Mania score</td>
<td>.21</td>
<td>.01</td>
<td>.11*</td>
<td>34.7</td>
</tr>
<tr>
<td>Verbosity</td>
<td>1</td>
<td>Mania score</td>
<td>.21</td>
<td>.42**</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Inattentiveness</td>
<td>.22</td>
<td>.01</td>
<td>.13**</td>
<td>37.3</td>
</tr>
<tr>
<td>Poverty of speech</td>
<td>1</td>
<td>Inattentiveness</td>
<td>.07</td>
<td>.29**</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Mania score</td>
<td>.13</td>
<td>.06</td>
<td>-.26**</td>
<td>18.4</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>FLS of schizophrenia</td>
<td>.14</td>
<td>.01</td>
<td>.11*</td>
<td></td>
</tr>
<tr>
<td>Idiosyncratic speech</td>
<td>1</td>
<td>Mania score</td>
<td>.04</td>
<td>-.16**</td>
<td></td>
<td>7.6</td>
</tr>
<tr>
<td>Blocking</td>
<td>1</td>
<td>Inattentiveness</td>
<td>.14</td>
<td>.40**</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Mania score</td>
<td>.18</td>
<td>.04</td>
<td>-.20**</td>
<td>28.5</td>
</tr>
</tbody>
</table>

*Note: FLS, Familial Loading Score

$P < .01$, **$P < .001$

Discussion

**Hypothesis Testing**

FTDs, assessed using the TLC scale, are a multidimensional construct as indicated by the 5 interpretable factors that were obtained. Therefore, hypothesis A that FTDs are a unidimensional construct was not confirmed. Our finding of a multidimensional structure of the TLC is in accordance with results from previous studies that have used the TLC$^7,32,34,35$ and other scales$^{80}$ to rate FTDs.

Clinical distractibility loadings split into 2 factors, namely, disorganization and blocking. Although disorganization explained the largest amount of variance of the 5 FTD domains making it the main FTD component, distractibility also had a modest load on this factor. Moreover, distractibility did not load on the mania-related (verbosity) factor. Thus, the hypothesis that distractibility is a core feature of FTD, and more specifically, a core feature of manic thought disorder could not be confirmed. The TLC distractible speech item was not included in several previous factor analyses$^{8,34}$ but it loaded positively in the “fluent-disorganization”$^7$ and in an attentional factor (joined together with blocking item) in our previous study.$^{32}$

Attentional disturbance was moderately to strongly related to each FTD factor except for idiosyncratic thinking, even after partialling out confounding variables.
poor functioning in schizophrenia.43

FTD, as a persistent feature, is strongly predictive of speech.4 Differences in language coherence between the scores on poverty of speech and poverty of content of thinking, distractible speech, and circumstantiality and lower quantity of FTDs between manic and schizophrenia patients.4,38 In this regard, schizoaffective patients tend to resemble those with schizophrenia.7,39,40 Nonetheless, certain qualities of FTDs tend to be distinctive of manic patients, such as higher scores on pressured speech, clang- ing, distractible speech, and circumstantiality and lower scores on poverty of speech and poverty of content of speech.4 Differences in language coherence between the 2 groups were only found when the studies focused on the subset of patients experiencing FTDs but not in studies that included patients irrespective of their level of FTD.41,42 Finally, the persistence of some level of FTD over the course of the illness, or trait-related FTD, is more common in schizophrenia patients than in mania patients because in the later disorder, FTDs are much more state-dependent.7 Additionally, the severity of an FTD, as a persistent feature, is strongly predictive of poor functioning in schizophrenia.43

These aforementioned studies are consistent with our current results and conflict with the central point in Lake’s hypothesis that schizophrenia-related FTDs are actually mania-related FTDs. Our manic episode group, comprised schizoaffective and bipolar patients with current manic episodes, showed significantly higher scores on verbosity and disorganization factors but significant lower scores on poverty of speech and idiosyncratic thinking as compared with deficit and nondeficit schizophrenia groups.

In addition, when we moved away from the affective psychosis to nonaffective psychosis and schizophrenia, the amount of variance in FTDs explained by the mania decreased progressively.

**Attentional Impairment and FTD**

FTDs have been found to be related to several cognitive dysfunctions in schizophrenia, such as impairments in attention, information processing, working memory, discourse planning semantic processing, and executive dysfunction.17,20,44–46, and it seems these deficits in attention and information processing may be part of what causes FTDs. Furthermore, disorganization and negative syndromes were both significantly associated with impairments in executive function37,48 though showing different patterns of association with different executive tests.49

The relationship between attentional/information-processing deficits and FTDs has long been established in schizophrenia patients.50,51 In fact, a model of information-processing deficits similar to Lake’s defective attentional filter/prioritizer model has been proposed for schizophrenia.52 Until recently, research on information processing and neuropsychological performance had been mainly conducted in schizophrenia patients, which led to the impression that deficits were relatively specific for schizophrenia. Kerns and Berenbaum20 completed a meta-analysis of studies examining cognitive functioning associated with FTD in patients with schizophrenia. They found that 2 such impairments, executive dysfunction and impaired processing of semantic information, showed a substantial effect size. In contrast, 2 other cognitive impairments, increase spreading activation and impaired language production, were not consistently associated with FTD.

The aforementioned findings regarding cognitive impairments and their relationships with FTDs in schizophrenia should be integrated with current evidence suggesting that differences in neuropsychological performance between schizophrenia and affective psychoses are largely quantitative, with schizophrenia patients displaying more severe impairments.53 In this regard, while studies examining relapsed patients with bipolar disorder and schizophrenia have found them to be equally affected in measures of sustained and selective attention,54,55 studies focusing on remitted patients do not report attentional impairment.55 Furthermore, there is some evidence arguing that the attentional impairment seems to be associated with psychosis in general56 and also associated with positive FTDs across schizophrenia and bipolar disorder.57 Both cross-sectional and longitudinal differences of FTDs in psychoses may further suggest a shared pathophysiology, possibly involving information-processing disturbances along a gradient in different psychotic disorders. This may evolve from state-dependent FTDs in acute...
psychotic episodes to trait-related FTDs more prevalent in schizophrenia disorders.

Taken together, existing evidence and the results from this study do not support the notion that specific mania-related attentional impairment leads to FTD. Our data showing that inattentiveness was related to all 5 types of FTD does not support Lake's hypothesis.

One pending question that remains unanswered is the exact nature by which attentional and information-processing deficits are related. One possible reason for inconsistencies among studies could be related to discrepancies in the assessment methods for both FTDs and attention. Different sound standardized instruments and scales have been employed in the FTD assessment, but rates of concordance among them are low.58 There are also wide variations in the assessment of attention, ranging from studies evaluating distractibility at the clinical domain to studies using specific neuropsychological tests or neurocognitive batteries. Because FTD is not a unitary construct but a multidimensional structure,32 it is feasible that different FTD dimensions may be based on specific underlying cognitive impairments. This view requires new studies targeting each FTD dimension or subsyndromes to specific cognitive impairments.59 This approach might result in identifiable FTDs-cognitive impairment complexes that may be partially schizophrenia related, partially mania related, or independent of belonging to a particular diagnostic category.

In this regard, Luck and Gold60 recently proposed that 2 distinct constructs, closely tied to working memory and executive function, are the underpinnings of attention impairment in schizophrenia. These constructs are input selection (made up of 2 subprocesses, control and implementation selection) and rule selection. These authors hypothesized that a significant impairment in the control of input selection, but little or no impairment in the implementation of selection of input, is involved in the attentional impairment of schizophrenia patients. Thus, impairment in specific modalities and subprocesses of attention, such as visual sustained attention, may serve for the differentiation of schizophrenia from their first-degree relatives and schizophrenia from bipolar patients and their first-degree relatives even without a specific genetic risk for diagnosis.61 Thus, future research should explore to what extent specific FTD dimensions are better explained by impairments in specific modalities and subprocesses of attention, such as visual sustained attention, and particularly in the control of input selection.

FTDs and Familial Liability to Bipolar Disorder

Familial liability to bipolar disorder was not related to FTDs but it was related to mania scorings. Familial liability to schizophrenia did not show significant associations with the FTD dimensions. The development of FTD in schizophrenia might be due not to a direct genetic or familial effect but to an interaction between genetic and environmental factors.62 By affecting a growing child's environment, their risk for the development of a schizophrenia spectrum disorder may be increased.63 In this regard, results from the same group reported that the genetic risk of schizophrenia did not account for the stability or the severity of FTD, though other authors proposed the use of FTDs as endophenotype candidates for research in psychosis.57

Current diagnostic systems distinguish between schizophrenia and psychotic mood disorders mainly based upon psychosis being the core-defining feature of the schizophrenia diagnosis whereas in mood disorders, it is considered to be a secondary clinical phenomenon. Our study may help to clarify the boundaries and overlap of thought disorders between schizophrenia and bipolar disorder and particularly to determine the extent to which FTDs influence on how these disorders are being diagnosed. In this respect, while disorganized speech (eg, derailment or incoherence) is included among the characteristic symptoms of schizophrenia, it does not hold for the diagnosis of a manic episode. Specific symptoms of thought disorganization should be considered as characteristic symptoms of both schizophrenia and mania episodes, qualifying its severity.

Over the last 2 decades, there have been attempts to characterize FTD at either clinical or descriptive levels using positive and negative thought disorder constructs. This atheoretical approach has been consolidated within standardized clinical scales, and it is still used in research such as the present study. In addition, new methods to assess FTD include using psycholinguistic and neuroscience theory-based approaches to better characterize FTD clinical constructs in schizophrenia and other psychoses. Specifically, there have been attempts to describe FTD based on analyzing the language output of patients in terms of its statistical properties as well as its lexical, syntactic, and discourse structure.64,65 Other scientists have examined the neural correlates of FTD by using either neuroimaging techniques18 or neuropsychological procedures to assess the lexical semantic access store.49

In summary, the main FTD component of patients who suffered a relapse of psychosis was disorganization. Distractibility was also a core FTD factor, but one that was not accounted for by a mania-related attentional impairment. Lake's hypothesis of mutual interdependence between mania and attentional disturbance leading to FTDs was not confirmed; however, future studies using patients with nonaffective psychotic disorders or those with exclusively nonthought disorders are warranted to definitively discard the aforementioned hypothesis.

Limitations

Caution is warranted in drawing FTD trait inferences due to the cross-sectional design and the FTD state component. Future research is needed to discern differences between cross-sectional and longitudinal FTD factors.
We used a clinically based measure of inattentiveness rather than a specific attentional construct, which may have created results that are too crude and general to assess via a complex construct such as attentional disturbance. And we measured a final output of distractibility through FTD that might have been better addressed by targeting this variable in an early brain process at a neurophysiological level. Both caveats should be taken in mind because they may have obscured important relationships of the FTD components because different types of FTDs may reflect different underlying cognitive impairments. However, the SANS inattentive subscale has been found to be significantly correlated with other well-validated measures of inattentiveness such as the Trail Making Test, Continuous Performance Test, and Digit Span Distraction Task, which tap overlapping constructs such as attentional control processing, sustained attention, selective attention, and working memory. Taken together, our results should be validated in future studies using rigorous neuropsychological testing.

Some circularity may be inferred from trying to assess differences in FTDs in DSM psychotic groups because FTDs are within the set of diagnostic criteria for both manic and schizophrenic episodes. However, our sample was composed of consecutive admissions of patients with at least one prominent psychotic symptom as defined by DSM-IV criterion A of schizophrenia and mostly because illness exacerbation. Lake postulates the existence of a link between mania and FTDs that extends to all psychotic disorders. We reasoned that to definitively discard the above mentioned hypothesis, it should ideally be tested in a sample of patients with nonaffective psychotic disorders or tested in a sample comprising exclusively nonaffective disordered patients. However, a recent meta-analysis did not find significant differences in semantic priming between patients with and without thought disorder.

Funding

Supplementary Material
Supplementary material is available at http://schizophreniabulletin.oxfordjournals.org.

Acknowledgments
The authors have declared that there are no conflicts of interest in relation to the subject of this study.

References
findings from a functional magnetic resonance imaging study. *Arch Gen Psychiatry*. 2001;58:769–774.


