Formal thought disorder in first-episode psychosis

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Abstract

Formal thought disorder (FTD) is one of the fundamental symptom clusters of schizophrenia and it was found to be the strongest predictor determining conversion from first-episode acute transient psychotic disorder to schizophrenia. Our goal in the present study was to compare a first-episode psychosis (FEP) sample to a healthy control group in relation to subtypes of FTD. Fifty six patients aged between 15 and 45 years with FEP and forty five control subjects were included in the study. All the patients were under medication for less than six weeks or drug-naive. FTD was assessed using the Thought and Language Index (TLI), which is composed of impoverishment of thought and disorganization of thought subscales. FEP patients showed significantly higher scores on the items of poverty of speech, weakening of goal, perseveration, looseness, peculiar word use, peculiar sentence construction and peculiar logic compared to controls. Poverty of speech, perseveration and peculiar word use were the significant factors differentiating FEP patients from controls when controlling for years of education, family history of psychosis and drug abuse.
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1. Introduction

Formal thought disorder (FTD) is one of the fundamental symptom clusters of schizophrenia. Disorders of thought processes that are characterized by deficiency in organizing thought in a definite logical sequence for a certain goal are considered as FTD. Thomas and Frazer [1] defined FTD as multidimensional impairment including disorders in thought, language processing and social cognition.

Poverty of speech, poverty of content, pressure of speech, distractible speech, tangentiality, derailment, incoherence, illogicality, clanging, neologisms and word approximations were reported as more pathologic types of FTD [2]. Among types of FTD identified by Andreasen, derailment, loss of goal, poverty of content and tangentiality were stated to be the most frequently seen types in patients with schizophrenia [3].

FTD usually persists during the illness chronically in an attenuated form, yet it tends to deteriorate in acute episodes [4,5]. Antipsychotic treatment reduces thought pathology associated with acute episodes of schizophrenia [6].

Negative FTD, identified with poverty of speech and poverty in content of speech, remains stable over the course of schizophrenia [7]. It is associated with poor response to treatment [8] and schizophrenia patients having negative FTD are less likely to attain remission [7]. Positive FTD, determined by features like derailment, perseveration, circumstantiality, tangentiality, blocking and incoherence usually declines or disappears as the acute episode alleviates [7,9]. Patients with affective psychosis tend to have more explicit positive FTD in contrast to patients with schizophrenia who have more negative FTD [7]. Moreover, follow-up study of these patients indicated that patients with schizoaffective disorder and bipolar disorder with manic episode showed improvements in some subtypes of FTD over time, whereas patients with schizophrenia remained the same. The foremost determinant factor of this result was thought to be the existence of negative FTD present throughout schizophrenia [7].

FTD is reported to be highly heritable, being found in healthy relatives of patients with schizophrenia [10,11]. Specifically, deficiency in verbal fluency [12], peculiar word use [13], deviant verbalization [10], and grammatical oversimplification [4] are explicit in relatives of patients with schizophrenia compared to healthy controls. Moreover, adoption studies provide a basis for minimizing the

confounding effects of genetic and environmental factors. Adoptees with schizophrenia tend to have significant FTD compared to control adoptees and, likewise, biological relatives of adoptees with schizophrenia show more FTD than biological relatives of control adoptees [4,14]. These results indicate that the genetic factors increase the liability for schizophrenia rather than the rearing experiences [14]. A previous genome-wide linkage analysis and whole-genome sequencing showed that impaired MEF2A activity and genetic variation in the region 6q26–27 may be biologically relevant high-risk factors for FTD in schizophrenia [15].

The aim of this study is to compare an FEP sample to a healthy control group in relation to subtypes of FTD.

2. Materials and methods

2.1. Participants

Fifty six patients aged between 15 and 45 years with FEP were recruited from the inpatient unit of Manisa Psychiatric Hospital, which is a public psychiatric hospital in Turkey. First-time admitted patients during their first acute phase of psychotic illness were screened and the ones that fulfilled our inclusion criteria were included in the study. A trained psychologist (EA) carried out the clinical assessments (SCID, PANSS, TLI, neurocognitive battery). Diagnosis was made based on SCID-I (Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV), Axis I Disorders). As part of the differential diagnosis, potential organic causes of psychosis were screened by routine laboratory tests and brain CT examination was applied to all patients at admittance. There were no patients with psychosis due to general medical conditions. Patients with affective psychosis were excluded. All the patients were under medication for less than six weeks or drug-naive in order to restrain the risk of bias from medication effects. At the time of the assessment, 32 (57%) patients were taking atypical antipsychotics, 18 (33%) patients were taking combinations of atypical antipsychotics, 3 (5%) patients were taking combinations of atypical and typical antipsychotics and 3 (5%) patients were drug-naive. Of the 56 patients, 22 (40%) patients received adjunctive anticholinergic agents (biperiden) for extrapyramidal side effects and 21 (38%) patients received adjunctive benzodiazepines (diazepam, lorazepam) for agitation. FEP patients having electroconvulsive treatment were excluded from the study as ECT might influence cognitive functioning and thought processes.

Forty five age- and gender-matched healthy subjects who had no previous history of mental, psychiatric and neurological disorders were included in the study as the control group. The recruitment of the controls also took place at the Manisa Psychiatric Hospital. The controls were recruited from hospital staff who had no relation to the patients. SCID-I was also administered to the control group to out rule any comorbid condition. The ones who were taking medications for psychiatric, neurological or common medical diseases such as hypertension or diabetes at the time of assessment were excluded from the study.

Neurocognitive assessment, including executive function, verbal learning, verbal memory, visual memory, attention/vigilance, processing speed, verbal fluency, cognitive flexibility and working memory was performed on both the patient and the control groups in order to screen for conditions that might affect cognition or language.

A trained psychologist (ŞS) rated the TLI scores of the participants. All the participants were Turkish native-speaking. Written informed consents were attained from each participant at recruitment. The study was approved by the Ethics Committee of Dokuz Eylül University School of Medicine.

2.2. Measures

2.2.1. Formal thought disorder

2.2.1.1. The Thought and Language Index. The Thought and Language Index (TLI) was developed for assessing FTD under standardized conditions [16]. Participant is required to produce eight one-minute speech samples in response to the eight standard pictures taken from the Thematic Apperception Test (TAT) [17]. The two-factor structure of the Turkish version of TLI has a Cronbach alpha value of 0.75 with a high interrater and test–retest reliability [18]. It comprises impoverishment of thought and disorganization of thought subscales. Impoverishment of thought subscale consists of three items: Poverty of speech, weakening of goal and perseveration. Disorganization of thought subscale includes five items: Looseness, peculiar word use, peculiar sentence construction, peculiar logic and distractibility. The entire interview is recorded on audiotape and then transcribed. These transcribed speech samples are assessed according to the TLI manual. As to the TLI manual, a score of 0.25, 0.50, 0.75 or 1.0 is given to each TAT picture depending on the severity of FTD. For one picture, a score of 0.25 indicates that the abnormality is questionable. A score of 0.50 or above indicates that the abnormality is clear. The sum scores of the eight TAT pictures give the mean severity of each TLI item.

2.2.2. Psychiatric symptom assessment

2.2.2.1. The Positive and Negative Syndrome Scale. The Positive and Negative Syndrome Scale (PANSS) [19,20] was used to assess the symptom severity in FEP patients. PANSS includes Positive Symptoms Subscale, Negative Symptoms Subscale and General Psychopathology Subscale.

2.3. Statistical analyses

The Statistical Package for the Social Sciences (SPSS) version 15.0 for Windows was used for all the analyses. Due to the condition that our data were not normally distributed, the Mann–Whitney U nonparametric test was used to

determine the significance of intergroup differences for continuous variables (age, years of education, TLI scores) and Spearman correlation coefficient was used to calculate the correlations between variables. Chi-square tests were used to analyze any differences between the groups for categorical variables (gender, family history of psychosis, sexual abuse, threatening life events, alcohol abuse, drug abuse).

In order to demonstrate how TLI items differentiate FEP patients from controls, logistic regression was conducted. Being patient/control was the dependent variable and all the TLI items were included as independent variables, while controlling for years of education, family history of psychosis and drug abuse.

3. Results

3.1. The study flowchart

Flowchart of the patients from screening to the study endpoint is shown in Fig. 1.

3.2. Demographic and clinical features

Demographic and clinical features of the FEP patients and the healthy controls are shown in Table 1. There were no
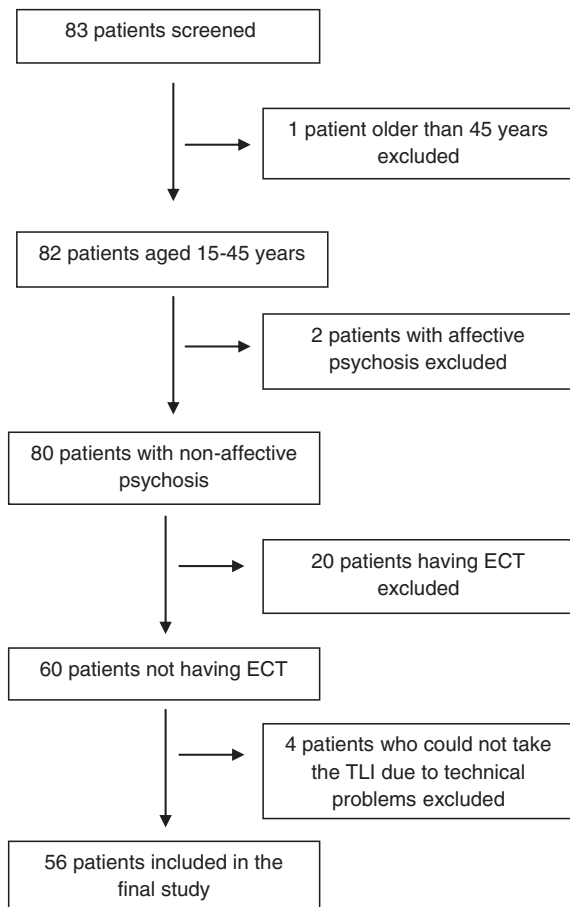

Fig. 1. Flowchart describing study subjects.

significant group differences between patient and control groups in age or gender. The FEP patients had significantly less education in years compared to the control group. The mean duration of untreated psychosis (DUP) of patients was 10.91 months. Seven of the 56 FEP patients (12%) were abusing drugs, including cannabis, cocaine and heroin. Psychosis was significantly more common in first degree relatives of FEP patients compared to that of controls.

3.3. Comparison of TLI items between FEP patients and healthy controls

As shown in Table 2, the FEP patients showed significantly higher scores on the items of poverty of speech (U = 701, p < 0.01), weakening of goal (U = 647, p < 0.01), perseveration (U = 193.5, p < 0.01), looseness (U = 1000.5, p = 0.05), peculiar word use (U = 479, p < 0.01), peculiar sentence construction (U = 726.5, p < 0.01) and peculiar logic (U = 415.5, p < 0.01). There were significant differences between the FEP patients and the controls with regard to impoverishment of thought subscale scores (U = 383.5, p < 0.01), disorganization of thought subscale scores (U = 338.5, p < 0.01) and total scores of TLI (U = 139, p < 0.01).

3.4. Association between TLI subscales and PANSS items P2 and N6

As to the previous research by Liddle et al. [16], impoverishment of thought subscale of TLI was found to be correlated with SANS alogia global score and disorganization of thought subscale with SAPS positive thought disorder global score. Regarding this finding, we thought it would be relevant to examine the correlations between TLI subscales and PANSS items P2 (conceptual disorganization) and N6 (lack of spontaneity and flow of conversation) in our FEP sample. There were no significant correlations between impoverishment of thought subscale and PANSS item N6 (rho = 0.03, p = 0.81), and between disorganization of thought subscale and PANSS item P2 (rho = 0.08, p = 0.56).

3.5. Severity of TLI items

Severity of TLI items in FEP patients and controls are shown on a bar chart (Fig. 2).

3.6. Prevalence of TLI items

A score of 0.50 or above for each of the eight pictures used in TLI refers that abnormality in one item is clear [16]. In this regard, we computed the average scores of the eight pictures for each TLI item. The percentage of FEP patients and controls that demonstrate FTD items at an average score between 0.50 and 1.00 are displayed in Fig. 3.

32% (n = 18) of the FEP group and 16% (n = 7) of the control group displayed poverty of speech. 4% (n = 2) of the FEP patients showed weakening of goal, 5% (n = 3) displayed perseveration, 7% (n = 4) displayed peculiar

Table 1
Demographic and clinical features of FEP and control groups.

Variable (mean ± S.D.)	FEP group (n = 56)	Control group (n = 45)	Test statistic	p
Age (years)	26.68 ± 5.78	28.02 ± 7.49	U = 1200.5	0.68
Gender (M/F), n	36/20	25/20	X^2 = 0.79	0.38
Education (years)	9.04 ± 2.97	10.16 ± 2.73	U = 928	0.02
Family history of psychosis	14 (25%)	3 (6.67%)	X^2 = 5.93	0.02
Sexual abuse	11 (19.64%)	5 (11.11%)	X^2 = 0.22	0.64
Threatening life events	42 (75%)	22 (48.89%)	X^2 = 0.4	0.53
Alcohol abuse	25 (44.64%)	18 (40%)	X^2 = 0.14	0.71
Drug abuse	7 (12.5%)	0	X^2 = 5.86	0.02
DUP (months)	10.91 ± 7.59	-	-	-
PANSS score	100.61 ± 17.41	-	-	-
Positive symptoms scale	26.21 ± 5.88			
Negative symptoms scale	22.75 ± 5.05			
General psychopathology scale	51.64 ± 10.17			

FEP = first-episode psychosis; S.D. = standard deviation; PANSS = Positive and Negative Syndrome Scale.

sentence construction and 9% (n = 5) showed peculiar logic at a level of 0.50 or above.

3.7. Logistic regression analysis

We used a forced entry logistic regression to determine the relative predictive values of FTD subtypes in differentiating FEP cases from controls. All the demographic/clinical variables showing significant group differences in Table 1 and the items of TLI in Table 2 were submitted to binary logistic regression analysis. As shown in Table 3, poverty of speech, perseveration and peculiar word use were found to differentiate FEP patients from controls while controlling for years of education, family history of psychosis and drug abuse. When all these variables are taken into analysis, they explain the 91% variance in the dependent variable (Nagelkerke R^2 = 0.91).

4. Discussion

Our goal in the present study was to compare an FEP sample to a healthy control group in relation to subtypes of FTD. We described the demographic and clinical correlates of FTD and demonstrated how TLI items differentiate FEP

patients from healthy controls when controlling for relevant demographic/clinical variables. In line with the vast amount of research on FTD, our results demonstrate that FEP patients had significant thought abnormalities compared to healthy controls in terms of impoverishment and disorganization of thought processes. Additionally, we found that poverty of speech, perseveration and peculiar word use were the significant thought impairments that differentiated FEP patients from controls after controlling for years of education, family history of psychosis and drug abuse.

People at high risk for psychosis and at prodrome stage of psychosis are shown to have FTD and communication deviance [21]. As a result of this basic impairment of the disorder, these people might end their education earlier, which in turn might cause impoverishment in their thought processes. On the other hand, education might serve as a protective factor and the ones with more years of education might show less impoverishment of thought. In FEP patients, we found that as the years of education increase, impoverishment in thought processes decreases. We found no association between years of education and disorganization of thought, revealing that rather than disorganized thought, impoverishment of thought might be more related to education.

Table 2
Comparison of TLI scores between FEP and control groups.

Variable (mean ± SD)	FEP group (n = 56)	Control group (n = 45)	U	p
Poverty of speech	3.28 ± 2.04	1.84 ± 1.51	701	<0.01
Weakening of goal	0.86 ± 1.22	0.12 ± 0.34	647	<0.01
Perseveration	1.20 ± 1.03	0.12 ± 0.21	193.5	<0.01
Looseness	0.21 ± 0.41	0.08 ± 0.23	1000.5	0.03
Peculiar word use	0.54 ± 0.65	0.05 ± 0.17	479	<0.01
Peculiar sentence construction	1.20 ± 1.83	0.08 ± 0.27	726.5	<0.01
Peculiar logic	1.59 ± 1.72	0.19 ± 0.37	415.5	<0.01
Distractibility	0	0	1260	1
Impoverishment of thought subscale	5.33 ± 3.14	2.08 ± 1.57	383.5	<0.01
Disorganization of thought subscale	3.53 ± 3.61	0.40 ± 0.52	338.5	<0.01
TLI total	8.87 ± 5.06	2.48 ± 1.47	139	<0.01

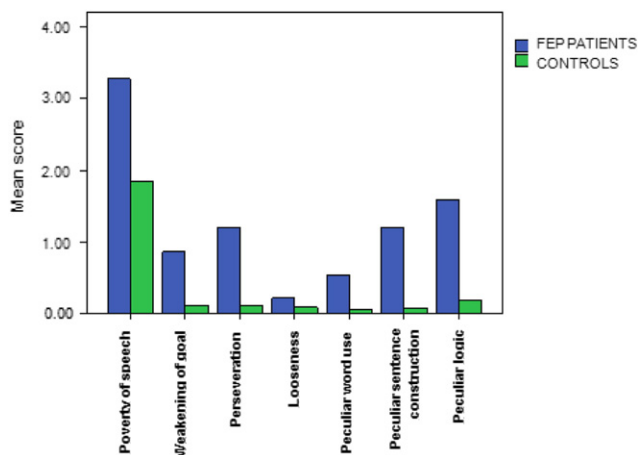FEP = first-episode psychosis; SD = standard deviation; TLI = Thought and Language Index.

Fig. 2. Severity of TLI items (mean scores) in FEP patients and controls.

Table 3
Logistic regression analysis of variables associated with FEP.

Measure	B	Wald	p	OR (95%CI)
Poverty of speech	−1.28	4.69	0.03	0.28 (0.09–0.89)
Weakening of goal	−0.45	0.18	0.67	0.64 (0.08–5.01)
Perseveration	−7.16	4.93	0.03	0.01 (0.00–0.43)
Looseness	−2.94	0.54	0.46	0.05 (0.00–139.17)
Peculiar word use	−4.62	3.96	0.05	0.01 (0.00–0.93)
Peculiar sentence construction	0.47	0.14	0.71	1.60 (0.13–19.21)
Peculiar logic	−2.98	3.79	0.05	0.05 (0.00–1.02)
Years of education	0.15	0.21	0.65	1.16 (0.61–2.19)
Family history of psychosis	−2.07	0.82	0.37	0.13 (0.00–11.12)
Drug abuse	19.64	0.00	1	-

CI, confidence interval; OR, odds ratio.

Liddle et al. [16], examined the correlation of the two TLI subscale scores with the SANS and SAPS global scores in patients with schizophrenia. Impoverishment of thought subscale was found to be correlated with the SANS alogia global score and disorganization of thought subscale with the SAPS positive thought disorder global score. Based upon this finding, we examined the possible correlations between impoverishment of thought subscale and PANSS item N6 (lack of spontaneity and flow of conversation), and between disorganization of thought subscale and PANSS item P2 (conceptual disorganization). We did not find this overlap between the TLI subscales and PANSS items P2 and N6. This might be because of our sample being not large enough to get this correlation or it might be that it was too early to be able to see such a correlation in an FEP sample that might develop later on.

In FTD research, there is wide range of assessment tools used for evaluation such as Thought, Language and Communication Scale [22], Thought Disorder Index [23], Bizarre-Idiosyncratic Thinking [24], Clinical Language Disorder Rating Scale [25], and Formal Thought Disorder-Patient and Carer Scale [26]. As for the FTD studies on FEP patients, FTD was mostly evaluated indirectly using the subscales of the other scales used for
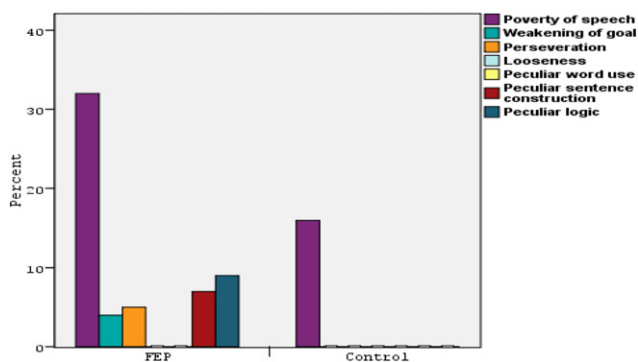
evaluating psychotic symptoms, such as the disorganized syndrome subscale of the Brief Psychiatric Rating Scale (BPRS) [27] or by using items from the Scale for the Assessment of Positive Symptoms (SAPS) and Scale for the Assessment of Negative Symptoms (SANS) [28,29]. In the study of Goldstein et al. [30], FTD was assessed by taking the average score of the three items (impaired understandability, derailment and illogical thinking) from the Schedule for Affective Disorders and Schizophrenia Change Version with Psychosis and Disorganization Items rating scale. Other FTD scales that have been used in first-episode samples are Thought, Language and Communication Scale [31], Clinical Language Disorder Rating Scale [9] and Bizarre-Idiosyncratic Thinking [32].

In FTD literature, there has not been a consensus about clinical conceptualization of FTD that researchers have agreed upon, which leads these principle scales to take different domains in attention. Although all these scales provide reliability and validity, we thought that TLI might be more suitable for our research. Thought, Language and Communication Scale was reported not to be sensitive to subtle thought anomalies [16], which might be disadvantageous for an FEP sample. Thought Disorder Index was defined as too time-consuming and extensive training is needed for its scoring [16]. Bizarre-Idiosyncratic Thinking focuses only on positive FTD. CLANG just assesses psycholinguistic levels as syntax, semantics and production. Formal Thought Disorder-Patient and Carer Scale does not involve a clinical interview, which makes the evaluation depend on the subjective responses of patients and carers. We thought that TLI might provide comprehensive information about FTD in an FEP sample. It is sensitive to subtle thought abnormalities, it is not time-consuming, it assesses both negative and positive FTD consisting of impoverishment and disorganization of thought categories and it makes assessments due to the clinician's objective evaluation. Additionally, TLI is the only FTD scale available in Turkish with strong reliability and validity measures [18].

As FTD has predictive value over the course of psychosis, it is a substantial subject to study. FTD was found to be the strongest predictor determining conversion from first-episode acute transient psychotic disorder to schizophrenia [33].

Fig. 3. Presence of TLI items in FEP and control groups identified at a level ≥ 0.50.

Moreover, FTD may predict relapse [34], is associated with poor quality of life [35] and may indicate a more severe form of psychotic illness [36]. Patients with psychotic depression who had FTD were found to have a relapse within a seven-year period more than other people with depression [34]. In particular, negative FTD tends to predict a chronic and persistent course of illness [31]. Poverty of thought present in the prodromal phase is predictive of conversion to psychosis and future deterioration [37]. FTD also has predictive value over functioning (objective quality of life) and life satisfaction (subjective quality of life). The disorganization dimension of FTD was associated with occupational and social functioning [32]. Verbal underproductivity tends to influence daily functioning and relations with others, while pressured speech affects satisfaction with life [35]. FTD, being considered a marker of illness severity, is substantial for predicting prognosis in psychosis [36]. These findings suggest that FTD is an important target for remission and recovery in psychosis.

FTD was qualified as a "complex multi-dimensional construct" [38]. It is noteworthy that certain FTD items, such as weakening of goal, looseness, peculiar sentence construction and peculiar logic, did not distinguish FEP sample from healthy controls in our study. This result points out the concept of FTD representing a dimensional construct distributed throughout the population and suggests that there may be a need to refine our clinical conceptualization of FTD and identify its etiological factors.

This study has various strengths and limitations. Our use of reliable and valid tools provided thorough clinical assessment of the sample. The study sample was representative of inpatient, non-affective FEP patients. The possible confounding effect of medication was restrained. A limitation of our study is that the psychologist who rated the TLI scores of the participants was not blinded to diagnosis. Another limitation is that we did not find any correlations between the TLI subscale scores and PANSS items P2 and N6, which might raise a potential question over the validity of the TLI scores in FEP samples. We used a neurocognitive battery in order to screen for conditions that might affect cognition and language but we did not include its scores in our regression analyses. It would be interesting to examine the predictors of FTD in this sample when controlling for neurocognitive deficits in future research. Additionally, longitudinal study of this sample might establish the prognostic value of FTD dimensions over psychosis.

Characterizing the possible changes in the categories of disorganization and impoverishment of thought after the first-episode of the diagnoses at follow-up might provide more information about the long-term outcomes of FTD in schizophrenia-spectrum disorders.

5. Conclusions

The results of this study implicate FTD in FEP patients. FTD seems to be a stable characteristic of the disorder. The evidence of disorganization and impoverishment in

thought processes already present during first-episode provides important information for the clinical manifestations of the disorder. Understanding persistent FTD as a predictor of early stage of psychosis may help the identification of these patients and the application of appropriate treatment strategies.

Role of the funding source

Conflict of interest

Acknowledgment

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