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Language comprehension and neurocognition independently and concurrently contribute to formal thought disorder severity in schizophrenia

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ABSTRACT

Formal thought disorder (FTD) in schizophrenia is a prevalent symptom that has a significant impact on patients but low remediation options. This is largely due to a still unclear aetiology, where both neurocognitive and language dysfunction have been shown to contribute. Given established relationships between neurocognition and language themselves, this study aimed to examine if language comprehension impairments have a significant effect on FTD severity independent of neurocognition. 54 schizophrenia/schizoaffective disorder patients ($M = 43.35$, $SD = 10.74$) completed three measures of language comprehension along with the MATRICS Consensus Cognitive Battery and the D-KEFS Colour Word Interference Test. Symptomatology was assessed using the Positive and Negative Symptom Scale and the Scale for the Assessment of Thought, Language and Communication. Hierarchical linear regression analyses revealed syntactic sentence processing had a significant, and independent, contribution to positive FTD severity above neurocognition, while semantic sentence processing and single word semantic processing did not. The findings support the existence of a specific relationship between language comprehension dysfunction and FTD; however the question of generalisation to all aspects of language processing or FTD types needs further investigation. The establishment of a specific language-related impairment in schizophrenia which contributes independently to FTD severity supports the benefit of language-based remediation approaches for alleviating FTD symptoms and their effects. Clinical, aetiological and nosological implications of the results are discussed.

1. Introduction

Formal thought disorder (FTD) is a core schizophrenia symptom that is characterized by aberrant patterns of speech and word use that hamper communicative ability. FTD is prevalent in the disorder (Roche et al., 2015a), and has critically been related to reduced functioning (Bowie et al., 2011) and poorer quality of life (Tan et al., 2014). It is also predictive of future social functioning from the first episode of psychosis (Roche et al., 2016), and is associated with increased social isolation (de Sousa et al., 2015). FTD is thus a logical and important treatment target for patients, however, current avenues for remediation are limited by a still inadequate understanding of the mechanisms underlying FTD manifestations.

There is substantial evidence for relationships between FTD and impairments in both neurocognition (Stirling et al., 2006; Tan and Rossell, 2014; Tan and Rossell, 2017) and language (Kuperberg et al., 2000; Rodriguez-Ferrera et al., 2001; Tan et al., 2016), which are currently the two primary candidates in the mechanistic literature. While the role of neurocognition, particularly semantic and executive dysfunction, is well-established with regards to FTD (McKenna and Oh, 2005), the contribution of language dysfunction to FTD manifestations is less straightforward (Bagner et al., 2003; Condray et al., 1996), and is yet to be rigorously investigated. Unlike the demonstrated co-existence of semantic and executive dysfunction in FTD (Stirling et al., 2006; Tan and Rossell, 2014), the concurrent roles of neurocognition and language in FTD have yet to be clearly delineated in a single sample.

1.1. Language dysfunction and FTD

Language dysfunction has always seemed a logical pathway to FTD, stemming from the early work of Kleist (1914) and Chaika (1974) to more recent conceptualisations (DeLisi, 2001; Kuperberg, 2010). Language processing impairments have been observed on many levels in schizophrenia (Covington et al., 2005). Kuperberg (2010) characterized

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FTD as the most severe form of language and communication deficits that occur across the schizophrenia spectrum. Investigating the relationship between FTD and language dysfunction has therefore been intuitive. Several studies have confirmed this relationship, showing that – when compared to schizophrenia patients without FTD – patients with FTD demonstrate exacerbated abnormalities in both lexical-semantic and syntactic processing (Allen, 1983; Faber and Reichstein, 1981; Manschreck et al., 1981). This is further reinforced by neuroimaging work demonstrating a relationship between FTD and neural abnormalities in language areas of the brain (Sans-Sansa et al., 2013; Sumner et al., 2018).

Language processing has two aspects: production and comprehension. While there has been work examining at the relationship between FTD and the former (Levine et al., 1996; Rodriguez-Ferrera et al., 2001), there is much less with the latter. The assessment of production has the benefits of increased ecological validity when unstructured, while the assessment of language comprehension is advantageous as it is not dependent on motor mechanisms that facilitate speech production (Tan et al., 2016) that may confound performance data. However, language comprehension tasks can be limited by other factors such as mode of delivery and individual verbal intelligence levels. Given that language production and comprehension occur in a loop (Cummings, 2008), it logically follows that aspects of language comprehension would be related to the manifestation of FTD (production). We have previously demonstrated this relationship (Tan et al., 2016). Consequently, the next logical question would be whether language comprehension deficits have an independent and distinct contribution to language production problems in schizophrenia, i.e. FTD. This is aligned with the recent Research Domain Criteria approach to understanding the causes of symptom manifestations in psychotic disorders (Insel et al., 2010).

1.2. The current study

The present study thus sought to examine the relationship between FTD and language comprehension at two levels: single words and sentences. Given previously mentioned evidence linking neurocognition to language processing in schizophrenia (Bagner et al., 2003; Condray et al., 1996), the aim was to investigate if performance on language tasks contributes to FTD symptoms independent of general neurocognition, including semantic and executive function. The language comprehension tasks used here assess the ability to correctly identify synonyms and appreciate sentential deep structure, while the neurocognitive tasks are standardized measures that correspond to characteristic domains of cognition (e.g. processing speed, attention) that are distinct from language processing components (e.g. syntax, pragmatics).

FTD is a heterogeneous disorder, with a number of differing language and cognitive abnormalities (Kircher and Thienel, 2005; Tan and Rossell, 2017); therefore the investigation of language as an orthogonal mechanism of FTD aetiology alongside neurocognition is both important and justified. While this heterogeneity suggests that the mechanisms of individual FTD symptoms may differ, there is still very limited work on this. From previous theoretical and empirical work, it was hypothesised that language task performance would have a significant contribution to FTD symptoms above neurocognition here.

2. Method

2.1. Participants

Fifty-four patients with DSM-IV schizophrenia/schizoaffective disorder were recruited from the Alfred Hospital and surrounding community clinics in Melbourne, Australia. All patients were on stable doses of antipsychotic medication and screened for previous traumatic brain injury, previous neurological illness, current substance abuse (previous 6 months), and English proficiency. All participants provided written voluntary informed consent prior to commencing assessment. Demographic and clinical characteristics are presented in Table 1. Ethical approval for this research was obtained from the Alfred Hospital Human Research Ethics Committee, Melbourne.

Table 1
Demographic and clinical characteristics of the sample ($n = 54$).

Variable	Mean	SD
Age (years)	43.35	10.74
Gender (% male)	51.9	–
Years of education	14.31	2.65
Premorbid intelligence (WTAR)	101.76	13.88
Age of onset	23.55	6.67
Length of illness	19.77	11.59
Medication (CPZE)	489.85	439.13
PANSS positive	14.04	4.65
PANSS negative (minus N6)	12.06	4.82
PANSS cognitive	9.31	3.85
PANSS excitement	4.85	1.50
PANSS emotional distress	9.70	3.31

Note. SD: standard deviation. WTAR = Wechsler Test of Adult Reading. CPZE = Chlorpromazine equivalence. PANSS = Positive and Negative Syndrome Scale. All PANSS scores calculated from van der Gaag et al. (2006), except PANSS negative which excludes item N6 (negative FTD).

2.2. Measures

2.2.1. Symptom assessment

FTD symptoms were assessed using the Scale for the Assessment of Thought, Language and Communication (TLC; Andreasen, 1986). Speech samples were collected during an audiotaped interview between the patient and the examiner (EJT and a trained PhD student). FTD ratings were done post-hoc from the audiotapes. Schizophrenia symptoms were assessed using the Positive and Negative Symptom Scale (PANSS; Kay et al., 1987).

2.2.2. Neurocognitive assessment

Neurocognition assessed using the MATRICS Consensus Cognitive Battery (MCCB; Nuechterlein et al., 2008), supplemented with the Delis-Kaplan Executive Function System Colour-Word Interference Test as a measure of inhibition (DKEFS Stroop; Delis et al., 2001). The MCCB individual domain t-scores and Overall Cognitive Score (OCS) were calculated using the prescribed MCCB scoring program and used in the subsequent analyses. Only the MCCB OCS was used in the regressions to minimise the number of variables and maximise the power of the analysis. The Inhibition vs. Colour Naming scaled score from the DKEFS Stroop was used as a measure of inhibition (INHB).

2.2.3. Language assessment

Two language tasks were used which provided three measures of language comprehension. These tasks were chosen to permit examination of language comprehension at both the single word and sentence levels. Lexical semantics was examined using a synonym identification task where participants were presented a target word then asked to choose the word with the most similar meaning (synonym) from three options: a synonym, a distracter (either a homophone or an antonym[1]), or an unrelated word. This was a paper-and-pencil task in which participants were asked to circle their chosen response without a time limit. There were 102 trials with the option positions of the synonym, distracter and unrelated word counterbalanced to prevent a visual bias in response. These were also pseudo-randomised such that no option appeared more than twice consecutively in the same position. Task accuracy and errors were recorded.

[1] Homophones are words that sound identical when pronounced (e.g. VEIL-VALE), while antonyms are words with opposite meanings (e.g. HOT-COLD).

Syntactic ability was examined using the Sentential Pairs and Meanings (SPAM) Task that we developed in a previous study (Tan et al., 2016). Participants were presented with 56 sentence pairs and asked to indicate if the two sentences in a pair had an identical meaning or not. There were two sentence pair types (28 each) – semantic (the object or subject of the sentence is changed to a similar or completely different word) and syntactic (the form of the sentence is changed such that the meaning is either retained or altered to assess the appreciation of deep structure). In both manipulations, the meaning of the second sentence is either kept the same as the first, or made different (see Tan et al., 2016 for more task details). Task accuracy and errors were recorded. This task yielded one set of scores each for the semantic and syntactic sentence conditions.

2.3. Statistical analysis

Spearman's correlations were conducted between all the neurocognitive and language variables and FTD symptoms measured using the TLC. To ensure the validity of the correlations, only symptoms present in >10% of the sample were examined (see Tan et al., 2015): poverty of speech (14.8%), tangentiality (22.2%), derailment (13%), circumstantiality (31.5%), loss of goal (13%) and perseveration (11.1%). Bonferroni correction for multiple comparisons was employed. Significant relationships between language and FTD variables were further explored using hierarchical linear regressions. A composite positive FTD score was created for this to simplify interpretations.

The main aim of the regression analyses was to examine the effect of language on FTD independent of neurocognition. This was achieved by entering the neurocognitive variables MCCB OCS and INHB in Block 1. In Block 2, the total correct responses to the language task being examined was entered. The specific ordering of the blocks was for the purposes of controlling for the influence of neurocognition in language performance. For language performance to be established as predicting variance in positive FTD independent of neurocognition, a significant increase in explained variance would have to be observed when Block 2 was added. If this is indeed the case, the contribution of language-specific abilities to positive FTD presentation can then be more confidently attributed. Given that correlations were expected between the neurocognitive and language variables, multicollinearity between predictors was gauged by examining the Variance Inflation Factor (VIF) before the results were interpreted.

3. Results

3.1. Relationship between FTD, neurocognition and language performance

Spearman's correlations between FTD scores and the neurocognition and language task variables are presented in Table 2. Means and standard deviations of patient scores on the TLC, MCCB and language tasks are presented in Supplementary Table 1. Significant correlations were observed between at least one language task and all FTD symptoms except poverty of speech and perseveration. It was then decided to exclude these two symptoms from subsequent analyses, with the latter excluded from the composite positive FTD score. Semantic sentence task accuracy was not significantly associated with the positive FTD score, and thus also excluded from further analyses.

3.2. The independent effect of language on positive FTD

The first regression examined the independent relationship between positive FTD and synonym identification. The predictive model was significant with the neurocognitive variables, $F(2,51) = 3.47$, $p = .039$, explaining 12% of the variance in positive FTD scores. No significant change in R^2 was observed when synonym identification accuracy was added to the model, $\beta = -0.12$, $p > .05$, $F(1,50) = 0.46$, $p = .50$, explaining just 0.8% of the variance in positive FTD scores.

The second regression examined the independent relationship between positive FTD and syntactic sentence task accuracy. Neurocognitive variables produced the same significant change in R^2, $F(2,51) = 3.47$, $p = .039$. An additional 10% of the variance was explained upon entering syntactic performance, $\beta = -0.39$, $p = .016$, $F(1,50) = 6.25$, $p = .016$. In both regressions, the VIFs (<2) were well within commonly accepted levels (O'Brien, 2007), thus allaying multicollinearity concerns regarding the regression outcomes.

4. Discussion

The aim of this study was to examine whether language comprehension deficits had a discrete impact on FTD severity independent of neurocognition. To the best of our knowledge, this study extends the literature on the relationship between language and neurocognition and FTD (Bagner et al., 2003; Rodriguez-Ferrera et al., 2001). The hypotheses were partially supported. After controlling for neurocognition, syntactic sentence task accuracy, but not synonym identification accuracy, significantly predicted positive FTD severity.

4.1. Language task performance and FTD

The findings support the proposition that a specific relationship exists between language dysfunction and FTD. The significant finding with the syntactic sentence task suggests that a poor appreciation of sentential deep structure has an independent impact on the presentation of positive FTD symptoms. This contrasts with the non-significant association between FTD and sentential semantics, which suggests that this phenomenon may not be generalised to all aspects of language processing. The ability to comprehend deep structure from surface form is an aspect of transformational grammar (Chomsky, 1965). Consequently, we can conclude that poor transformational grammar ability appears to induce FTD symptoms. This provides definitive evidence for a language-specific impairment of syntactic processing in the mechanisms of positive FTD. This finding is also aligned with and contributes to previous work highlighting syntactic-level language deficits in schizophrenia (Condray et al., 2002; Kuperberg et al., 2006).

Conversely, language processing at the word level did not significantly predict the severity of positive FTD symptoms, after controlling for the effects of neurocognition. This further highlights the non-generalisability of language impairment in FTD and there are two plausible explanations for the finding. First, lexical-semantic problems may not be related to the selected FTD symptoms that comprise the composite score used here. This would imply that FTD symptoms such as tangentiality and derailment do not ensue from misinterpretations of single words. Due to the heterogeneity of FTD we consequently propose that the investigation of lexical-semantic issues in relation to other individual FTD symptoms, such as word approximations or neologisms, would be a useful endeavour. Alternatively, problems with understanding word meanings may be more strongly associated with neurocognitive than linguistic processes. This would imply that single word language processing has a significant neurocognitive component, aligned with previous work (Bagner et al., 2003; Condray et al., 1996) and supported by the positive correlations observed in this sample. This does not, however, discount a relationship between single word processing and speech abnormalities but hints at a different pathway, particularly in FTD where neurocognitive problems are well-established. More work is required to clarify this.

It should also be noted that no significant associations were found between the language tasks and negative FTD. This suggests that the observations of reduced and monosyllabic speech are not related to problems with processing words or sentences but may have a different aetiology, such as problems with regulating situationally appropriate behaviour (Tan and Rossell, 2017). Alongside evidence of prognostic differences between positive and negative FTD (Roche et al., 2016), their individual mechanisms may thus differ as well.

Table 2
Spearman's correlations between FTD symptoms and neurocognitive and language measures ($N = 54$).

	MCCB OCS	DKEFS inhibition[a]	Poverty of speech[c]	Tangentiality	Derailment	Circumstantiality	Loss of goal	Perseveration	Positive FTD score
Neurocognition									
MCCB OCS	–	0.17	−0.12	−0.30*	−0.20	−0.24	−0.33*	−0.097	−0.33*
DKEFS inhibition[a]	0.17	–	0.061	−0.16	−0.17	−0.10	−0.32*	−0.25	−0.19
Language comprehension[b]									
Synonym identification task accuracy	0.48**	0.27*	0.17	−0.23	−0.17	−0.35**	−0.32*	−0.25	−0.33*
Semantic sentence task accuracy	0.35**	0.011	−0.19	−0.30*	−0.12	−0.18	−0.24	−0.24	−0.25
Syntactic sentence task accuracy	0.53**	0.36**	−0.056	−0.32*	−0.39**	−0.36**	−0.36**	−0.25	−0.46**

Note: MCCB OCS = MATRICS Consensus Cognitive Battery Overall Cognitive Score. Positive FTD score = Tangentiality + Derailment + Circumstantiality + Loss of Goal.
* $p < .05$.
** $p \leq .01$.
[a] Score from the Delis-Kaplan Executive Functioning System Color-Word Interference Test.
[b] Total correct responses.
[c] Also the negative FTD score.

In summary, these findings point to a language-specific impairment of syntactic function, that co-occurs with neurocognitive deficits, in the mechanisms of some FTD symptoms. The poor appreciation of transformational grammar rules of deep structure may contribute to some of the aberrant speech patterns in schizophrenia. A similar conclusion could not be reached for problems with understanding individual word meanings. As this is the first study to demonstrate this, these findings need replication.

4.2. Clinical, aetiological and nosological implications

The establishment of a specific language-related impairment in schizophrenia which contributes independently to FTD severity opens the possibility that language-based remediation approaches may be beneficial in alleviating FTD symptoms and their effects. In the wake of promising cognitive remediation outcomes, particularly those that target specific capabilities such as auditory and visual processing (Contreras et al., 2018; Fisher et al., 2009), a language-specific remediation approach could be plausible and effective.

At present no specific language-remediation package/s exist for FTD, however we are hopeful that the improved theoretical understanding provided by the research findings here will facilitate this process. Our data suggests abnormal deep structure processing as a potential target. To this end, the Treatment of Underlying Forms approach (Thompson and Shapiro, 2005) has been specifically developed to address deep structure processing in agrammatic aphasia, and can thus be potentially employed in FTD patients as well. Ameliorated FTD and improved communication would consequently lead to better clinical interactions for patients as well as better capacity for obtaining and maintaining both employment and social networks. These would then reduce issues with social isolation (de Sousa et al., 2015) and have positive impacts on quality of life.

On a related note, the relationship between FTD and language could potentially be harnessed to develop an objective measure of speech abnormalities. Traditionally used measures of FTD are primarily clinician-rated which is inherently subjective. A measure assessing language components related to FTD could theoretically circumvent these issues and lead to improved symptom classification. Admittedly this would require a battery assessing a number of FTD-related neurocognitive and language deficits. Apart from being tedious to compile and validate, the current elusiveness of an aetiological model for FTD presents a major challenge; however the current findings lend support to this eventual possibility. Similar work has already begun in the schizophrenia using both automated (Elvevag et al., 2007; Gupta et al., 2018; Minor et al., 2018) and trained rater instruments (Docherty, 2012; Minor et al., 2016; Rubino et al., 2011) to assess disturbances in speech patterns.

On an aetiological level, a distinct language impairment in FTD in schizophrenia becomes the fourth mechanistic component alongside semantic and executive dysfunction (Stirling et al., 2006; Tan and Rossell, 2014) as well as affect (Minor et al., 2016; Rubino et al., 2011). This should be confirmed through examining the FTD mechanisms in other disorders such as bipolar disorder and autism. Given the differences in FTD presentation across the different diagnoses (McKenna and Oh, 2005), the examination of the language-FTD relationship in other disorders would be beneficial to understanding if language dysfunction is partly responsible for the observed cross-diagnostic differences.

In terms of psychiatric nosology, FTD is currently classified as a psychotic symptom in the spectrum of schizophrenia. The results demonstrate clear roles for neurocognition and language in FTD in schizophrenia and further support a change in its nosological status (Tan and Rossell, 2015). They also further highlight the differences between positive and negative FTD.

4.3. Limitations

These findings should be considered with some caveats. First, the composite positive FTD score used here does not represent the gamut of positive FTD symptoms and so limits the generalisability of the findings. Recent factor analyses have proposed as many as six FTD symptom domains (Roche et al., 2015b). The four symptoms that comprise the composite score used here belong to the Disorganization domain, so it remains possible that language is not related to all aspects of FTD. Subsequent work should examine the current findings with other FTD symptoms and domains.

Second, the overall levels of FTD in this sample are low, which is likely related to the primarily community-dwelling sample who tend to be more symptomatically stable. While we have mitigated this by analysing only the more prominent FTD symptoms in this sample, we cannot fully discount lower overall FTD as a factor that may have influenced some of the correlations. Collectively, lower FTD levels and the use of a composite score, while appropriate for the study aims, also precluded our ability to directly investigate the relationship between language impairment and individual FTD symptoms. This is an important step for future research with larger samples – and thus more variability in FTD severity – to address. This is not to disregard the value of composite scores in the whole investigative process. Rather, they are one of a number of valuable tools that complement each other and help build up a comprehensive picture.

Third, this study only investigated a small portion of language processing abilities with much more needing to be done in relation to the varying manifestations of FTD. The same can be said for the breadth of neurocognitive assessments used here; for example, source monitoring which has been related to FTD (Nienow and Docherty, 2005). Future similar studies should consider a broader assessment of both language and neurocognition to replicate these findings and further specify the concurrent contributions of neurocognitive and language dysfunction to FTD. The present findings are ultimately just one piece of an intricate aetiological puzzle. Future work should be conducted with additional aspects of language processing in samples with higher and more diverse levels of FTD to confirm and expand on this finding beyond the FTD dimensions investigated here (i.e. verbosity). This would greatly improve the characterization of language impairment in FTD and lay the groundwork for potential avenues for remediation and improving patient outcomes.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.schres.2018.08.019.

Conflict of interest

The authors report no conflicts of interest in the reported research.

Contributors

ET was responsible for collecting the data, analysis and writing the manuscript. SR oversaw data collection and contributed to the analysis and manuscript.

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