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Original article

Altered syntactic abilities in first episode patients: An inner phenomenon characterizing psychosis

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ABSTRACT

Background: Research has consistently shown that language abilities represent a core dimension of psychosis; however, to date, very little is known about syntactic comprehension performance in the early stages of psychosis. This study aims to compare the linguistic abilities involved in syntactic comprehension in a large group of First Episode Psychosis (FEP) patients and healthy controls (HCs).
Methods: A multiple choice test of comprehension of syntax was administered to 218 FEP patients (166 non-affective FEP patients [FEP-NA] and 52 affective FEP patients [FEP-A]) and 106 HCs. All participants were asked to match a sentence they listen with one out of four vignettes on a pc screen. Only one vignette represents the stimulus target, while the others are grammatical or non-grammatical (visual) distractors. Both grammatical and non-grammatical errors and performance in different syntactic constructions were considered.
Results: FEP committed greater number of errors in the majority of TCGB language domains compared to HCs. Moreover, FEP-NA patients committed significantly more non-grammatical ($z = -3.2$, $p = 0.007$), locative ($z = -4.7$, $p < 0.001$), passive-negative ($z = -3.2$, $p = 0.02$), and relative ($z = -4.6$, $p < 0.001$) errors compared to HCs as well as more passive-affirmative errors compared to both HCs ($z = -4.3$, $p < 0.001$) and FEP-A ($z = 3.1$, $p = 0.04$). Finally, we also found that both FEP-NA and FEP-A committed more grammatical (FEP-NA: $z = -9.2$, $p < 0.001$ and FEP-A: $z = -4.4$, $p < 0.001$), total (FEP-NA: $z = -8.2$, $p < 0.001$ and FEP-A: $z = 3.9$, $p = 0.002$), and active-negative (FEP-NA: $z = -5.8$, $p < 0.001$ and FEP-A: $z = -3.5$, $p = 0.01$) errors compared to HCs.
Conclusions: This study shows that the access to syntactic structures is already impaired in FEP patients, especially in those with FEP-NA, ultimately suggesting that language impairments represent a core and inner feature of psychosis even at early stages.

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1. Introduction

Psychosis has been found to be associated with linguistic deficits [1–3] and poorer social and clinical outcomes [4,5]. The central role of language in the development of schizophrenia (SKZ) has been first hypothesized by Crow [6] who correlated the origin of psychotic symptoms with an altered hemispheric lateralization [7]. Furthermore, language comprehension deficits have been observed in the premorbid phase of SKZ [8], further suggesting that linguistic assessment is important for predicting the development of psychosis [5,9–11]. Additionally, syntactic deficits have been found in both First Episode Psychosis (FEP) patients [12] and in individuals at high-risk for psychosis [13].

Moreover, another pressing issue of clinical research is represented by the investigation of similarities and differences between affective and non-affective psychosis in the linguistic domain [14]. Interestingly, although speech deficits have been observed in both affective and non-affective FEP [15,16], syntactic comprehension abilities in these patients have not yet been clearly explored [15]. In general, language is generally divided in comprehension processing and syntactic processing. Comprehension has been described as sufficient vocabulary and knowing the meanings of enough words, while syntax has been described as set of rules, specific for each language, used to combine words in sentences, each word requiring for the generation of well-formed sentences [17].

Although only a few behavioral studies explored linguistic abilities in FEP patients, they have been consistently investigated in both patients with SKZ and BD. Indeed, two previous studies from our group explored the linguistic performance in chronic psychotic patients [18,19]. In particular, Tavano et al. [18] showed that patients with SKZ were significantly less able to produce appropriate interpretations, indicating the presence of abnormal pragmatic inferential abilities.

Also, the presence of pragmatic deficits in SKZ was further confirmed by a more recent study carried out by Bambini et al. [20], which reported altered pragmatic abilities, especially in comprehending discourse and non-literal meanings, in 77% of their patients with SKZ, ultimately suggesting that these abilities might be considered a core feature of SKZ.

Similarly, Perlini et al. [19] suggested that the syntactic receptive verbal abilities were impaired in both chronic SKZ and BD, being, however, more severe and generalized in SKZ than in BD. Also, impairments in syntactic abilities were suggested by Moro et al. [21] in patients with SKZ while processing of an anomaly detection task, which allow to investigate either the syntactic or semantic knowledge. The authors also reported that the syntactic impairments were independent from cognitive abilities and psychopathological measures.

Interestingly, these studies further aligned with the evidence reported by several other independent studies, which showed that patients with SKZ had severe and generalized deficits in terms of language impairments [6,7,22–25].

Therefore, it seems that language abilities are important to be studied in psychosis, especially because language is a complex dynamic cognitive system, which brings to integration of multiple levels of linguistic and cognitive processing [26]. Indeed, psychotic patients showed word-finding difficulties and lexical processing impairments [27] as well as they have the speech usually filled with irrelevant pieces of information and derailments [28].

In this context, this study aims to compare, for the first time, the linguistic abilities involved in syntactic comprehension in a large group of FEP patients and healthy controls (HCs), by considering both affective (FEP-A) and non-affective (FEP-NA) psychosis. In particular, we expected that a) FEP patients would show deficits in linguistic performance compared to HCs and b) FEP-NA patients would display more severe disturbances compared to both FEP-A and HCs.

2. Methods

2.1. Subjects

Patients were recruited in the frame of the 'Genetics Endophenotypes and Treatment: Understanding early Psychosis' (GET UP) Study (see Ruggeri et al. [29,30] for a detailed description of subjects' enrolment). ICD-10 diagnoses were obtained after 9 months from the first contact with participating psychiatric services using the Item Group Checklist of the Schedule for Clinical Assessment in Neuropsychiatry (IGC-SCAN) [31]. Overall, 218 FEP patients and 106 HCs were evaluated. Among FEP, 166 were diagnosed with non-affective psychosis (FEP-NA) and 52 with affective psychosis (FEP-A). Specifically, for FEP-NA patients the diagnoses were schizophrenia (F20; N = 64), schizotypal disorder (F21; N = 4), delusional disorder (F22; N = 33), brief psychotic disorder (F23; N = 33), schizoaffective disorder (F25; N = 20), unspecified psychosis not due to a substance or known physiological condition (F29; N = 12). For FEP-A patients the diagnoses were mania with psychotic symptoms (F30.2; N = 13), bipolar affective disorder (F31; N = 6), bipolar affective disorder, current manic episode without psychotic symptoms (F31.1; N = 1), bipolar affective disorder, current manic episode with psychotic symptoms (F31.2; N = 4), bipolar affective disorder, current episode of severe depression with psychotic symptoms (F31.5; N = 1), bipolar affective disorder, current mixed episode (F31.6; N = 2), bipolar affective disorder, unspecified (F31.9; N = 2), mild depressive episode (F32; N = 1), severe depressive episode with psychotic symptoms (F32.3; N = 22). Symptoms were assessed using the Positive and Negative Syndrome Scale (PANSS) [32], which is formed by one total score (PANSS-Total) and three sub-scales evaluating positive symptoms (PANSS-Positive), negative symptoms (PANSS-Negative) and general psychopathology (PANSS-Psychopathology), the Hamilton Depression Rating Scale (HDRS) [33], and the Bech–Rafaelsen Mania Rating Scale (BRMRS) [34]. Also, the Global Assessment of Functioning (GAF) [35] was administered. Finally, the Brief Intelligence Test (TIB) [36] was used to obtain a measure of the Intelligence Quotient (IQ). Patients with other mental and behavioural disorders, alcohol or substance abuse in the six months preceding the assessment, history of traumatic head injury, neurological or medical disease and mental retardation were excluded from the study. Notably, 99 out of 218 FEP patients (27 FEP-A and 72 FEP-NA) were drug-free. In contrast, 116 FEP patients (23 FEP-A and 93 FEP-NA) were taking different antipsychotic medications, either typical or atypical, and 3 FEP patients were taking only antidepressants (2 FEP-A and 1 FEP-NA). Specifically, FEP-A patients were taking haloperidol (N = 1), aripiprazole (N = 4), olanzapine (N = 8), paliperidone (N = 1), quetiapine (N = 5), risperidone (N = 6), and ziprasidone (N = 1). In contrast, FEP-NA were taking: haloperidol (N = 9), aripiprazole (N = 14), clozapine (N = 1), perphenazine (N = 2), olanzapine (N = 28), paliperidone (N = 8), quetiapine (N = 6), risperidone (N = 31) and ziprasidone (N = 1). With regards to antidepressants, three patients were taking only sertraline (N = 2, FEP-A) or paroxetine (N = 1, FEP-NA). Finally, within the groups of FEP-A patients, 11 were taking antidepressants or mood stabilizers in association with antipsychotics. HCs were recruited by word of mouth and leaflets. Subjects with a history of psychiatric symptoms, also in first degree relatives, were excluded from the study. All participants had Italian as native language. The GET UP was approved by the Ethics Committee of the Azienda Ospedaliera of Verona (http://www.ospedaliverona.it/Istituzionale/Comitati-Etici/Sperimentazione) on 6 May 2009 (Prot. N. 20406/CE, Date 14/

05/2009), and by the ethics committee of each participating unit [29]. All participants signed inform consent after having understood all issues involved in the study design.

2.2. Syntactic comprehension measures

A multiple choice test of comprehension of syntax was administered to all participants. In particular, an adapted computer based version of the 'Test di Comprensione Grammaticale per Bambini' (TCGB) [37] assessing syntactic comprehension was used. This test has been used in previous research conducted by our group, showing good psychometric properties [18,19]. Shortly, subjects were asked to match a sentence they hear with one out of four vignettes on a PC screen. Only one vignette represents the stimulus target, while the others are grammatical (which have a role of syntactic contrast with respect to the target) or non-grammatical (visual) (which do not have any specific role of syntactic contrast) distractors. The task analyses different grammatical structure such as locative (e.g." The dog is above the chair"), active negative (e.g. "The girl doesn't run"), passive-negative (e.g. "The piano is not played"), passive-affirmative (e.g. "The car is washed by the child"), and relative (e.g. "The vase that the child is painting is on the chair"). For a more detailed description of the test please refer to Perlini et al. [19].

2.3. Statistical analyses

All the analyses were conducted using R [38]. For exploring the presence of differences between the groups on clinical and sociodemographic variables we performed a chi–square test (χ^2), for qualitative variables (i.e. gender), and t -tests or Analysis of Variance (ANOVA), for quantitative variables. Then, we employed a hierarchical approach for investigating the differences between the groups in TCGB variables [39]. First, a general Multivariate Analyses of variance (MANOVA) with all TCGB variables as dependent variables as well as group, age, TIB and educational level as covariates were carried out in order to explore whether the variable "group" was significant. The MANOVA was carried out between the two groups (whole group of FEP vs HCs) and between the three groups (FEP-NA, FEP-A and HCs). Second, since the assumption of normality, necessary for a standard linear model, was not satisfied, a gamma generalized linear model with identity link function, corrected for Bonferroni, with group, age, TIB and educational level as covariates, was performed separately after we found that the variable group was significant in the MANOVA. Then, for each significant model, a post-hoc analysis was performed and the Holm correction for multiple comparisons was applied. Finally, ANOVAs based on gamma generalized linear model with identity link function with age, TIB and educational level as covariates, were carried out in order to analyse the relationship between clinical features and TCGB scales. We used Bonferroni to correct for multiple testing. Additionally, Cohen's f was employed for measuring the effect size of the regression in order to provide measures of magnitude of the observed correlations. Cohen's f^2 values can be interpreted as small (0.02), medium (0.15) and large (0.35) [40]. Notably, the regressions were considered significant based on both p-value and effect sizes, as suggested by Sullivan and Feinn [41].

3. Results

3.1. Socio demographic and clinical variables

No statistically significant differences were found in any of the socio-demographic variables between the whole group of FEP patients vs HCs as well as between FEP-NA, FEP-A and HCs, except for the educational level. Specifically, we observed that the whole group of FEP patients had lower educational level compared to HCs ($t = 10$, $df = 227.3$, $p < 0.001$). Similarly, we also found that educational level was different between the FEP-NA, FEP-A and HCs ($F_{(2,321)} = 46.5$, $p < 0.001$). Specifically, post-hoc tests showed that FEP-A ($z = 5.4$, $p < 0.001$) and FEP-NA ($z = 8.3$, $p < 0.001$) had lower educational level compared to HCs. Furthermore, significant differences were observed between FEP-NA and FEP-A patients on some clinical variables. Specifically, we found that FEP-NA patients showed higher PANSS-Total ($t = 4.3$, $df = 112.4$, $p < 0.001$), PANSS-Positive ($t = 6.1$, $df = 113.4$, $p < 0.001$) and PANSS-Psychopathology ($t = 3.1$, $df = 111.4$, $p = 0.03$) compared to FEP-A. Also, FEP-NA patients showed lower GAF scores compared to FEP-A ($t = -3.4$, $df = 79.0$, $p = 0.01$). Finally, the two groups did not differ in terms of PANSS-Negative, HDRS and BRMRS scores as well as in terms of dose of antipsychotics. Socio-demographic and clinical data are shown in Tables 1 and 2.

3.2. Syntactic comprehension

3.2.1. FEP patients vs healthy controls

Table 3 and Fig. 1 showed the significant results emerged from the post-hoc analysis.

Overall, the results showed that FEP patients committed more total errors than HCs in the comprehension of syntactic constructions ($z = -8.1$, $p < 0.001$). Specifically, they produced

Table 1
Socio-demographic and clinical variables in the whole group of first episode psychosis (FEP) patients and healthy controls (HCs).

	FEP patients (n = 218)	HCs (n = 106)	Statistics[a]	P-value, Bonferroni corrected
Age (years), mean ± SD	30.5 ± 10.01	31.8 ± 9.0	t = 1.1, df = 228.3	p = 1
Gender (males/females)	118/100	48/58	χ^2 = 1.8, df = 1	p = 1
Educational level (years), mean ± SD	11.7 ± 3.2	15.2 ± 2.9	t = 10, df = 227.3	p < 0.001
Race	Caucasian	Caucasian		
Age on onset (years), mean ± SD	30.1 ± 9.9	–	–	–
TIB Total, mean ± SD	109.9 ± 6.5	109.8 ± 3.7	t = -0.3, df = 315.6	p = 1
PANSS-Positive, mean ± SD	15.2 ± 5.7	–	–	–
PANSS-Negative, mean ± SD	16.4 ± 6.8	–	–	–
PANSS-Psychopathology, mean ± SD	35.6 ± 9.2	–	–	–
PANSS Total scores, mean ± SD	67.2 ± 17.8	–	–	–
BRMRS Total scores, mean ± SD	2.4 ± 3.7	–	–	–
HDRS Total scores, mean ± SD	15.8 ± 7.5	–	–	–
GAF Total scores, mean ± SD	47.8 ± 14.0	–	–	–
Dose of antipsychotics (Chlorpromazine equivalent doses)	245.5 ± 218.5			

BRMRS = Bech-Rafaelsen Manic Rating Scale; df = Degree of Freedom; PANSS = Positive and Negative Syndrome Scale; HDRS = Hamilton Depressive Rating Scale; FEP = First Episode Psychosis; GAF = Global Assessment of Functioning; HCs = Healthy controls; SD = Standard Deviation; TIB = Brief Intelligence Test.

[a] The statistical tests applied were the chi–square test for qualitative variables and t –tests for quantitative variables.

Table 2
Socio-demographic and clinical variables in the three study groups.

	FEP-NA (n = 166)	FEP-A (n = 52)	HCs (n = 106)	Statistics[a]	P-value, Bonferroni corrected	Post-hoc results (after correction for multiple comparisons with Holm method)
Age (years), mean ± SD	30.4 ± 9.9	31.1 ± 10.4	31.8 ± 9	$F_{(2,321)}$ = 0.7	p =0.5	
Gender (males/females)	91/75	27/25	48/58	χ^2 = 2.4, df = 2	p = 1	
Educational level (years), mean ± SD	11.56± 3.1	11.9 ± 3.5	15.2 ± 2.9	$F_{(2,231)}$ = 46.6	p < 0.001	FEP-NA = FEP-A<HCs
Ethnic group	Caucasian	Caucasian	Caucasian	–	–	
Age on onset (years), mean ± SD	30.1 ± 9.9	30.7 ± 10.5	–	t = −0.4, df = 81.06	p = 1	
TIB Total, mean ± SD	109.6 ± 6.3	111.1 ± 6.9	109.8 ± 3.7	$F_{(2,321)}$ = 1.1	p = 1	
PANSS-Positive, mean ± SD	16.2 ± 5.7	11.78 ± 4.3	–	t = 6.1, df = 113.4	p < 0.001	FEP-NA > FEP-A
PANSS-Negative, mean ± SD	16.8 ± 7.1	15.0 ± 5.4	–	t = 2.0, df = 112.8	p = 0.5	
PANSS-Psychopathology, mean ± SD	36.5 ± 9.6	32.7 ± 7.3	–	t = 3.1, df = 111.4	p = 0.03	FEP-NA > FEP-A
PANSS Total scores, mean ± SD	69.6 ± 18.2	59.4 ± 13.7		t = 4.3, df = 112.4	p < 0.001	FEP-NA > FEP-A
BRMRS Total scores, mean ± SD	2.5 ± 3.8	2.2 ±3.3	–	t = 0.5, df = 96.8	p = 1	
HDRS Total scores, mean ± SD	16.2 ± 7.6	14.6 ± 6.8	–	t = 1.4, df = 94.9	p = 1	
GAF Total scores, mean ± SD	45.9 ± 13.3	53.6 ± 14.7	–	t = −3.4, df = 79.0	p = 0.01	FEP-A > FEP-NA
Dose of antipsychotics (Chlorpromazine equivalent doses), mean ± SD	252 ± 243	224 ± 110	–	t = 1.2, df = 188.7	p = 1	

BRMRS = Bech-Rafaelsen Mania Rating Scale; df = Degree of Freedom; PANSS = Positive and Negative Syndrome Scale; HDRS = Hamilton Depressive Rating Scale; GAF = Global Assessment of Functioning; FEP-A = Affective First Episode Psychosis; FEP-NA = Non-Affective First Episode Psychosis; HCs = Healthy Controls; SD = Standard Deviation; TIB = Brief Intelligence Test.
[a] The statistical tests applied were the chi–square test for qualitative variables and t –tests or Analysis of Variance (ANOVA) for quantitative variables.

Table 3
Differences in syntactic comprehension between first episode psychosis (FEP) patients and healthy controls (HCs).

	FEP patients (n = 218)	HCs (n = 106)	Statistics[a]	P-value, Bonferroni corrected
TCGB Grammatical Errors, mean ± SD	2.8 ± 2.7	1.1 ± 1.4	z = −9.2	p < 0.001
TCGB Non Grammatical Errors, mean ± SD	0.4 ± 1.2	0.06 ± 0.2	z = −3.2	p = 0.005
TCGB Total Errors, mean ± SD	1.9 ± 2.3	0.6 ± 0.8	z = −8.1	p < 0.001
TCGB Locative Item, mean ± SD	0.7 ± 1.1	0.3 ± 0.6	z = −4.4	p < 0.001
TCGB Active-Negative Item, mean ± SD	0.9 ± 1.1	0.3 ± 0.5	z = −6.1	p < 0.001
TCGB Passive-Affirmative Item, mean ± SD	0.4 ± 1.0	0.1 ± 0.4	z = −3.5	p = 0.002
TCGB Passive-Negative Item, mean ± SD	0.4 ± 1.0	0.2 ± 0.6	z = −2.6	p = 0.07
TCGB Relative Item, mean ± SD	0.5 ± 1.1	0.1 ± 0.5	z = −4.3	p < 0.001

FEP = First Episode Psychosis; HCs = Healthy Controls; SD = Standard Deviation; TCGB = Test di Comprensione Grammaticale per Bambini.
[a] The post-hoc tests were calculated on the coefficient of a generalized linear model with gamma and identity link function corrected for multiple testing with Bonferroni correction.

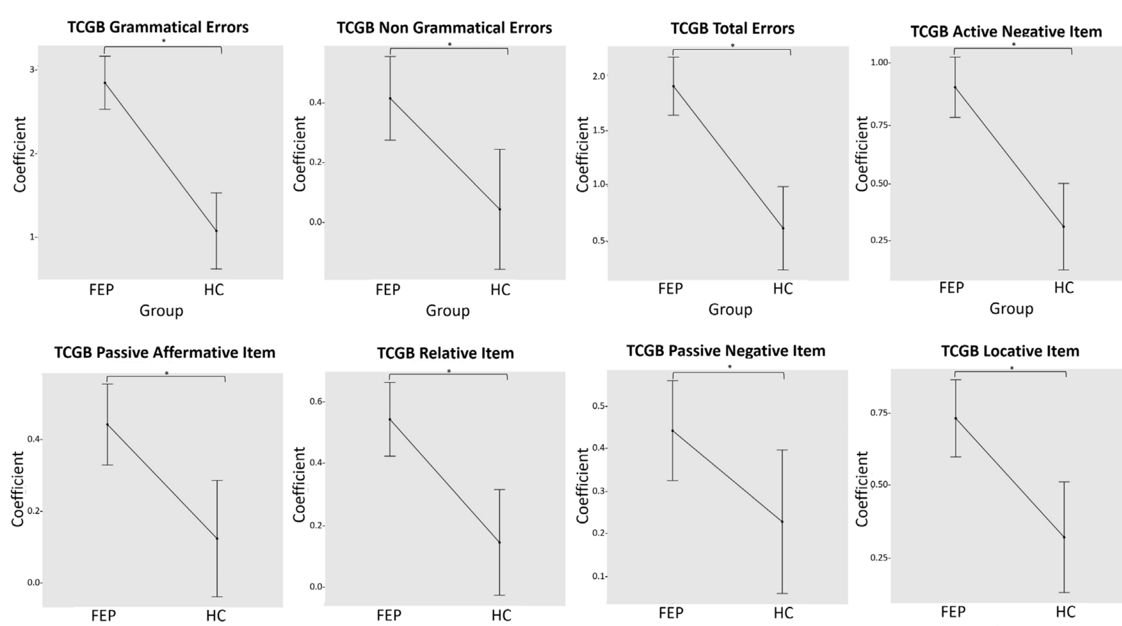

Fig. 1. Significant mean differences in TCGB syntactic comprehension measures between first episode psychosis (FEP) patients and healthy controls (HCs). The post-hoc tests were calculated on the coefficient of a generalized linear model with gamma and identity link function corrected for multiple testing with Bonferroni correction.

Table 4
Differences in syntactic comprehension among the three study groups.

	FEP-NA (n = 166)	FEP-A (n = 52)	HCs (n = 106)	Statistics[a]	P-value, Bonferroni corrected	Post-hoc results (after correction for multiple comparisons with Holm method)
TCGB Grammatical Errors	2.9 ± 2.8	2.4 ± 2.2	1.1 ± 1.4	HCsvsFEP-NA; z = -9.2 HCsvsFEP-A; z = -4.4 FEP-NAvsFEP-A; z = 2.4	HCsvsFEP-NA; p < 0.001 HCsvsFEP-A; p < 0.001 FEP-NAvsFEP-A; p = 0.2	FEP-NA = FEP-A> HCs
TCGB Non Grammatical Errors	0.5 ± 1.4	0.3 ± 0.5	0.06 ± 0.2	HCsvsFEP-NA; z = -3.2 HCsvsFEP-A; z = -1.6 FEP-NAvsFEP-A; z = 1.1	HCsvsFEP-NA; p = 0.007 HCsvsFEP-A; p = 1 FEP-NAvsFEP-A;p = 1	FEP-NA>HCs
TCGB Total Errors	2.0 ± 2.5	1.5 ± 1.5	0.6 ± 0.8	HCsvsFEP-NA; z = -8.2 HCsvsFEP-A; z = -3.9 FEP-NAvsFEP-A; z = 2.3	HCsvsFEP-NA; p < 0.001 HCsvsFEP-A; p = 0.002 FEP-NAvsFEP-A; p = 0.3	FEP-NA = FEP-A> HCs
TCGB Locative Item	0.8 ± 1.2	0.60 ± 0.9	0.3 ± 0.6	HCsvsFEP-NA; z = -4.7 HCsvsFEP-A; z = -1.8 FEP-NAvsFEP-A; z = 1.7	HCsvsFEP-NA; p < 0.001 HCsvsFEP-A; p = 1 FEP-NAvsFEP-A; p = 1	FEP-NA>HCs
TCGB Active Negative Item	0.9 ± 1.2	0.8 ± 0.8	0.3 ± 0.6	HCsvsFEP-NA; z = -5.8 HCsvsFEP-A; z = -3.5 FEP-NAvsFEP-A; z = 0.6	HCsvsFEP-NA; p < 0.001 HCsvsFEP-A; p = 0.01 FEP-NAvsFEP-A; p = 1	FEP-NA = FEP-A > HCs
TCGB Passive Affirmative Item	0.5 ± 1.1	0.2 ± 0.4	0.1 ± 0.4	HCsvsFEP-NA; z = -4.3 HCsvsFEP-A; z = -0.4 FEP-NAvsFEP-A; z = 3.1	HCsvsFEP-NA; p < 0.001 HCsvsFEP-A; p = 1 FEP-NAvsFEP-A; p = 0.04	FEP-NA > FEP-A and HCs
TCGB Passive Negative Item	0.5 ± 1.1	0.2 ± 0.4	0.2 ± 0.6	HCsvsFEP-NA; z = -3.2 HCsvsFEP-A; z = 0.07 FEP-NAvsFEP-A; z = 2.7	HCsvsFEP-NA; p = 0.02 HCsvsFEP-A; p = 1 FEP-NAvsFEP-A; p = 0.1	FEP-NA>HCs
TCGB Relative Item	0.6 ± 1.1	0.5 ± 1	0.1 ± 0.5	HCsvsFEP-NA; z = -4.6 HCsvsFEP-A; z = -2.0 FEP-NAvsFEP-A; z = 1.4	HCsvsFEP-NA; p < 0.001 HCsvsFEP-A; p = 0.7 FEP-NAvsFEP-A; p = 1	FEP-NA>HCs

FEP-A = Affective First Episode psychosis; FEP-NA = Non-affective First Episode Psychosis; HCs = Healthy Controls; TCGB = Test di Comprensione Grammaticale per Bambini.
[a] The post-hoc tests were calculated on the coefficient of a generalized linear model with gamma and identity link function, corrected for multiple comparisons with Holm method and for multiple testing with Bonferroni correction.

significantly greater grammatical ($z = -9.2$, $p < 0.001$) and non grammatical ($z = -3.2$, $p = 0.005$) errors as well as locative ($z = -4.4$, $p < 0.001$), active-negative ($z = -6.1$, $p < 0.001$), passive-affirmative ($z = -3.5$, $p = 0.002$) and relative ($z = -4.3$, $p < 0.001$) errors compared to HCs. No differences were observed in passive-negative sentences ($z = -2.6$, $p = 0.07$).

3.2.2. Affective FEP patients vs non-affective FEP patients vs healthy controls

Table 4 and Fig. 2 showed the significant results emerged from the post-hoc analysis.

Comparison between the three groups showed that FEP-NA and FEP-A patients committed more grammatical (FEP-NA: $z = -9.2$, $p < 0.001$; FEP-A: $z = -4.4$, $p < 0.001$), total (FEP-NA: $z = -8.2$, $p < 0.001$; FEP-A: $z = -3.9$, $p = 0.002$) and active-negative (FEP-NA: $z = -5.8$, $p < 0.001$; FEP-A: $z = -3.5$, $p = 0.01$) errors compared to HCs. Interestingly, FEP-NA patients also committed more non-grammatical ($z = -3.2$, $p = 0.007$), locative ($z = -4.7$, $p < 0.001$), passive negative ($z = -3.2$, $p = 0.02$) and relative ($z = -4.6$, $p < 0.001$) errors compared to HCs. Finally, FEP-NA patients produced more passive-affirmative errors compared to HCs ($z = -4.3$, $p < 0.001$) and FEP-A ($z = 3.1$, $p = 0.04$).

3.3. Correlations between syntactic comprehension and clinical or sociodemographic variables in FEP patients

No statistical significant correlations were observed between TCGB measures and educational level, PANSS-Positive, PANSS-Psychopathology, HDRS scores, BRMRS scores, GAF scores and dose of antipsychotics in the whole FEP group, except for PANSS-Negative that significantly positively correlated with TCGB grammatical errors ($p = 0.04$; effect size = 0.06). Additionally, no statistical significant correlations were observed between TCGB measures and educational level, PANNS-Negative, PANSS-Positive, PANSS-Psychopathology, PANSS-Total, HDRS scores, BRMRS scores, GAF scores and dose of antipsychotics in FEP-NA. Similarly, we found no statistical significant correlations between all TCGB measures and these scales also in FEP-A patients, except for TCGB grammatical errors, which were significantly positively correlated with GAF scores ($p = 0.049$; effect size = 0.04). Finally, with regards to HCs, no statistical significant correlations were observed between TCGB measures and educational level scores.

Please refer to Supplementary Materials for all the tables showing the p-values and effect sizes of the correlations performed between all TCGB measures and clinical or sociodemographic variables in the whole groups of FEP (Table S1), FEP-NA (Table S2), FEP-A (Table S3) and HCs (Table S4).

4. Discussion

To the best of our knowledge, this is the first study in the literature that explored syntactic comprehension language abilities in a large sample of FEP patients.

Overall, we found a greater number of errors in performing the syntactic comprehension test in the group of FEP patients as compared to HCs. This finding is consistent with previous research on patients with SKZ both conducted by our [18,19] and other

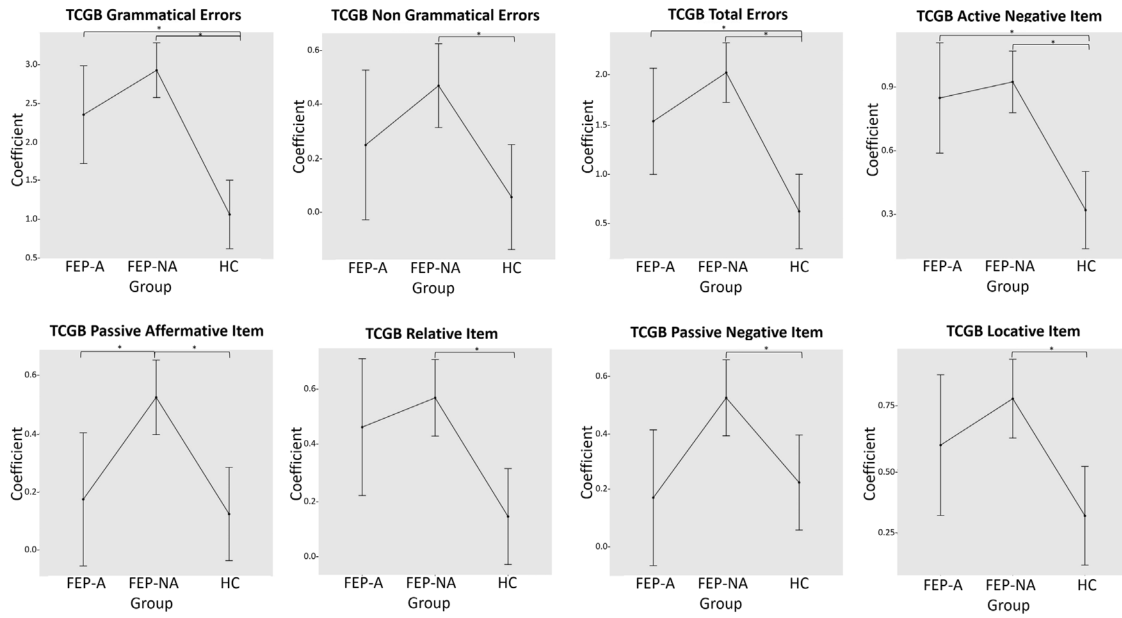

Fig. 2. Significant mean differences in TCGB syntactic comprehension measures between affective first episode psychosis (FEP) patients, non-affective FEP patients and healthy controls (HCs). The post-hoc tests were calculated on the coefficient of a generalized linear model with gamma and identity link function, corrected for multiple comparisons with Holm method and for multiple testing with Bonferroni correction.

[12,15,16] research groups. Indeed, in Tavano et al. [18] patients with SKZ showed significantly poorer syntactic diversity skills, including narrative and conversational speech, than HCs. Similarly, Perlini et al. [19] reported that patients with SKZ had selective impairments in active-negative sentences, as measured by the same TCGB test employed in our study, compared to HCs. Furthermore, the study also showed that patients with longer history of illness had a more generalized deficit in correctly identifying syntactic constructions compared to HCs [19]. Taken together, these findings suggest that syntactic deficits are a core dimension of psychosis, as also hypothesized by Crow et al. [6,7]. Specifically, according to Crow's hypothesis, the nuclear symptoms of psychoses represent a failure in establishing the left hemisphere dominance for language, which is one of the most lateralized dimension (most commonly to the left hemisphere) [7]. Indeed, it has to be noted that in the healthy brain syntactic abilities are anatomically sustained by a distributed fronto-temporal network within the left hemisphere, including the inferior frontal gyrus and the posterior superior temporal sulcus [42–46]. Therefore, altered lateralization, which is defined as an inverse asymmetry or a lack of prevalence of one hemisphere on the other, is one of the most replicated behavioral and neuroimaging findings in psychosis, being also present in FEP and in subjects at genetic risk to develop psychosis [47–50]. In this context, we might hypothesize that cerebral asymmetry changes may possibly explain the deterioration of syntactic abilities that we observed in our group of FEP subjects. However, further studies are necessary to confirm these alterations over time.

Moreover, our findings showed that both FEP-NA and FEP-A patients committed more grammatical and active negative errors compared to HCs, ultimately suggesting a shared syntactic deficit between the two diagnostic groups. These common syntactic impairments may be understood within the psychosis continuum theoretical framework [51]. The adoption of categorical system alone to classify psychotic disorders has been, indeed, widely questioned in light of evidence showing shared cognitive and brain deficits between non-affective and affective psychosis [52–54]. Notably, a recent study carried out by our group also reported similar deficits in linguistic and emotional prosodic [55] as well as in comprehension of figurative language [56] deficits between affective and non-affective FEP patients. Therefore, in line with these evidence, the syntactic deficits observed in both FEP-NA and FEP-A patients may represent a common clinical feature consistent with a possible nosological overlap. However, it is worth noticing that FEP-NA patients showed unique syntactic impairments, with worse performance in non-grammatical, locative, passive-affirmative, passive-negative and relative sentences compared to HCs as well as in passive-affirmative constructions compared to FEP-A patients, ultimately suggesting a more extensive language dysfunction in these patients. This result is also in line with our previous study [55] showing more prominent prosodic deficits in FEP-NA patients compared to FEP-A, as well as with previous research showing more severe neuropsychological deficits in SKZ as compared to BD [57,58], even when matched for clinical and demographic characteristics [57]. Furthermore, the more extensive language deficits found in our group of FEP-NA patients could be anatomically sustained by a more remarkable disruption of leftward functional hemispheric lateralization for language observed in SKZ compared to BD, independently of task performance, severity of symptoms, age and gender, as suggested by previous studies [59–61].

Therefore, based on these evidence, language disturbances seem to have a central role in the presentation of psychotic disorders and it should be considered as a potential target of intervention in FEP patients, as also suggested by a previous study [5].

4.1. Correlations between TCGB measures and clinical variables

Our results showed the presence of significant correlations between clinical symptoms and syntactic abilities only in the whole group of FEP and FEP-A patients. Specifically, we found that PANSS-Negative, for the whole group of FEP patients, and GAF scores, for only FEP-A patients, positively correlated with TCGB grammatical errors, ultimately suggesting that illness severity played a key role in influencing the performance in this test. Interestingly, these results seemed to partially align with the evidence reported by our previous study investigating prosody abilities in a partially overlapping sample, which showed that emotional prosody impairments were significantly correlated with illness severity [55]. Moreover, our results are also in agreement with evidence reporting significant correlations between illness severity and cognitive impairments in BD [62] and SKZ [63]. Indeed, it has been found that in BD the performance in executive functions was negatively correlated with the number of manic or depressive episodes [62]. Similarly, Heydebrand et al. [63] also observed that negative symptoms were associated with deficits in memory, verbal fluency and executive functions in first episode SKZ.

Therefore, our study further suggests that clinical symptomatology might play a key role on language deficits in FEP, ultimately proposing the need of a clear clinical stratification of FEP patients for a better understanding of language deficits in these patients. However, it is important to point out that the significant correlations found in our study were characterized by small effect sizes and therefore further studies are warranted to confirm our results.

4.2. Limitations

Although this study investigated language abilities in a large sample of FEP patients, some limitations might have reduced the generalizability of the results and therefore should be taken into account. First, all participating patients were on medication, which may have a potential confounding role. Therefore, future studies on medication-free FEP patients are warranted for ruling out the possible medication effects on language abilities. Second, the specific cognitive abilities were not assessed and they should be considered in future studies, especially because executive functions and working memory have an important role in language abilities, as suggested by previous investigations [64–66]. Nevertheless, in this study we controlled for an estimated measure of the IQ in all the statistical analyses.

5. Conclusion

This study shows that the syntactic comprehension impairments are already present in both FEP-NA and FEP-A patients, confirming that reduced access to syntactic structures is a core impairment of psychoses, in particular in FEP-NA patients. Therefore, given the centrality of language domain for functional outcome, the assessment of different aspects of language and the remediation of linguistic comprehension alterations should be included in routine clinical practice in the early phases of psychosis. Finally, further neuroimaging studies should be warranted in order to explore the relationship between syntactic comprehension impairment and cerebral asymmetry and connectivity at different illness stages.

Declaration of interest

None.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.eurpsy.2019.08.001.

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