Disorganization dimension in early psychosis

Emanuela Leuci, Lorenzo Pelizza*, & the Pr-EP Program Group

*Department of Biomedical and Neuromotor Sciences
Alma Mater Studiorum – University of Bologna
&
Department of Mental Health and Pathological Addictions
AUSL di Parma

lorenzo.pelizza@unibo.it

Starting questions in our research

Why did we decide to investigate disorganization in early psychosis?

And specifically in First Episode Schizophrenia (FES)?

INTRODUCTION -1

(1) Disorganization remains a crucial psychopathological dimension close to the "core" of schizophrenia (Ventura et al., 2009).

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In his unitary theory of schizophrenia, Bleuler (1911) stated: "…I call dementia praecox "Schizophrenia" because (as I hope to demonstrate) the "splitting" of the different psychic functions is one of its most important characteristics"; and he proposed "…loosening of associations" as the central mechanism underlying disturbances in *thinking* (thought and speech), *motivation*, and *affective expression*.

Psychopathology of schizophrenia

Loosening of associations

- thought/speech disturbances
  - FTD
  - Alogia
- affective incongruence
  - Inappropriate affect
  - Blunted affect
- volitional indeterminacy
  - Avolition
  - Non-purposeful behavior
- withdrawal from reality
  - Autism
  - Social isolation

Primary/Basic symptoms

Secondary/Accessory symptoms

Open questions - 1

Are disorganization and negative symptoms really two *different* psychopathological dimensions?

Or could they be considered as at two *opposite ends* of the same, unitary dimension?

FTD

Inappropriate affect

Non-purposeful behavior

As severity levels of disorganization increases, psychic mechanisms underlying thought, affect and motivation gradually get stuck

alogia

Blunted affect

Avolition

Social isolation

INTRODUCTION - 2

(2) Disorganization is significantly associated with poor prognosis and socio-occupational functioning decline (Rocca et al., 2018).

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From a treatment perspective, targeted interventions on disorganization may specifically lead to improve daily real-world functioning and patient's quality of life.

Open questions - 2

What effective interventions for the disorganization dimension?

…especially at the onset of illness, i.e., a particularly crucial period to favor positive outcomes and prognosis (McGorry, 2016)

Unfortunately, to date, most of the empirical research on disorganization has been conducted in patients with prolonged schizophrenia, and studies in early phases of the disorder are still relatively poor. Moreover, most of these investigations had a cross-sectional design and a lack of knowledge still affects the longitudinal course of disorganization in schizophrenia and their potential response to specific psychosocial and/or pharmacological treatments.

INTRODUCTION - 3

However, disorganization in schizophrenia has attracted much less attention (in both clinical and research studies) than positive and negative symptoms.

This relative neglect (mostly at the onset of illness) may be traced back to early models of schizophrenia psychopathology, which incorporated disorganization with symptoms of "reality distortion" (delusions, hallucinations) to define a "positive dimension".

The most common psychometric scales for the assessment of schizophrenia psychopathology (e.g., PANSS and SAPS) maintain this "old" conceptualization. Therefore, these scales and their main statistical dimension resulted from factor analyses (included the "disorganization" domain) did not originally develop for examining disorganization in schizophrenia and are composed of items not specifically centered on disorganized symptoms.

More suitable scales for assessing disorganization features (not only for thought and speech, but also for affect and motivation) in schizophrenia are thus needed.

AIMS

(1) to investigate the longitudinal stability of disorganization in young patients (aged 12-25 years) with FES treated within an "Early Intervention in Psychosis" (EIP) program across a 2-year follow-up period;

(2) to examine any significant association of disorganization with schizophrenia symptomatology, functioning, sociodemographic and clinical features, as well as with the specialized treatment components of our program across the follow-up.

SETTING: the Pr-EP program

The "Parma Early Psychosis" program

The Pr-EP program is not a stand-alone ("centralized") EIP service, but a diffused infrastructure implemented in all adolescent and adult mental healthcare services of the Parma Department of Mental Health, in Northern Italy (Leuci et al., 2019).

This allows us (a) to spread the EIP culture; (b) to improve the quality and effectiveness of treatments in accordance with well-defined guidelines on EIP; (c) to reduce the variability of interventions, standardizing them in both Child/Adolescent and Adult Mental Health Services (d) to make an accurate evaluation of the adherence of EIP treatments to the evidence-based recommendations.

Indeed, the PrEP program is a "real-world", non-academic setting, primarily engaged in the identification of optimal clinical care pathways in standard, public community mental health services within NHS. This model is spead in all DMH of the Emilia-Romagna region.

INSTRUMENTS

(1) the Positive and Negative Syndrome Scale (PANSS)
(2) the Global Assessment of Functioning (GAF) scale

These instruments were administered by trained Pr-EP team members both at baseline and every 12 months during the 2-year follow-up period.
Regular supervision sessions and scoring workshops were used to ensure the inter-rater reliability.

PANSS: disorganization factor

We clustered PANSS items following the 5 main dimensions proposed by Shafer & Dazzi (2019) in a recent meta-analysis on the PANSS factor structure: "Positive Symptoms", "Negative Symptoms", "Disorganization", "Affect" (Depression/Anxiety) and "Resistance/Activation".

Specifically, the "Disorganization" dimension included 8 PANSS items: P2 "Conceptual Disorganization", N5 "Difficulty in Abstract Thinking", N7 "Stereotyped Thinking", G5 "Mannerisms and Posturing", G10 "Disorientation", G11 "Poor Attention", G13 "Disturbance of Volition" and G15 "Preoccupation".

Baseline results

159 FES patients recruited from January 2013 to December to June 2019

Table 2
Baseline associations of PANSS "Disorganization" dimension score with func tioning, psychopathology, clinical and sociodemographic characteristics in th FES total group (n = 159).

Variables		PANSS "Disorganization" factor score (ρ)
PANSS dimensions		
Positive Symptoms		0.374[a]
Negative Symptoms		0.501[a]
Affect (Depression/Anxiety)		0.296[a]
Resistance/Activation		0.335[a]
PANSS items		
P1 Delusions		0.330[a]
P3 Hallucinations		0.181
P4 Excitement		0.081
P5 Grandiosity		0.131
P6 Suspiciousness/Persecution		0.284[a]
P7 Hostility		0.283[a]
N1 Blunted Affect		0.356[a]
N2 Emotional Withdrawal		0.384[a]
N3 Poor Rapport		0.362[a]
N4 Passive/Apathetic Social Withdrawal		0.307[a]
N6 Lack of Spontaneity/Flow of Conversation		0.408[a]
G1 Somatic Concern		0.169
G2 Anxiety		0.266[b]
G3 Guilt Feelings		0.130
G4 Tension		0.375[a]
G6 Depression		0.021
G7 Motor retardation		0.323[a]
G8 Uncooperativeness		0.254[b]
G9 Unusual Thought Content		0.340[a]
G12 Lack of Judgment and Insight		0.390[a]
G14 Poor Impulse Control		0.228
G16 Active Social Avoidance		[illegible][b]
GAF		−0.189[b]
Age at entry (in years)		[illegible]
Education (in years)		−0.115
DUP (in weeks)		−0.023
Males (n = 116)	Females (n = 43)	z (PANSS "Disorganization" subscale score)
20.29 ± 7.56	18.67 ± 7.04	−1.033
White Caucasian (n = 130)	Other Ethnic Group (n = 29)	Z (PANSS "Disorganization" subscale score)
20.00 ± 7.53	19.21 ± 7.10	−0.351

At **baseline** (T0), the PANSS Disorganization dimension score had significant positive correlation with all PANSS factor subscores (and "Lack of judgment/insight" item score). The statistically **strongest** association was with the **PANSS "Negative" domain** score.

Moreover, it had a statistically significant negative correlation with the **GAF** score.

Longitudinal results - 1

Table 3
PANSS "Disorganization" dimension subscores and their associations with psychopathology, functioning, specialized treatment components of the Pr-E program, sociodemographic and clinical features across the 2-year follow-u period in the FES total sample.

Variable (n = 98)	Baseline (T0)	2-year (T2) follow-up assessment time	z
PANSS "Disorganization" scores	19.63 ± 7.75	15.11 ± 6.46	−6.124[a]
Variables (n = 98) (T0-T2 Delta PANSS scores)		T0-T2 Delta PANSS "Disorganization" score (ρ)	
PANSS dimensions			
Positive Symptoms		0.536[a]	
Negative Symptoms		0.566[a]	
Affect (Depression/Anxiety)		0.404[a]	
Resistance/Activation		0.420[a]	
PANSS items			
P1 Delusions		0.540[a]	
P3 Hallucinations		0.238	
P4 Excitement		0.297	
P5 Grandiosity		0.251	
P6 Suspiciousness/Persecution		0.380[a]	
P7 Hostility		0.283	
N1 Blunted Affect		0.335[a]	
N2 Emotional Withdrawal		0.505[a]	
N3 Poor Rapport		0.365[a]	
N4 Passive/Apathetic Social Withdrawal		0.446[a]	
N6 Lack of Spontaneity/Flow of Conversation		0.227	
G1 Somatic Concern		0.203	
G2 Anxiety		0.279	
G3 Guilt Feelings		0.219	
G4 Tension		0.264	
G6 Depression		0.316	
G7 Motor retardation		0.519[a]	
G8 Uncooperativeness		0.257	
G9 Unusual Thought Content		0.366[a]	
G12 Lack of Judgment and Insight		0.360[a]	
G14 Poor Impulse Control		0.258	
G16 Active Social Avoidance		0.429[a]	
GAF		−0.351[a]	

Across the follow-up, a **significant decrease** in the PANSS "Disorganization" factor subscores was found.

The difference (delta) between T0 and T2 PANSS "Disorganization" dimension subscores maintained significant positive correlations with deltas in T0 and T2 scores of all other PANSS domains, especially with the **PANSS "Negative" dimension** (and with "Lack of judgment/insight" item scores)

Similarly, the delta between T0 and T2 PANSS "Disorganization" dimension scores maintained a statistically relevant negative correlation with the delta in T0 and T2 **GAF** scores.

Longitudinal results - 2

Table 4
Multiple linear regression analysis results of the difference in T0 and T1 or T2 PANSS "Disorganization" factor scores by specialized treatment components of the Pr-EP program across the 2-year follow-up period in the FES total sample.

T0-T1 Delta "Disorganization" score (n = 135)	B	SE	95% CI for B Lower	Upper	β	p	
Constant	1.357	1.088	−0.797	3.510	–	0.215	$R^2 = 0.089$
T0 equivalent dose of Chlorpromazine (mg/day)	0.270	0.181	−0.087	0.627	0.133	0.137	$F_{[df\ -\ 4]} = 3.041$ p = 0.020
T1 number of individual psychotherapy sessions	0.145	0.063	0.020	0.270	0.218	0.023	
T1 number of psychoeducational sessions for family members	0.068	0.096	−0.122	0.257	0.071	0.481	
T1 number of case management sessions	−0.001	0.025	−0.050	0.048	−0.003	0.978	
T0-T2 Delta "Disorganization" score (n = 98)	**B**	**SE**	**95% CI for B Lower**	**Upper**	**β**	**p**	$R^2 = 0.052$
							$F_{[df\ -\ 6]} = 0.751$ p = 0.610
Constant	2.263	1.713	−1.145	5.670	–	0.190	
T0 equivalent dose of Chlorpromazine (mg/day)	0.402	0.246	−0.088	0.891	0.192	0.106	
T1 equivalent dose of Chlorpromazine (mg/day)	0.017	0.016	−0.015	0.049	0.114	0.298	
T2 equivalent dose of Chlorpromazine (mg/day)	−0.113	0.183	−0.476	0.250	−0.072	0.539	
T2 number of individual psychotherapy sessions	0.040	0.049	−0.057	0.138	0.095	0.415	
T2 number of psychoeducational sessions for family members	−0.013	0.090	−0.192	0.167	−0.017	0.888	
T2 number of case management sessions	−0.002	0.019	−0.040	0.036	−0.011	0.924	

Our multiple linear regression analysis results showed that exclusively the T1 total number of individual psychotherapy sessions predicted improvements in the delta between T0 and T1 PANSS "Disorganization" dimension subscores after the first year of follow. This interesting association was not confirmed at T2.
(*most individual psychotherapy sessions were provided in the first year*)

CONCLUSIONS

Disorganization in FES patients represents a longitudinally stable index of psychopathological severity (already at the onset of illness and at the recruitment within specialized EIP programs). Particularly, disorganization in FES had significant enduring associations with functioning deterioration, psychopathology severity (especially negative symptoms) and some clinical aspects specifically involved in treatment resistance (i.e, lack of judgment/insight).

Moreover, longitudinal improvement in disorganization was predicted by the intensity of individual psychotherapy sessions offered to FES individuals in the first year of our intervention. Therefore, targeted psychotherapy interventions on disorganization in young people with early schizophrenia are recommended. Similarly, maintaining the intensity of these intervention on FES patients and their retention in care within specialized EIP as frequent as in the first year of treatment could further consolidate the longitudinal improvement of disorganization and successfully promote clinical, functional and personal recovery of FES patients in their belonging community.

LIMITATIONS

1) We examined FES individuals within a real-world setting, primarily involved in the delivery of optimal clinical care pathways within community mental healthcare services. Thus, our results are exclusively generalizable to similar populations.

2) The present research was conducted within an EIP program that did not specifically focus on disorganization. Indeed, the psychometric evaluation of major psychopathology was performed with the PANSS, which is not originally developed for measuring disorganization. However, given the widespread use of the PANSS in similar samples, our results have the potential to be replicated in other FES populations. This is of primary importance, since research in this topic is still relatively scarce and disorganization has a detrimental effect both on functioning and real-world performance.

3) Another limitation is that we could not evaluate the potential link between disorganization and neurocognitive functioning (although recent evidence suggests that they are separate dimensions) (Rocca et al., 2018). Thus, further research investigating this association in FES individuals is needed.

Thanks for your attention

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