Disorganization in first episode schizophrenia: treatment response and psychopathological findings from the 2-year follow-up of the "Parma Early Psychosis" program

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Background - *Disorganization* is a core dimension of schizophrenia (Ventura et al., 2009), yet it is relatively under-investigated compared to positive and negative symptoms, especially at the illness onset, although it has been considered as a crucial psychopathological domain significantly associated with poor prognosis (Minor and Lysaker, 2014) and functioning decline (presumably for its impact on social communication) (Rocca et al., 2018). Indeed, most of the empirical studies investigating the disorganized domain included patients with prolonged schizophrenia. This relative neglect may be traced back to early models of schizophrenia psychopathology, which incorporated disorganization with symptoms of "reality distortion" (i.e. delusions and hallucinations) to define a "positive dimension" (Tsuang and Winokur, 1974). This conflation of the disorganized and positive dimension persists even today: indeed, the most common psychometric scales for the assessment of schizophrenia psychopathology (both in research and in clinical practice) maintain this outdated conceptualization (Marneros et al., 1991). Therefore, the aims of this research were (1) to monitor the longitudinal stability of disorganized symptoms in young patients with *First Episode Schizophrenia* (FES) along a 2-year follow-up period, and (2) to examine any significant association of disorganization with functioning, psychopathology and the specific treatment components of an "Early Intervention in Psychosis" (EIP) program across the 2 years of follow-up.

Methods – At baseline, 159 FES individuals (aged 12–35 years) completed the Positive And Negative Syndrome Scale (PANSS) and the Global Assessment of Functioning (GAF). Spearman's correlation coefficients and multiple linear regression analysis were carried out. We clustered the PANSS 30 items in the following 5 main dimensions: "Positive Symptoms", "Negative Symptoms", "Disorganization", "Affect" (Depression/Anxiety) and "Resistance/Activation" (Shafer & Dazzi, 2019). 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".

Results – Our findings showed that FES patients had relevant levels of disorganized symptoms at the enrollment within a specialized EIP program. During the follow-up period, disorganization had relevant enduring positive associations with PANSS negative symptoms, lack of judgment/insight and positive symptoms, as well as significant enduring negative correlation with GAF scores. Along the 2 years of follow-up, FES patients also showed a relevant improvement in disorganization symptoms. This reduction was specifically associated with the number of individual psychotherapy sessions provided during the first year of treatment.

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]

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]

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**	
Constant	2.263	1.713	−1.145	5.670	–	0.190	$R^2 = 0.052$
T0 equivalent dose of Chlorpromazine (mg/day)	0.402	0.246	−0.088	0.891	0.192	0.106	$F_{[df = 6]} = 0.751$ p = 0.610
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	

The statistically strongest correlation of disorganization was with negative symptoms, both at baseline and along the 2 years of follow-up. These results cohere with Blueler's conceptualization of schizophrenia, suggesting that other crucial clinical features (currently classified as negative symptoms [i.e. affective incongruence, volitional indeterminacy and withdrawal from reality]) could be considered as "basic" (i.e. "nuclear") symptoms of the disorder, together with thought and speech disorganization (McNally, 2016). This leads to hypothesize an early and enduring link between disorganized and negative symptoms in schizophrenia, with a putative potentiating detrimental effect on daily functioning and social participation. our findings also showed significant baseline correlations of disorganized symptoms with a lack of judgment/insight and other PANSS items representing an index of potential treatment resistance (i.e. uncooperativeness and hostility).
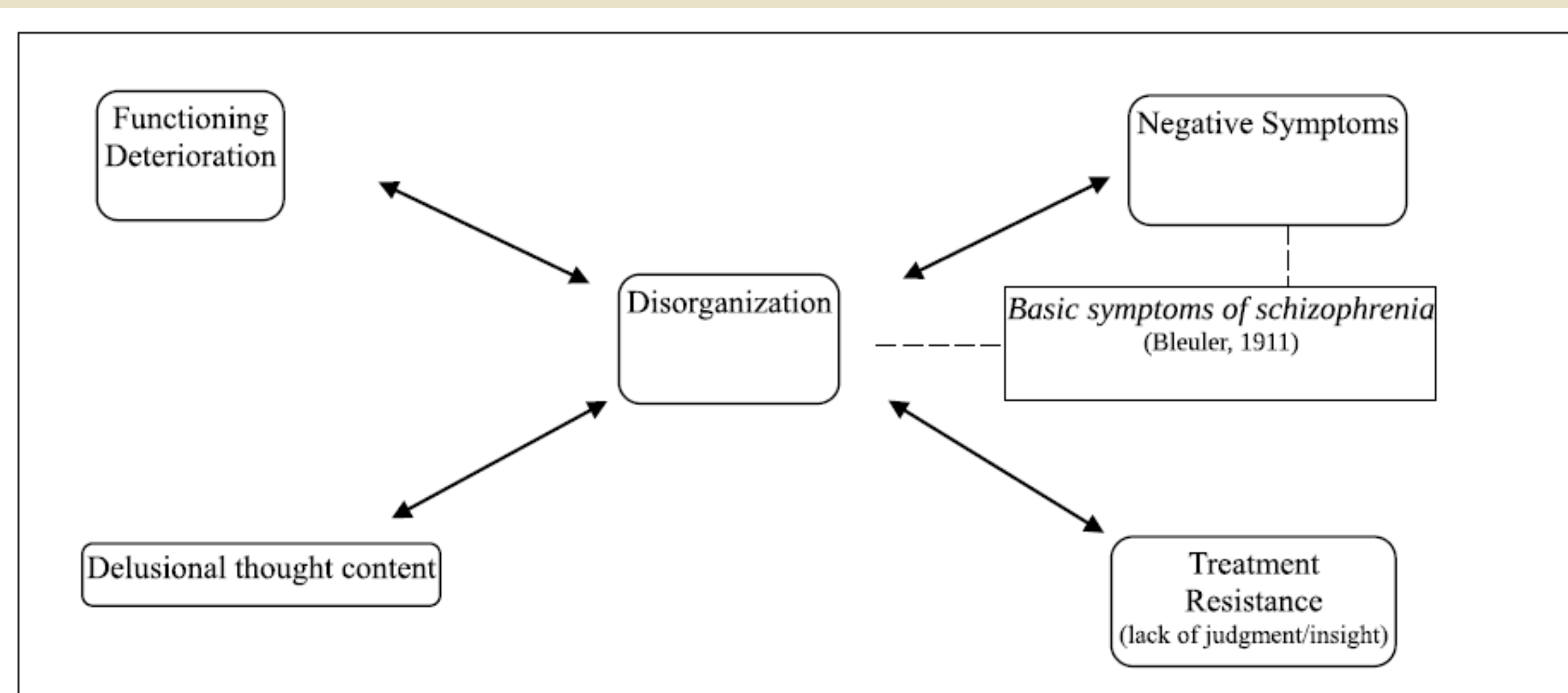

Fig. 1. Enduring associations of disorganization with other clinical dimensions in first-episode schizophrenia: psychopathological considerations.

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However, the effectiveness of psychotherapy was not confirmed at the end of the 2-year follow-up period. Considering that most of the Pr-EP individual psychotherapy sessions were offered within the first 12 months of treatment, maintaining a similar intensity of individual psychotherapy (and, more in general, a high intensity of FES patient's taking charge within mental healthcare services) at least still along the first 2–3 years of our EIP protocol could further promote the longitudinal improvement of disorganization and a better clinical/functional recovery of young people with FES. No associations between disorganized symptoms and equivalent dose of antipsychotic medication along the 2-year follow-up period were found.

In **conclusion**, Disorganization is clinically relevant in FES patients, in which it seems to represent a longitudinally stable index of psychopathological severity (already at the recruitment within specialized EIP programs). However, its temporal trajectory reveals a decrease over time, together with the delivery of specific, patient-tailored EIP interventions.