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The interplay between functioning problems and symptoms in first episode of psychosis: An approach from network analysis

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ABSTRACT

The relationship between psychotic symptoms and global measures of functioning has been widely studied. No previous study has assessed so far the interplay between specific clinical symptoms and particular areas of functioning in first-episode psychosis (FEP) using network analysis methods. A total of 191 patients with FEP (age 24.45 ± 6.28 years, 64.9% male) participating in an observational and longitudinal study (AGES-CM) comprised the study sample. Functioning problems were assessed with the WHO *Disability Assessment Schedule (WHODAS)*, whereas the *Positive and Negative Syndrome Scale* (PANSS) was used to assess symptom severity. Network analysis were conducted with the aim of analysing the patterns of relationships between the different dimensions of functioning and PANSS symptoms and factors at baseline. According to our results, the most important nodes were "conceptual disorganization", "emotional withdrawal", "lack of spontaneity and flow of conversation", "delusions", "unusual thought content", "dealing with strangers" and "poor rapport". Our findings suggest that these symptoms and functioning dimensions should be prioritized in the clinical assessment and management of patients with FEP. These areas may also become targets of future early intervention strategies, so as to improve quality of life in this population.

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1. Introduction

Psychotic disorders are associated with a worse quality of life (Malla et al., 2004), a wide and diverse array of psychosocial difficulties (Switaj et al., 2012), and an increase in Morbi-Mortality (Morgan et al., 2014), resulting in a life expectancy of approximately 20 years below that of the general population (Laursen et al., 2014).

The relationship between psychotic symptoms and functional outcomes has been widely studied with mixed results (Siegel et al., 2006; Stouten et al., 2017; Strassnig et al., 2015). Special attention has been paid to negative symptoms, which have been related to poor functional outcomes (Akinsulore et al., 2015; Apiquian et al., 2007; Ayesa-Arriola et al., 2013; Hunter and Barry, 2012; Rabinowitz et al., 2012), particularly regarding occupational impairment (Marwaha and Johnson, 2004), financial dependence (Ho et al., 1998; Malla, 2005), difficulties in social relationships (Galderisi et al., 2013), losses in daily activities (Juckel et al., 2008; Siegel et al., 2006), social withdrawal and cognitive impairment (Cullen et al., 2011). Positive symptoms have been related to work performance (Hatta et al., 2003) and social difficulties (Lyngstad et al., 2018), whereas disorganized symptoms seem to be related to poorer functioning (Galderisi et al., 2013). Finally, regarding depressive symptoms, some authors defended their role in predicting social inclusion (Gardner et al., 2019) and their relation to severity of disability (Lyngstad et al., 2018), especially regarding interpersonal functioning (Chudleigh et al., 2011; Galderisi et al., 2013; Sabbag et al., 2012).

Psychotic symptoms seem to impact on daily functioning even when the symptoms do not reach the clinical threshold for a disorder (Nuevo et al., 2012). People with psychotic experiences appear to have poorer global functioning than clinical samples without psychotic experiences (Kelleher et al., 2015). What is more, the relationship between psychosis and functioning has also been reported in patients who had already achieved syndrome recovery (Diaz et al., 2013).Therefore, although remission may be a necessary step to recovery, it is not sufficient, as patients that achieve symptomatic remission are not necessarily functioning well (AlAqeel and Margolese, 2012; Grau et al., 2016; Os et al., 2006; San et al., 2007). Consequently, obtaining symptomatic improvement as the only treatment goal bears the risk of overestimating the patients' overall functioning (Schennach-Wolff et al., 2009).

However, most of the previous studies have analysed both functioning and psychopathology using global scores measures (Switaj et al., 2012), which do not provide information on the interplay between specific symptoms and particular areas of functioning. Considering the multidimensional nature of both clinical symptoms (van Os et al., 2009) and functioning (Navarro-Mateu et al., 2017; World Health Organization, 2001) in psychotic disorders, such information may be essential to disentangle the complex interaction patterns between both kinds of outcomes, as dysfunction in each domain may be driven by different aspects of the illness (Cotter et al., 2017).

Innovative approaches to psychopathology argue that mental disorders could be described as a syndromic constellation of symptoms that hang together empirically, often for unknown reasons (Borsboom, 2017). From this perspective, the interplay among symptoms and biopsychosocial components, such as functional domains, could be conceptualized as a complex system, forming a network of interacting or even reinforcing elements (Borsboom and Cramer, 2013).

Network analysis represents an important innovation in the study of the interplay among variables (Galderisi et al., 2018b). With this technique, it is possible to verify the simultaneous relations between variables, unlike traditional methods, such as regression analysis and principal component analysis, in which statistical models are obtained that can bring answers to the research hypotheses by adjustments and data reduction (Leme et al., 2020). Moreover, in contrast to other techniques like structural equation models, it neither requires a priori assumption regarding the association among the variables nor the selection of predictors, mediators, and outcome measures (Galderisi et al., 2018b). Network analysis has been previously applied in order to explore the interactions between psychotic symptoms (Bak et al., 2016; Isvoranu et al, 2016, 2017; van Rooijen et al., 2017), as well as to review the interplay between psychopathological variables and functioning in patients with schizophrenia (Galderisi et al., 2018b, 2020) and with first episode of psychosis (FEP)(Chang et al., 2019). However, all these previous studies have used overall functioning scores, which may not capture the heterogeneity of outcome (Bratlien et al., 2013).

Improving knowledge of the interactions between clinical symptoms and specific areas of functioning may be useful for designing more personalized early intervention and rehabilitation programs during the first few years after the FEP, which have been described as a window of opportunity for intervention (Birchwood et al., 1998) that can positively impact long-term outcome (Díaz-Caneja et al., 2015; Lambert et al., 2006). Therefore, the aim of the present study is to evaluate how different areas of functioning are inter-related with specific clinical symptomatology in patients with FEP from a multidimensional and transdiagnostic perspective.

2. Material and methods

2.1. Study sample

All the study subjects were participants in an observational and longitudinal study of patients with first episode of psychosis (AGES-CM), carried out at the outpatient clinic and inpatient unit at the seven largest University Hospitals in the Community of Madrid, Spain. The study protocol was approved by the appropriate institutional ethics committee according to the principles of Good Clinical Practices (CPMP/ICH/135/95). 208 patients provided informed consent from February 2013 to May 2019. The patients should meet the following criteria to be included in this study: a) age between 7 and 40 years; and b) experiencing their first episode of psychosis (per DSM-IV-TR or DSM-5 criteria) with a total lifetime duration of positive psychotic symptoms lower than 24 months. Exclusion criteria were: a) meeting diagnostic criteria for other current Axis-I mental disorders (except substance use disorder); b) meeting DSM-IV-TR criteria for mental retardation; c) history of neurodevelopmental disorders or head injury with loss of consciousness; and d) pregnancy.

Subjects with missing values (n = 17) were excluded from our analysis, after checking that data were missing completely at random (Little's MCAR test: χ^2=.384.644, DF = 341, $p > .05$). Accordingly, 191 patients took part in our analytical sample.

2.2. Measures

Sociodemographic information was collected from patients and medical records. It included: age, sex, marital status (single, steady partner or divorced), level of education (elementary, secondary or university), parental socioeconomic status following the Hollingshead's Index of Social Position (Hollingshead, 1957), and occupational status (un/employed, student or pensioned). Functional and clinical assessments were conducted by a trained psychiatrist and psychologist. Diagnosis was established according to the Structured Clinical Interview for DSM-IV Axis-I disorders (SCID-I)(FIRST, 1997) and the Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS-PL), Spanish version (Ulloa et al., 2006).

Functioning was assessed with the WHO *Disability Assessment Schedule (WHODAS 2.0)*. It was designed for the evaluation of health and disability at population level or in clinical practice, providing a common metric of the impact of any health condition in terms of functioning (Ustun et al., 2010). This instrument captures the level of functioning within the last 30 days in six domains of life: Cognition, Mobility, Self-care, Getting along with others, Life activities, and Participation. The 12 items are assessed in a 5-point Likert-scale (from 0 = "no disability" to 5 = "extreme disability"). For the purposes of this work, we included the 12 items in our network as a measure of different

dimensions of functioning. Its internal consistency, measured by Cronbach's alpha, was 0.88 for the total scale in our sample.

The *Positive and Negative Syndrome Scale* (PANSS)(Kay et al., 1987) was used to assess symptom severity in a 7 point Likert-scale, which represents increasing levels of psychopathology (from 1 = "absent," to 7 = "extreme"). In line with previous research (Campellone et al., 2018; Capatina and Miclutia, 2018; Keane et al., 2018; Robinson et al., 2019), the scores for the dimensions "positive," "negative," "disorganized," "excited," and "depressed" symptoms were calculated in accordance with the 5-factor solution proposed by Wallwork (Wallwork et al., 2012), which has shown good psychometric properties in Spanish patients with schizophrenia (Rodriguez-Jimenez et al., 2013). Individual scores for each factor were calculated by dividing the sum of the included item scores by the number of items in the factor (Wallwork et al., 2012). The PANSS scale has shown an adequate internal consistency in our sample. Cronbach's alpha coefficients for each factor were: 0.77 for Positive factor, 0.92 for Negative factor, 0.70 for Disorganized factor, 0.77 for Excited factor, and 0.73 for Depressed factor.

The Hamilton Depression Rating Scale (Hamilton, 1960) was used as a measure of depression severity. The scale contains 17 items, distributed in a 3- or 5-point Likert-scale. Global score was calculated. In the present study, internal consistency, measured by Cronbach's alpha, was 0.81 for the total scale.

The Young Mania Rating Scale (Young et al., 1978) was applied in order to evaluate the intensity of manic symptoms. It is composed by 11 items, rated in a 5-point Likert-scale. The total score was calculated. In our sample, its internal consistency was $\alpha = 0.78$.

2.3. Statistical analysis

Frequency analysis and Mean and SD statistics were applied in order to describe the characteristics of the sample. In addition, network analysis was conducted with the aim of analysing the patterns of relationships between the different dimensions of functioning and the PANSS factors. From this perspective, nodes represent areas of functioning and symptoms, whereas edges represent the statistical relationships between them. To limit the number of spurious connections, we applied the regularization method "least absolute shrinkage and selection operator (LASSO)," which limits the total sum of absolute parameter values, leading many edge estimates to shrink to exactly zero and dropping out of the model (Epskamp et al., 2018). LASSO is commonly used to estimate a collection of networks (Epskamp and Fried, 2018). In order to optimize the fit of the network to the data, we implemented the Extended Bayesian Information Criterion (EBIC) under γ value of 0.50.

As our data were ordinal and not normally distributed, we estimated our network using Spearman correlations. Three centrality indices were computed in order to assess the relative influence of each node within the network structure: node strength (the sum of absolute edge weights connected to each node), closeness (the inverse of the sum of distances from one node to the others), and betweenness (which quantifies how often one node is in the shortest path between other nodes) (Epskamp and Fried, 2018). The higher the values, the more important the nodes are in the network. According to the network theories (Borsboom and Cramer, 2013), central symptoms were hypothesized to be responsible for maintaining mental disorders, as they are involved in stronger interactions or in the majority of interactions that constitute psychopathological networks.

To test the accuracy and stability of our network parameters, we estimated confidence intervals on the edge-weights under non-parametric bootstrapping (Epskamp et al., 2018) and the *Correlation Stability Coefficient*, which represents the maximum proportion of cases that can be dropped to retain a correlation of at least 0.7 with the original centrality indices. It should not be below 0.25 and is preferably above 0.50. However, these cut-off scores are somewhat arbitrary and should not be taken as definite guidelines (Epskamp and Fried, 2018).

Sensitivity analyses have been carried out in order to control the influence of the following variables: diagnosis, treatment, treatment compliance, treatment duration, long-acting injectable use, insight, comorbidity with substance use disorders, onset of illness, premorbid functioning, and prodromal status (results under request). Descriptive analyses were carried out using SPSS software, version 25 (IBM Corp, 2017), whereas network analyses were conducted with R Core Software, packages: *qgraph* (Epskamp et al., 2012) and *bootnet* (Epskamp et al., 2018).

3. Results

The mean age of our sample was 24.45 ± 6.28 years (range 11–44 years). A total of 124 were men (64.9%). Schizophrenia (21.9%), Psychosis not otherwise specified (NOS) (30.8%), and Schizophreniform disorder (18.3%) were the most common diagnoses. Most of the participants were single (89.5%), with secondary studies (60.2%) and unemployed (41.8%). Further details on sociodemographic and clinical characteristics of the sample can be seen in Table 1.

The domains of functioning in which the participants experienced the most difficulties were participation, consisting of the items "Joining in community activities," "Being emotionally affected by their health condition," and work performance. Even though the degree of difficulty that they experienced was mild, it had a mild-moderate interference in their lives, with a mean of 16.2 days a month in which these difficulties were present. In relation to symptoms, negative symptoms were the most severe.

The estimated network is shown in Fig. 1. Correlations found were ranging from rho = 0.003 (between excitement and poor rapport) to rho = 0.803 (between getting dressed and washing the whole body).

Almost all symptomatic factors were directly interconnected with functioning dimensions, except for the Excited factor, whose relationship with functioning was mediated by Positive, Depressive, and Disorganized factors. Regarding the relationship between specific symptoms and functioning domains and, after controlling the influence of all the other nodes, we found the following connections: i) self-care (getting dressed and washing the whole body) was related with lack of spontaneity and with conceptual disorganization, which also acted as a mediator between self-care and positive symptoms (hallucinatory behaviour, delusions and unusual thought content), excitement symptoms (excitement and uncooperativeness), and other disorganized symptoms (i.e., difficulty in abstract thinking); ii) concentration difficulties were related with hallucinatory behaviour, difficulty in abstract thinking, and conceptual disorganization, which mediated its relation with excitement symptoms (excitement, poor impulse control, hostility and uncooperativeness), moreover, concentration difficulties were directly related with guilt feelings, which mediated their connection with anxiety, depression, all the elements of the negative factor, and poor attention; iii) the latter pattern was also found for learning difficulties and being emotionally affected by the health condition; iv) social functioning (joining in community activities and maintaining a friendship) was related with depression, which connected social functioning with guilt feelings, anxiety, motor retardation, blunted affect, and emotional withdrawal; v) difficulties in joining in the community were related with passive/apathetic social withdrawal, which mediated its relation with poor rapport and emotional withdrawal; and vi) difficulties in dealing with strangers were directly connected to hallucinatory behaviour, conceptual disorganization, guilt feelings, poor attention, lack of spontaneity, blunted affect, and passive social withdrawal.

Fig. 2 represents the centrality indices for our network. According to their values in centrality measures, the most important nodes would be "conceptual disorganization" (weight = 6.668), "emotional withdrawal" (weight = 3.490), "lack of spontaneity and flow of conversation" (weight = 3.283), "delusions" (weight = 2.639), "unusual thought content" (weight = 2.560), "dealing with strangers" (weight = 2.540), and

Table 1
Demographic and clinical characteristics of the study sample.

Variables	Study sample (n = 191)
Gender, n (%)	
Female	67 (35.1)
Male	124 (64.9)
Age (years), Mean (SD)	24.45 (6.28)
Marital status, n (%)	
Single	170 (89.5)
Steady partner	15 (7.9)
Divorced	5 (2.6)
Diagnosis, n (%)	
Schizophrenia	42 (21.9)
Brief psychotic disorder	27 (14.1)
Psychosis NOS	59 (30.8)
Schizophreniform disorder	35 (18.3)
Schizoaffective disorder	2 (1.0)
Delusional disorder	2 (1.0)
Bipolar disorder with psychotic features	14 (7.3)
Major depressive disorder with psychotic features	6 (3.1)
Manic episode with psychotic symptoms	4 (2.0)
Parental socio-economic status, Mean (SD)	38.09 (18.41)
Level of education, n (%)	
Elementary school	19 (9.9)
Secondary school	115 (60.2)
University	53 (27.7)
Others	4 (2.1)
Occupational status, n (%)	
Employed	32 (18.1)
Unemployed	74 (41.8)
Student	70 (39.5)
Pensioned	1 (0.6)
Treatment, n (%)	
Antipsychotic treatment	
Amilsupride	18 (9.9)
Aripiprazole	35 (19.3)
Asenapine	3 (1.7)
Clozapine	4 (2.2)
Olanzapine	29 (16.0)
Paliperidone	18 (10.0)
Quetiapine	11 (6.1)
Risperidone	63 (34.8)
Antidepressants	39 (20.4)
Anticholinergics	23 (12.0)
Benzodiazepines	93 (48.7)
Lithium	9 (4.7)
Non-Benzodiazepines hypnotics	1 (0.5)
Stimulants	1 (0.5)
WHODAS, Mean (SD)	22.97 (8.65)
Standing for long periods	1.61 (.85)
Household responsibilities	1.83 (1.05)
Learning a new task	1.95 (1.11)
Joining in community activities	2.34 (1.28)
Emotionally affected	2.60 (1.31)
Concentrating	2.15 (1.18)
Walking	1.50 (.911)
Washing	1.23 (.63)
Getting dressed	1.15 (.48)
Dealing with strangers	2.17 (1.23)
Maintaining a friendship	2.06 (1.16)
Work/School	2.41 (1.36)
How much did these difficulties interfere?	2.75 (1.26)
How many days?	16.2 (12.5)
Days unable to carry out usual activities	7.8 (10.91)
Days reducing usual activities	11.08 (11.94)
PANSS, Mean (SD)	
PANSS positive factor	2.33 (1.23)
PANSS negative factor	2.52 (1.18)
PANSS disorganized factor	2.16 (1.12)
PANSS excited factor	1.18 (.68)
PANSS depressed factor	2.26 (1.15)
HAMILTON, Mean (SD)	7.97 (6.36)
YOUNG, Mean (SD)	5.21 (7.23)

Abbreviations: WHODAS, World Health Organization Disability Assessment Schedule; PANSS, Positive and Negative Syndrome Scale; HAMILTON, Hamilton Depression Rating Scale; YOUNG, Young Mania Rating Scale.

"poor rapport" (weight = 2.272). Within each PANSS symptoms domain, the most central node was: "delusions" for the Positive factor, "emotional withdrawal" in the Negative factor, "conceptual disorganization" in the Disorganized factor, "poor impulse control" in the Excited factor, and "guilt feelings" in the Depressed factor. Within the WHODAS items "dealing with strangers" was the most central one.

Significant differences have been found in *edge-weights* that connects nodes 28(getting dressed)-29(washing the whole body), 1(delusions)-18 (unusual thought content), 7(blunted affect)-8(emotional withdrawal), 31(maintaining a friendship)-32(work functioning), 8(emotional withdrawal)-10(passive social withdrawal), 9(poor rapport)-12(lack of spontaneity), 17(Uncooperativeness)-20(Poor impulse control), 14 (Guilt feelings)-15(Depression), 8(emotional withdrawal)-9(poor rapport), 12(lack of spontaneity)-16(Motor retardation), 1(delusions)-3(Hallucinatory behaviour), 1(delusions)-2(Conceptual disorganization), 6(Hostility)-20(Poor impulse control), 24(Joining in community activities)-30(Dealing with strangers), 30(Dealing with strangers)-31 (maintaining a friendship), 2(Conceptual disorganization)-3 (Hallucinatory behaviour), 2(Conceptual disorganization)-11 (Difficulty in abstract thinking) and 4(Excitement)-5(Grandiosity), which means that they are reliably the strongest edges in the network. As we can see in Fig. 3, differences are also present in *strength*. Stability of centrality indices drop steeply for betweenness (*CS*(cor = 0.7) = 0.052) and closeness (*CS*(cor = 0.7) = 0.126), but seems to be better for strength (*CS*(cor = 0.7) = 0.204) (see Fig. 4 for further details).

4. Discussion

Psychosis has been described as an imprecise group of symptoms of sufficient severity to disrupt everyday functioning (Nevarez-Flores et al., 2019). Although the relationship between psychotic symptoms and functional outcomes has been widely recognized, no previous studies have examined the interrelation between psychotic symptoms and specific areas of functioning applying network analysis methods. This study aimed to shed light on the way in which specific areas of functioning are connected with clinical symptomatology in patients with FEP, using a relatively large sample of patients within the first two years after the onset of psychotic symptoms.

Our findings showed that nodes that belong to the same construct were highly interconnected, being particularly outstanding in functioning areas, depressive factor items, and negative factor items. Contrary to our results, Galderisi (Galderisi et al., 2018b) found that everyday life skills were the most central nodes of their network. This difference may be due to the fact that we have not only included patients diagnosed with schizophrenia, but we have taken a transdiagnostic perspective, comprising also affective psychosis and psychosis not otherwise specified. Another possible explanation could be that their study was not carried out in patients with first episode, so it is possible these patterns change over time once the disease is more chronic.

Although specific areas of functioning revealed singular interrelations with symptoms, the most interrelated symptoms were "conceptual disorganization", "hallucinatory behaviour", "apathetic social withdrawal", "depression", "guilt feelings", and "difficulty in abstract thinking", which acted as bridge items in the connection between functioning and other clinical symptoms. According to the network basis (van Rooijen et al., 2017), these nodes might play an important role in maintaining and linking symptoms and disability. Previous prospective studies in schizophrenia patients have reported links between i) disorganized symptom and functional capacity (Galderisi et al., 2013), ii) avolition and patient's social dysfunction (Foussias and Remington, 2010; Galderisi et al., 2018a; Juckel et al., 2008; Strauss et al., 2013), iii) positive symptoms and concentration difficulties (Cuesta et al., 2012; Kim et al., 2021), and iv) depression and severity of disability (Lyngstad et al., 2018), especially regarding interpersonal functioning (Chudleigh et al., 2011; Galderisi et al., 2013;

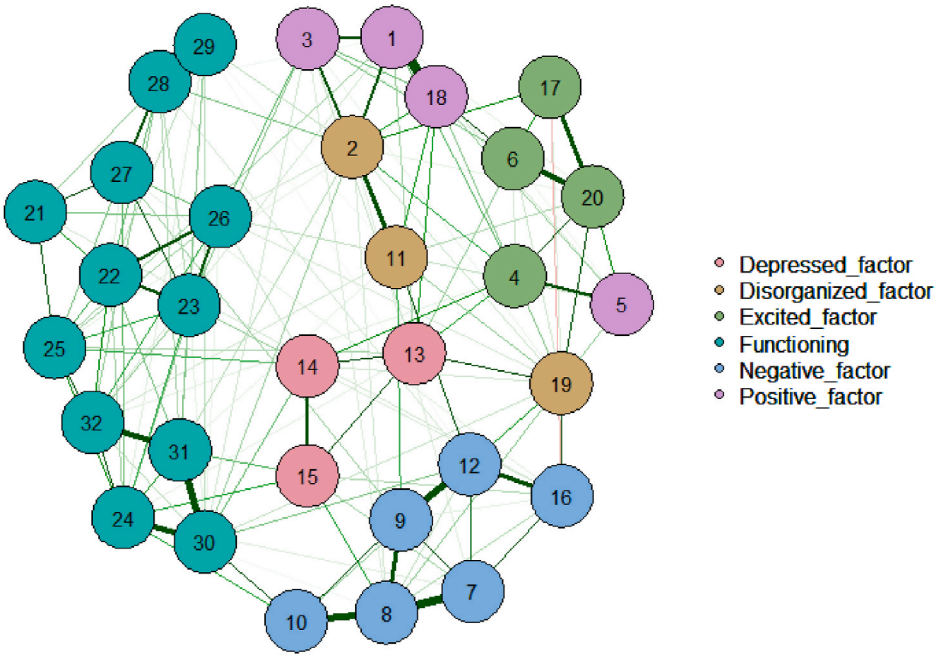

Fig. 1. Network showing the associations among functional dimensions and PANSS factors.
The PANSS Positive factor includes the items "(1) Delusions", "(3) Hallucinatory behaviour", "(5) Grandiosity" and "(18) Unusual thought content". The Negative factor includes the items "(7) Blunted affect", "(8) Emotional withdrawal", "(9) Poor rapport", "(10) Passive/apathetic social withdrawal", "(12) Lack of spontaneity". and "(16) Motor retardation". The Disorganized factor contains "(2) Conceptual disorganization", "(11) Difficulty in abstract thinking", and "(19) Poor attention". The Excited factor includes the items "(4) Excitement", "(6) Hostility", "(17) Uncooperativeness". and "(20) Poor impulse control". The Depressed Factor includes the items "(13) Anxiety", "(14) Guilt feelings", and "(15) Depression". The WHODAS items are "(21) Standing for long periods", "(22) Household responsibilities", "(23) Learning a new task", "(24) Joining in community activities", "(25) Being emotionally affected", "(26) Concentrating", "(27) Walking", "(28) Washing the whole body", "(29) Getting dressed", "(30) Dealing with strangers", "(31) Maintaining a friendship", and "(32) Work/School performance".

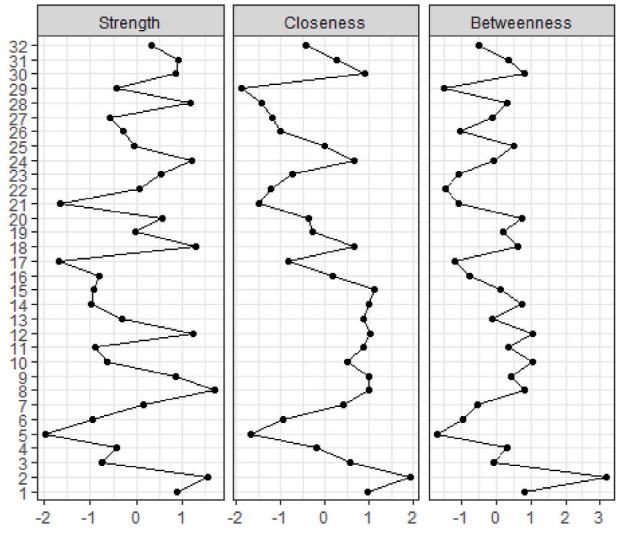

Fig. 2. Standardized centrality indices of each node.
The PANSS items are: (1) Delusions, (2) Conceptual disorganization, (3) Hallucinatory behaviour, (4) Excitement, (5) Grandiosity, (6) Hostility, (7) Blunted affect, (8) Emotional withdrawal, (9) Poor rapport, (10) Passive/apathetic social withdrawal, (11) Difficulty in abstract thinking, (12) Lack of spontaneity, (13) Anxiety, (14) Guilt feelings, (15) Depression, (16) Motor retardation, (17) Uncooperativeness, (18) Unusual thought content, (19) Poor attention, (20) Poor impulse control. The WHODAS items are: (21) Standing for long periods, (22) Household responsibilities, (23) Learning a new task, (24) Joining in community activities, (25) Being emotionally affected, (26) Concentrating, (27) Walking, (28) Washing the whole body, (29) Getting dressed, (30) Dealing with strangers, (31) Maintaining a friendship, and (32) Work/School performance.

Sabbag et al., 2012). Surprisingly, although guilt feelings have been related to social isolation (Ludwig et al., 2019), risk of suicide (Duffy et al., 2019; Palmier-Claus et al., 2013; Ventriglio et al., 2016), and severity of psychotic symptoms (Rekhi et al., 2018), its essential role regarding functioning in patients with first episode has been scarcely reported in previous literature. Nevertheless, the relation between cognition and positive symptoms has been explained by some authors on the basis of the abnormal function of the default mode network (DMN) found in psychotic disorders, according to which the hyperactivation of the DMN could be interpreted as a failure to allocate attentional resources to tasks at hand, with consequent impairment in cognitive task performance (Whitfield-Gabrieli and Ford, 2012). Significant correlations have been found between greater DMN activation and cognitive deficits (Whitfield-Gabrieli and Ford, 2012), as well as between DMN and positive symptoms of psychosis (Whitfield-Gabrieli et al., 2009).

Our results seem to indicate that "dealing with strangers" plays a central role in the disability of patients with first episode of psychosis. Velthorst (Velthorst et al., 2010) argued its critical role in predicting the transition to psychosis in people clinically at risk of developing the disorder and its relation with negative and dysphoric mood symptoms. Nevertheless, as far as we know, its impact in other areas of functioning had been explored very little previously. According to our results, this area seems to be related with participation in society, problems with maintaining a friendship, learning and concentrating difficulties, and work performance, even after controlling the influence of negative and depressive symptoms. Hogan (Horan et al., 2006) theorized that social difficulties in patients with first episode of psychosis may result in reduced participation and motivation, increasing social isolation and avoidance in these patients. This idea was supported by Chudleig et al. (2011), who argued that the development of early signs and symptoms of the illness may increase feelings of alienation and isolation, as young people who had experienced recent onset of psychosis reported losing contact with friends and 'feeling different' from others. Meanwhile, Velligan et al. (2014) theorized a negative symptom maintenance loop, in which limited initiation and withdrawal leads to decreased exposure to situations, which likely might lead to decreased interest, decreased events, minimized participation in conversation with others, decreased opportunities for reinforcement from the environment, and finally atrophy of work and social skills, which subsequently evoked higher negative symptoms. An additional explanation about the impact of psychotic symptoms in social functioning could be related to the presence of suspiciousness (Bliksted et al., 2019). Previous studies have associated persecutory delusions with lower social skills (Cameron, 1959), and this relationship may be mediated by Theory of Mind difficulties (i.e., the ability to understand the motivations, attitudes and intentions of others) (Corcoran et al., 1995; Phalen et al., 2017).

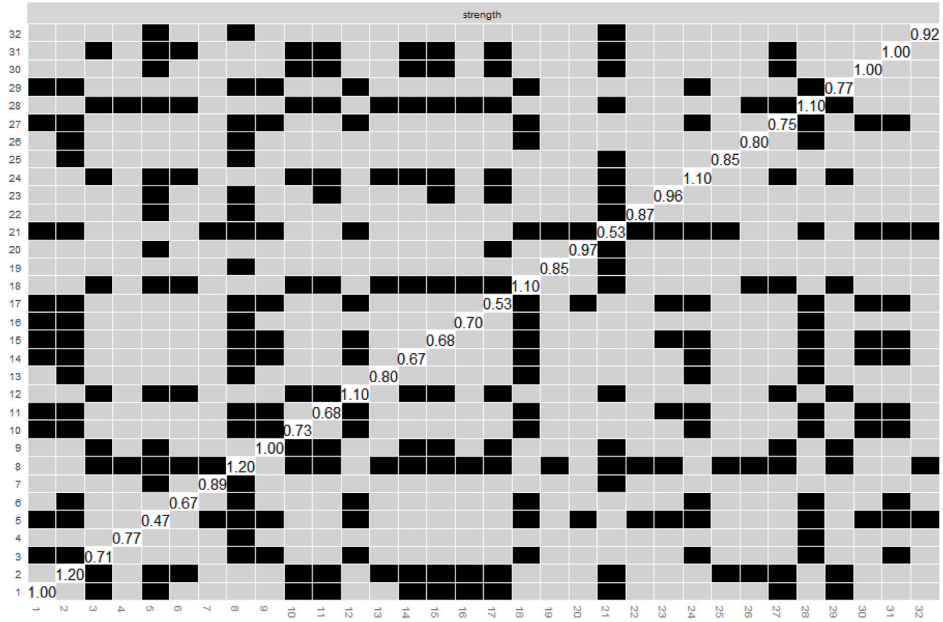

Fig. 3. Bootstrapped difference tests between the node strength. *Black boxes* represent nodes that differ significantly from the others, whereas *gray boxes* indicate nodes that do not differ significantly from one-another and *white boxes* show the value of each node strength.

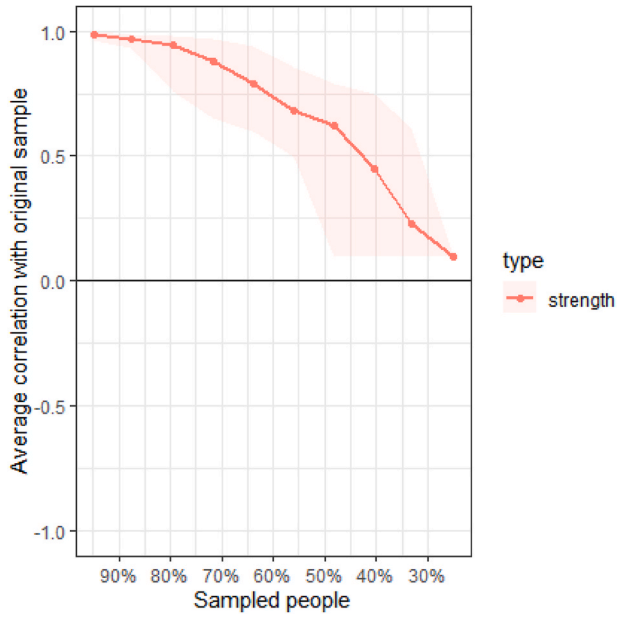

Fig. 4. Average correlations between strength index of network sampled with persons dropped and the original sample. This figure represents the maximum proportion of cases that can be dropped to retain a correlation of at least 0.7 with the original strength centrality. *Lines* represent the means and *areas* represent the range.

Our results may have clinical implications, since these findings could allow the identification of potential symptoms and functioning dimensions to be prioritized in the assessment and management of patients with FEP. According to our findings, "conceptual disorganization", "emotional withdrawal", "lack of spontaneity and flow of conversation", "delusions", "unusual thought content", "dealing with strangers" and "poor rapport" could be high-priority target areas of treatment, since they seem to be central nodes within the network. Within these areas, conceptual disorganization seems to have the most prominent role connecting functioning dimensions and clinical symptoms, which is in accordance with results reported by Kurtz (2006), who suggested that disorganization symptoms show a robust link to how well persons can form and sustain relationships (Phalen et al., 2017). At clinical research level, all these areas should also be specifically measured when assessing the effectiveness of interventions.

In addition, these results are in line with the relevance of social skills and cognitive training (Galderisi et al., 2018a) in early phases of psychotic disorders, not only for improving functional outcomes in other areas, but also for stopping the feedback loops that could appear between these functioning difficulties and clinical symptoms.

Limitations of the present study should be considered. First of all, the use of network modelling in psychology is still a young field and it is not without challenges (Epskamp and Fried, 2018; Forbes et al., 2019). Secondly, our results should be carefully considered due to the instability of our centrality measures. Thirdly, our data were based on a cross-sectional assessment, which precludes ascertaining the direction of the associations between clinical and functional domains. Using a sample of patients with FEP, regardless of specific DSM/ICD diagnosis, provides advantages over previous studies (i.e., it enables the identification of potential targets for early intervention strategies from a transdiagnostic perspective). However, carrying out the assessments at their study entry has the disadvantage that the measures could be unstable. In addition, our study included only help-seeking patients, so a certain selection bias cannot be ruled out. Further longitudinal and prospective studies will be needed to explore the relationships between specific areas of functioning and clinical symptoms in first-episode psychosis using a network approach. This research could guide novel treatment strategies targeting these areas, so as to improve the clinical and functional prognosis of FEP.

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Author contributions

Ana Izquierdo: Investigation, Conceptualization, Data curation, Formal analysis, Writing -original draft; **María Cabello:** Conceptualization, Supervision, Writing - review & editing; **Itziar Leal:** Resources; **Blanca Mellor-Marsá:** Investigation, Resources, Writing - review & editing; **Miriam Ayora:** Project administration, Investigation, Resources, Data curation, Writing - review & editing; **María-Fé Bravo-Ortiz**: Investigation, Resources, Funding acquisition, Writing - review; **Roberto Rodriguez-Jimenez**: Investigation, Resources, Funding acquisition, Writing - review & editing; **Ángela Ibáñez:** Investigation, Resources, Funding acquisition, Writing - review & editing; **Karina S. MacDowell**: Investigation, Resources, Writing - review & editing; **Norberto Malpica:** Investigation, Resources, Funding acquisition, Writing – review; **Marina Díaz-Marsá:** Investigation, Resources, Funding acquisition, Writing - review; **Enrique Baca-García:** Investigation, Resources, Funding acquisition; **Natalia Fares-Otero:** Investigation, Resources, Writing – review; **Helena Melero:** Investigation, Resources, Writing – review & editing; **Pilar López-García:** Supervision; **Covadonga M. Díaz-Caneja**: Project administration, Funding acquisition, Investigation, Resources, Data curation, Writing - review & editing; **Celso Arango:** Project administration, Funding acquisition, Investigation, Resources, Data curation, Writing - review & editing; **Jose Luis Ayuso-Mateos**: Funding acquisition, Investigation, Resources, Supervision, Writing - review & editing.

Declaration of competing interest

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