Schizophrenia Research 243 (2022) 43–54

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

# (Attenuated) hallucinations join basic symptoms in a transdiagnostic network cluster analysis

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ARTICLE INFO

*Keywords:*
hallucination
attenuated psychotic symptom
basic symptom
modularity analysis
psychosis
depression

ABSTRACT

Hallucinations are considered characteristic symptoms of psychosis and part of the 'psychosis superspectrum' of the Hierarchical Taxonomy Of Psychopathology (HiTOP) initiative. To gain insight into their psychopathological relevance, we studied their dimensional placement within a single dense transdiagnostic network constituting of basic symptoms as well as of attenuated and frank psychotic, and related symptoms. Newman's modularity analysis was used to detect symptom clusters in an earlier generated network (Jimeno, N., et al., 2020. Main symptomatic treatment targets in suspected and early psychosis: New insights from network analysis. Schizophr. Bull. 46, 884–895. https://doi.org/10.1093/schbul/sbz140). The constituting 86 symptoms were assessed with the Schizophrenia Proneness Instrument, Adult version (SPI-A), the Structured Interview for Psychosis-Risk Syndromes (SIPS), and the Positive And Negative Syndrome Scale (PANSS) in three adult samples of an early detection service: clinical high-risk ($n = 203$), first-episode psychosis ($n = 153$), and major depression ($n = 104$). Three clusters were detected: "subjective disturbances", "positive symptoms and behaviors", and "negative and anxious-depressive symptoms". The predominately attenuated hallucinations of both SIPS and PANSS joined the basic symptoms in "subjective disturbances", whereas other positive symptoms entered "positive symptoms and behaviors". Our results underline the importance of insight in separating true psychotic hallucinations from other hallucinatory experiences that, albeit phenomenologically similar are still experienced with some insight, i.e., are present in an attenuated form. We conclude that, strictly, hallucinations held with any degree of insight should not be used to diagnose transition to or presence of frank psychoses and, relatedly, to justify antipsychotic medication.

## 1. Introduction

Transdiagnostic approaches have become increasingly important in psychiatry in order to address problems of arbitrary symptom and disorder boundaries, and the downfalls of traditional categorical diagnoses, by characterizing psychopathology in terms of dimensions rather than categories (such as in the Hierarchical Taxonomy Of Psychopathology (HiTOP) initiative; Kotov et al., 2018) and by developing dimensional constructs that integrate symptoms, observable behaviors and biology, especially genetics and neuroscience (such as in the National Institute of

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https://doi.org/10.1016/j.schres.2022.02.018
Received 26 May 2021; Received in revised form 31 January 2022; Accepted 13 February 2022
Available online 26 February 2022

Mental Health's Research Domain Criteria (RDoC) initiative; Kozak and Cuthbert, 2016). One group of phenomena that, esp. within the RDoC framework, have received special attention for their dimensional character are hallucinations, in particular auditory ones (Ben-Zeev et al., 2020; Ford et al., 2014).

### 1.1. Insight and the dimensional character of perceptual disturbances

Hallucinations are perceptions in any sensory modality that occur in the absence of corresponding sensory stimuli and, from the affected individual's subjective point of view, are indistinguishable from normal perceptions (Ohayon, 2000; Telles-Correia et al., 2015). Next to delusions and formal thought disorders, hallucinations experienced with full conviction (i.e., with complete lack of insight) are considered as characteristic of psychosis and are one of the three positive symptoms obligatorily required for the diagnosis of any psychotic disorders in both DSM-5 (American Psychiatric Association, 2013) and the up-coming ICD-11 (https://icd.who.int/en). Yet, just as other positive symptoms, hallucinations are no dichotomous events but can occur in attenuated forms or as 'pseudohallucinations', i.e., with various degrees of insight into their abnormal nature (Chapman and Chapman, 1980) (Fig. 1). Furthermore, perceptual aberrations might involve real stimuli that, despite good perception of these, are perceived as something else entirely, in form of illusions or delusional misperceptions (Telles-Correia et al., 2015), or that are perceived with immediate full insight in only a distorted way, in form of (body) perceptive basic symptoms (Jimeno and Vargas, 2018; Schultze-Lutter, 2009) (Fig. 1).

### 1.2. The transdiagnostic character of perceptual disturbances

Albeit considered a part of the subdimension 'reality distortion' of the 'psychosis superspectrum' of the HiTOP initiative (Kotov et al., 2020), hallucinations were linked to non-schizophrenia-spectrum psychotic disorders by the HiTOP initiative (Kotov et al., 2020).Moreover, hallucinations can appear in other mental or somatic disorders, and as the result of substance use, including medications (Ben-Zeev et al., 2020; Carota and Bogousslavsky, 2019; Coerver and Subramanian, 2020; Ford et al., 2014; Jean et al., 2020; Thakur and Gupta, 2020; Waters and Fernyhough, 2017). Hallucinatory experiences can also occur in hypnagogic or hypnopompic states; and, in these non-pathological forms, are most frequent in the community by far (Ohayon, 2000; Chapman and Chapman, 1980; Carota and Bogousslavsky, 2019).

### 1.3. Perceptual disturbances in the prediction of psychosis

Furthermore, hallucinations and other perceptual disturbances occur more frequently in children and adolescents compared to adults in both community and clinical samples (Maijer et al., 2019; Schimmelmann et al., 2015; Schultze-Lutter et al., 2017, 2020a, 2020b; Walger et al., 2020). Thus, it was cautioned that, in children and adolescents, the presence of hallucinations does not always justify a psychosis diagnosis (Driver et al., 2020; Maijer et al., 2019; Schultze-Lutter and Schmidt, 2016), not least because they would frequently spontaneously remit (Brink et al., 2020).

In the early detection of psychosis, both transient frank and attenuated hallucinations, including schizotypal unusual perceptual experiences, as well as visual and acoustic basic symptoms are part of current clinical high-risk (CHR) criteria (Schultze-Lutter et al., 2015). CHR criteria have been associated with lower conversion-to-psychosis rates in children and adolescents (Schultze-Lutter et al., 2015). There is indication that, in minors, positive symptoms, including perception-related symptoms, may play a lesser role compared to adults, while the role of negative symptoms may be more pronounced (Fux et al., 2013; Zhang et al., 2020). Furthermore, in examinations of the psychosis-predictive value of different attenuated positive symptoms, attenuated hallucinations did not differ in both prevalence and severity between converters and non-converters, independent of age (Zhang et al., 2020). This supports other reports from CHR samples on the low psychosis-predictive potential of attenuated hallucinations by themselves (Niles et al., 2019). Yet, specifically attenuated verbal auditory hallucinations (Niles et al., 2019) and concretization of hallucinatory experiences over time (Marshall et al., 2019) were associated with greater conversion risk, and multimodal hallucinations were linked to more adverse outcome and greater distress (Montagnese et al., 2021).

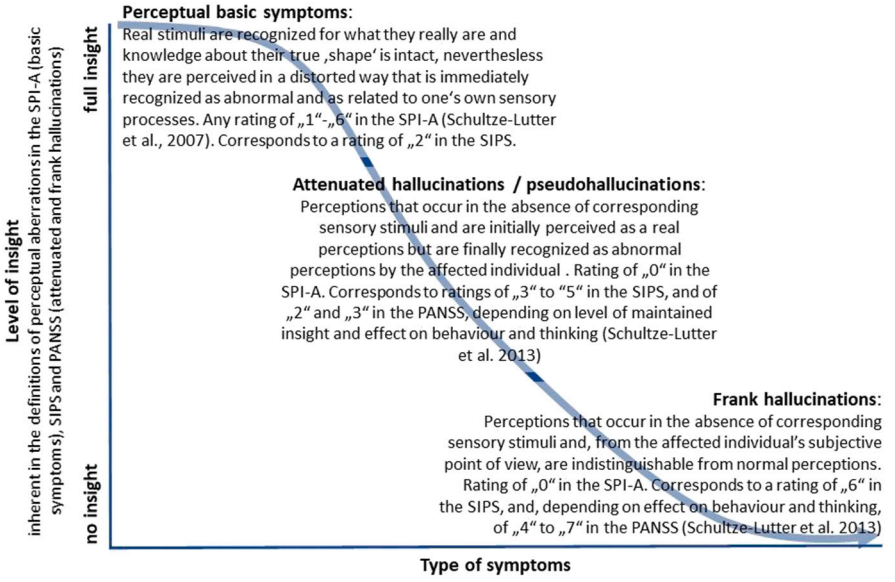


**Fig. 1.** The continuum of pathological perceptual aberrations in relation to the level of insight and examples of their operationalizations (Kay et al., 1987; McGlashan et al., 2010; Schultze-Lutter et al., 2007; Schultze-Lutter et al., 2013).

### 1.4. Perceptual disturbances and their association with other (positive) symptoms

Despite these indications that hallucinatory and other perceptual experiences might be less psychosis-specific compared to aberrations in thought content and processes, they were commonly closely linked to other positive symptoms in network analyses (Dodell-Feder et al., 2019; Fonseca-Pedrero et al., 2020; Moura et al., 2021; van Rooijen et al., 2017, 2018; Esfahlani et al., 2017). To examine this apparent close link between attenuated and frank positive symptoms, we proposed to empirically analyze the clusters formed by cognitive and perceptual basic symptoms as well as by attenuated and frank psychotic symptoms in a single dense network from a large transdiagnostic patient sample of an early detection of psychosis service (Jimeno et al., 2020). In our network, frank and attenuated positive symptoms appeared as strongly interrelated core symptoms. Five partly overlapping symptom subgroups were proposed by inspection of parameters and theoretical reasoning, with positive, negative, and cognitive-disorganized symptoms subgroups, including attenuated and basic symptoms relevant for CHR criteria, forming the core, and (body) perception and affective symptoms subgroups building the periphery (Jimeno et al., 2020).

### 1.5. Study aims

In order to avoid the subjectivities involved in our earlier visualization-based interpretation of possible network subgroups (Jimeno et al., 2020), we aimed to empirically study this inspection-based subgrouping and, in doing so, the dimensional placement of hallucinations using modularity analysis that examines the network structure by measuring the strength of division of a network into modules or clusters of items (Newman, 2006). Based on our previous results (Jimeno et al., 2020) and in line with the HiTOP's 'psychosis superspectrum', we hypothesized that hallucinations would belong to the same cluster as delusions and disorganized communication, i.e., a similar dimension as the HiTOP subdimension 'thought disorder symptoms' (Kotov et al., 2020).

## 2. Material and methods

### 2.1. Participants

The sample consisted of 460 patients of the Cologne Early Recognition and Intervention Centre for mental crises (FETZ; Schultze-Lutter et al., 2009), who had participated in either of two previous studies (Schultze-Lutter et al., 2007b, 2014). Patients belonged to any of the following three diagnostic groups: first-episode psychosis (FEP; $n = 153$, 33.3%), CHR ($n = 203$; 44.1%) according to ultra-high risk (UHR) and/or basic symptom criteria (Schultze-Lutter et al., 2015), and nonpsychotic, non-CHR major-depression episode (MD; $n = 104$; 22.6%) (Table 1). Patients were between 16 and 40 years-of-age, 65% were males (Table 1). Exclusion criteria of all groups were: presence of a somatic or drug-related condition explaining the mental condition as well as any missing data on any of the three target scales. Additionally, for CHR and MD, lifetime diagnosis of psychosis was an exclusion criterion. Further details on the sample are provided in Jimeno et al. (2020).

All patients provided written informed consent, and both studies were approved by the local Ethical Committee of the Medical Faculty of the University of Cologne.

### 2.2. Assessments

Participants were assessed for perception-related and other symptoms with three semi-structured clinical interviews: the Schizophrenia Proneness Instrument, Adult version (SPI-A; Schultze-Lutter et al., 2007a) for basic symptoms, the Structured Interview for Psychosis-Risk

**Table 1**
Sociodemographic and clinical characteristics of the help-seeking FETZ sample ($N = 460$). Kruskal-Wallis $H$-tests and $\chi^2$ tests were used to analyze group differences.

| | Major depression (n = 104) | Clinical high risk (CHR) (n = 203) | First-episode psychosis (n = 153) | Total sample[f] (N = 460) | $\chi^2$/U | df | p-value |
|---|---|---|---|---|---|---|---|
| Age in years: mean (SD) | 27.5 (7.4) | 25.3 (5.6) | 26.7 (6.5) | 26.2 (6.4) | 6.423 | 2 | 0.040 |
| Sex: % male | 51.0 | 65.0 | 74.5 | 65.0 | 15.091 | 2 | 0.001 |
| Current partnership: % single | 64.7 | 60.5 | 77.1 | 67.8 | 11.751 | 2 | 0.003 |
| Marital status: % never married | 77.7 | 88.2 | 83.0 | 84.1 | 5.844 | 2 | 0.059 |
| Highest school graduation[a]: % | | | | | 28.132 | 4 | <0.001 |
| still in school[b] | 7.9 | 15.2 | 3.3 | 9.7 | | | |
| ISCED 2 | 31.7 | 24.8 | 47.0 | 33.7 | | | |
| ISCED 3 | 60.4 | 59.9 | 49.7 | 56.6 | | | |
| Current occupation: % | | | | | 16.754 | 6 | 0.010 |
| regular occupation including school | 72.5 | 78.5 | 59.5 | 70.8 | | | |
| unemployed | 21.6 | 19.0 | 32.7 | 24.2 | | | |
| sheltered work place | 2.9 | 1.0 | 3.9 | 2.4 | | | |
| sporadic employment | 2.9 | 1.5 | 3.9 | 2.6 | | | |
| CHR type[c]: % | | | | | not applicable | | |
| only basic symptom criteria | | 25.5 | | | | | |
| only ultra-high risk criteria | | 4.9 | | | | | |
| both types of CHR criteria | | 69.5 | | | | | |
| Conversion to psychosis[d], % | 6.7 | 43.6 | | | 7.674 | 1 | 0.006 |
| SOFAS[e]: mean (SD) | 57.6 (17.5) | 52.5 (16.9) | 49.8 (10.5) | 49.1 (15.0) | 5.040 | 2 | 0.080 |
| Medication at baseline[f]: % any | 22.1 | 37.9 | 33.9 | 35.0 | 9.950 | 2 | 0.007 |
| Type of main medication[g]: % | | | | | 70.053 | 6 | <0.001 |
| antipsychotic | 0 | 28.1 | 37.9 | 25.0 | | | |
| antidepressant | 21.2 | 8.4 | 1.3 | 8.9 | | | |
| others | 1.0 | 2.0 | 0.7 | 1.3 | | | |

[a] ISCED: International Standard Classification of Education, 2011 revision (http://www.uis.unesco.org/Education/ Pages/international-standard-classification-of-education.aspx). Description of main categories: 2: lower secondary education; 3: upper secondary education.
[b] Mainly aiming for ISCED 3.
[c] Not including the genetic risk plus functional decline criterion.
[d] Numbers relate to those with a 48-months follow-up in the respective group (Schultze-Lutter et al., 2014).
[e] Social and Occupational Functioning Assessment Scale (American Psychiatric Association, 1994).
[f] Least medication in Major Depression group. Overall difference of only small effect size (Cramer's V = 0.147).
[g] Only n = 2 CHR patients received a combined medication. "Other" medications were mainly of the group of anti-anxiety agents.

Syndromes (SIPS; McGlashan et al., 2010) for attenuated symptoms, and the Positive And Negative Syndrome Scale (PANSS; Kay et al., 1987) for frank psychotic symptoms. In order to assess axis-I disorders, including FEP and MD, the German version of the Structured Clinical Interview for DSM-IV (Wittchen et al., 1997) was used. All the assessments were performed by previously trained mental health professionals.

### 2.3. Data analysis

The underlying network analysis is detailed in Jimeno et al. (2020) and, in brief, described in the Supplementary Information 1. Exceeding our earlier network analyses, modularity analysis was used to detect empirical groups of symptoms (nodes) in the network. Different modularity measures have been designed to measure the strength of division of a network into modules (also called clusters; Zhang et al., 2018). Networks with high modularity have more dense connections between the nodes within clusters as compared with the connections between nodes from different clusters (Fornito et al., 2016).

From the different methods developed to estimate the network modularity while avoiding the subjectivities involved in our earlier visual inspection (Jimeno et al., 2020), we used Newman's modularity (Newman, 2006) as an extended, reproducible and widely validated method (Miyauchi and Kawase, 2016). This eigenvector-based algorithm provides the specific partition of the network by maximizing the modularity function. The logic of this algorithm is based on the search for clusters (sets of nodes) among which the number of connections is significantly lower than those we would find by chance. Particularly, Newman's modularity was selected since it returns results of higher quality than competing methods in shorter running times (Newman, 2006).

## 3. Results

The modularity analysis identified three clusters including between 21 and 40 symptoms (Table 2, Fig. 2). The largest cluster 1, “subjective disturbances” (SD), included all of the 37 basic symptoms as assessed with the SPI-A, but also attenuated and frank hallucinations as assessed with both the SIPS (P4, “perceptual abnormalities/hallucinations”) and the PANSS (P3, “hallucinatory behavior”). Furthermore, “trouble with focus and attention” (SIPS-D3) was included into this cluster that, albeit also rating observed behaviors, has some phenomenological overlap with the B2 to B6 basic symptoms.

Other positive symptoms of both the SIPS (P1-P3, P5, D2) and the PANSS (P1, P5, P6) and, rating the bizarreness of thoughts (PANSS-G9, PANSS-P2, PANSS-N5) and attention (PANSS-G11), entered the smallest cluster 2, “positive symptoms and behaviors” (PS&B) (Table 2, Fig. 2). The other ten symptoms of cluster 2 referred to lack of judgement (PANSS-G8, PANSS-G10, PANSS-G12) and heightened emotions (PANSS-P4, P7, PANSS-G4, PANSS-G14) that often accompany positive psychotic symptoms. These were complemented by SIPS-D1 and PANSS-G5.

Finally, cluster 3, “negative and anxious-depressive symptoms” (N&ADS), with 25 symptoms (Table 2, Fig. 2) contained all but one (PANSS-N5) negative symptoms of both the SIPS and the PANSS, including functional deficits, the remaining general symptoms of these two scales as well as SIPS-D4 that phenomenologically overlaps with PANSS-N4. Thus, the non-negative symptoms refer to affective symptoms (PANSS-G1, PANSS-G2, PANSS-G3, PANSS-G6, SIPS-G2), motor disturbances (PANSS-G7, SIPS-G3), and self-absorbed, autistic behaviors (PANSS-G15).

We termed cluster 1 “subjective disturbances” (SD), cluster 2 “positive symptoms and behaviors” (PS&B), and cluster 3 “negative and anxious-depressive symptoms” (N&ADS).

## 4. Discussion

Using modularity analysis in a transdiagnostic single dense comprehensive network of 86 symptoms associated with and relevant for (early) psychosis, i.e., frank psychotic symptoms of the PANSS as well as attenuated psychotic, basic and related symptoms assessed with the SIPS and SPI-A, we detected three phenomenologically meaningful clusters: “subjective disturbances” (SD), “positive symptoms and behaviors” (PS&B), and “negative and anxious-depressive symptoms” (N&ADS). These clusters showed considerable overlap with the five earlier inspection-generated subgroups (Jimeno et al., 2020) and clarified some of the formerly inconclusive group memberships. Most importantly, however, the modularity analysis linked (attenuated) hallucinations to SD and not, as expected, to PS&B, thus indicating a clinical significance of these that differs from that of other positive symptoms.

### 4.1. Comparison of modularity- and inspection-generated symptom groups

Based on inspection of the network and its correlation matrix, and content-related consideration, five symptom subgroups were earlier proposed (Jimeno et al., 2020): (1) “(body) perception disturbances” consisting of perceptive and cenesthetic basic symptoms; (2) “cognitive-disorganized symptoms” with predominately cognitive basic symptoms and disorganized symptoms of both SIPS and PANSS; (3) “positive symptoms” including the most central positive symptoms and symptoms rating bizarreness of thought content; (4) “negative symptoms” containing negative symptoms and functional impairments assessed with both SIPS and PANSS, and adynamic basic symptoms; and (5) “affective symptoms” comprising of disturbances of emotions and rational judgement predominately of the PANSS (Table 2).

The modularity analysis now demonstrated that “affective symptoms” might be better perceived not as a single symptom dimension but, divided into symptoms of heightened-excessive and of anxious-depressive mood, as accessory symptoms of the clusters PS&B and N&ADS respectively (Table 2). In doing so, PS&B also comprised most symptoms of “positive symptoms”, N&ADS those of “negative symptoms”. The distinct placement of affective symptoms is further supported by earlier distinctions between an “excitement” and an “emotional distress” factor of the PANSS of that the “excitement” correlated with positive but not negative symptoms (van der Gaag et al., 2006), and by a recent network analysis on patients with schizophrenia-spectrum disorders that placed excitement symptoms close to positive symptoms and emotional-distress items close to negative symptoms (Moura et al., 2021). The placement of anxious-depressive symptoms together with negative symptoms in one cluster is also supported by a recent meta-analysis on non-affective psychosis samples reporting that negative symptoms were positively associated with depressive symptoms, though only with a small effect (Edwards et al., 2019).

The formerly proposed subgroups “(body) perception disturbances” and “cognitive-disorganized symptoms”, in particular their mainly constituting basic symptoms and the SIPS-D3 “trouble with focus and attention”, collapsed into SD. At the same time, SD included all basic symptoms formerly allocated to other subgroups and (attenuated) hallucinations of both SIPS and PANSS. The placement of “trouble with focus and attention” (SIPS-D3) had earlier been unclear (Jimeno et al., 2020); the results now indicate that it may be better understood as a cognitive-disorganized rather than as a negative symptom. Albeit its partly observation-based rating, its maintained placement with purely subjective cognitive basic symptoms seems justified by the inclusion of also subjectively described concentration, attention and memory problems that overlap phenomenologically with basic symptoms, of the SPI-A section B in particular. This inclusion of self-reported problems in SIPS-D3 might also explain its placement into a cluster different from that of the corresponding PANSS-item “poor attention” (G11) that is

**Table 2**
Cluster distribution of SPI-A, SIPS and PANSS symptoms according to the modularity analysis in comparison to the earlier inspection-based subgrouping (Jimeno et al., 2020), and frequency and its subgroup severity differences according to Jimeno et al. (2020).[b]

| Item number | Symptom name | Empirical cluster, number and name | Inspection-based subgroup[a] | % present[a] | Subgroup differences[a] |
|---|---|---|---|---|---|
| **SPI-A-A1** | **Impaired tolerance to unusual, unexpected or specific novel demands** | **1, subjective disturbances** | **negative symptoms** | **73.9** | **FEP > CHR = MD** |
| **SPI-A-A2** | **Impaired tolerance to certain social everyday situations** | **1, subjective disturbances** | **negative symptoms** | **74.5** | **FEP > CHR > MD** |
| **SPI-A-A3** | **Impaired tolerance to working under pressure of time or rapidly changing different demands** | **1, subjective disturbances** | **negative symptoms** | **77.1** | **FEP > CHR > MD** |
| **SPI-A-A4** | **Changes in mood and emotional responsiveness** | **1, subjective disturbances** | **affective symptoms** | **96.4** | **FEP > CHR = MD** |
| **SPI-A-A5** | **Decrease in positive emotional responsiveness toward others** | **1, subjective disturbances** | **affective symptoms** | **85.1** | **FEP = CHR > MD** |
| SPI-A-B1 | Inability to divide attention | 1, subjective disturbances | cognitive-disorg. symptoms | 41.8 | FEP > CHR > MD |
| SPI-A-B2 | Feeling overly distracted by stimuli | 1, subjective disturbances | cognitive-disorg. symptoms | 47.4 | FEP = CHR > MD |
| SPI-A-B3 | Difficulties concentrating | 1, subjective disturbances | cognitive-disorg. symptoms | 90.6 | FEP > CHR > MD |
| SPI-A-B4 | Difficulties to hold things in mind for less than half an hour | 1, subjective disturbances | cognitive-disorg. symptoms | 62.6 | FEP = CHR > MD |
| SPI-A-B5 | Slowed-down thinking | 1, subjective disturbances | cognitive-disorg. symptoms | 62.6 | FEP = CHR > MD |
| SPI-A-B6 | Lack of thought energy. Purposive thoughts | 1, subjective disturbances | cognitive-disorg. symptoms | 64.2 | FEP > CHR > MD |
| SPI-A-C1 | Increased indecisiveness with regard to insignificant choices between equal alternatives | 1, subjective disturbances | cognitive-disorg. symptoms | 61.5 | FEP = CHR > MD |
| SPI-A-C2 | Thought interference | 1, subjective disturbances | cognitive-disorg. symptoms | 47.6 | FEP > CHR > MD |
| SPI-A-C3 | Thought blockages | 1, subjective disturbances | cognitive-disorg. symptoms | 55.9 | FEP = CHR > MD |
| SPI-A-C4 | Disturbance of receptive speech | 1, subjective disturbances | cognitive-disorg. symptoms | 54.4 | FEP = CHR > MD |
| SPI-A-C5 | Disturbance of expressive speech | 1, subjective disturbances | cognitive-disorg. Symptoms | 55.2 | FEP = CHR > MD |
| SPI-A-C6 | Disturbance of immediate recall | 1, subjective disturbances | cognitive-disorg. symptoms | 53.8 | FEP = CHR > MD |
| SPI-A-D1 | Decreased capacity to discriminate between different kinds of emotions | 1, subjective disturbances | cognitive-disorg. symptoms | 35.0 | FEP = CHR > MD |
| **SPI-A-D2** | **Increased emotional reactivity in response to routine social interactions** | **1, subjective disturbances** | **affective symptoms** | **82.8** | **FEP > CHR = MD** |
| SPI-A-D3 | Thought pressure | 1, subjective disturbances | cognitive-disorg. symptoms | 51.7 | FEP > CHR > MD |
| **SPI-A-D4** | **Unstable ideas of reference** | **1, subjective disturbances** | **positive symptoms** | **56.4** | **FEP > CHR > MD** |
| SPI-A-D5 | Changed perception of the face or body of others | 1, subjective disturbances | (body) perception disturbances | 13.1 | FEP > CHR > MD |
| SPI-A-E1 | Bodily sensations of numbness and stiffness | 1, subjective disturbances | (body) perception disturbances | 15.6 | FEP > CHR = MD |
| SPI-A-E2 | Bodily sensations of pain in a distinct area | 1, subjective disturbances | (body) perception disturbances | 17.5 | FEP = CHR > MD |
| SPI-A-E3 | Bodily sensations migrating through the body | 1, subjective disturbances | (body) perception disturbances | 5.3 | FEP = CHR > MD |
| SPI-A-E4 | Bodily sensations of being electrified | 1, subjective disturbances | (body) perception disturbances | 8.2 | FEP = CHR = MD |
| SPI-A-E5 | Bodily sensations of movement or pressure | 1, subjective disturbances | (body) perception disturbances | 1.1 | FEP = CHR > MD |
| SPI-A-E6 | Bodily sensations of body/body parts changing size | 1, subjective disturbances | (body) perception disturbances | 8.3 | FEP = CHR > MD |
| SPI-A-F1 | Hypersensitivity to light/optic stimuli | 1, subjective disturbances | (body) perception disturbances | 29.8 | FEP = CHR > MD |
| SPI-A-F2 | Photopsia | 1, subjective disturbances | (body) perception disturbances | 10.2 | FEP = CHR = MD |
| SPI-A-F3 | Micropsia. Macropsia | 1, subjective disturbances | (body) perception disturbances | 4.1 | FEP = CHR = MD |
| SPI-A-F4 | Hypersensitivity to sounds/noise | 1, subjective disturbances | (body) perception disturbances | 50.7 | FEP = CHR > MD |
| SPI-A-F5 | Changed intensity/quality of acoustic stimuli | 1, subjective disturbances | (body) perception disturbances | 33.5 | FEP > CHR > MD |
| SPI-A-F6 | Somatopsychic bodily depersonalization | 1, subjective disturbances | (body) perception disturbances | 8.1 | FEP = CHR > MD |
| SPI-A-O1 | Thought perseveration | 1, subjective disturbances | cognitive-disorg. symptoms | 45.6 | FEP > CHR > MD |
| SPI-A-O4.10 | Partial seeing including tubular vision | 1, subjective disturbances | (body) perception disturbances | 8.1 | FEP = CHR > MD |

(*continued on next page*)

**Table 2** (*continued*)

| Item number | Symptom name | Empirical cluster, number and name | Inspection-based subgroup[a] | % present[a] | Subgroup differences[a] |
|---|---|---|---|---|---|
| SPI-A-O11 | Loss of automatic skills | 1, subjective disturbances | (body) perception disturbances | 17.4 | FEP = CHR > MD |
| **SIPS-P4** | **Perceptual abnormalities/hallucinations** | **1, subjective disturbances** | **positive symptoms** | **51.5** | **FEP > CHR > MD** |
| SIPS-D3 | Trouble with focus and attention | 1, subjective disturbances | negative symptoms/cognitive-disorg. symptoms | 54.3 | FEP > CHR > MD |
| **PANSS-P3** | **Hallucinatory behavior** | **1, subjective disturbances** | **positive symptoms** | **42.3** | **FEP > CHR > MD** |
| SIPS-P1 | Unusual thought content/delusional ideas | 2, positive symptoms and behaviors | positive symptoms | 64.1 | FEP > CHR > MD |
| SIPS-P2 | Suspiciousness/persecutory ideas | 2, positive symptoms and behaviors | positive symptoms | 56.5 | FEP > CHR > MD |
| SIPS-P3 | Grandiosity | 2, positive symptoms and behaviors | positive symptoms | 16.7 | FEP > CHR > MD |
| SIPS-P5 | Disorganized communication | 2, positive symptoms and behaviors | positive symptoms/cognitive-disorg. symptoms | 44.6 | FEP > CHR > MD |
| **SIPS-D1** | **Odd behavior or appearance** | **2, positive symptoms and behaviors** | **cognitive-disorg. symptoms** | **25.1** | **FEP > CHR > MD** |
| SIPS-D2 | Bizarre thinking | 2, positive symptoms and behaviors | positive symptoms | 29.5 | FEP > CHR > MD |
| PANSS-P1 | Delusions | 2, positive symptoms and behaviors | positive symptoms | 54.1 | FEP > CHR > MD |
| PANSS-P2 | Conceptual disorganization | 2, positive symptoms and behaviors | positive symptoms/cognitive-disorg. symptoms | 42.5 | FEP > CHR > MD |
| **PANSS-P4** | **Excitement** | **2, positive symptoms and behaviors** | **affective symptoms** | **49.6** | **FEP > CHR > MD** |
| PANSS-P5 | Grandiosity | 2, positive symptoms and behaviors | positive symptoms | 14.1 | FEP > CHR > MD |
| PANSS-P6 | Suspiciousness | 2, positive symptoms and behaviors | positive symptoms | 52.0 | FEP > CHR > MD |
| PANSS-P7 | Hostility | 2, positive symptoms and behaviors | affective symptoms | 22.4 | FEP > CHR > MD |
| **PANSS-N5** | **Difficulty in abstract thinking** | **2, positive symptoms and behaviors** | **negative symptoms/cognitive-disorg. symptoms** | **33.5** | **FEP > CHR > MD** |
| PANSS-G4 | Tension | 2, positive symptoms and behaviors | affective symptoms | 79.1 | FEP > CHR > MD |
| **PANSS-G5** | **Mannerisms & posturing** | **2, positive symptoms and behaviors** | **negative symptoms** | **15.8** | **FEP > CHR > MD** |
| PANSS-G8 | Uncooperativeness | 2, positive symptoms and behaviors | affective symptoms | 19.6 | FEP > CHR = MD |
| PANSS-G9 | Unusual thought content | 2, positive symptoms and behaviors | positive symptoms | 33.7 | FEP > CHR > MD |
| PANSS-G10 | Disorientation | 2, positive symptoms and behaviors | affective symptoms | 7.4 | FEP > CHR = MD |
| **PANSS-G11** | **Poor attention** | **2, positive symptoms and behaviors** | **cognitive-disorg. symptoms** | **44.5** | **FEP > CHR > MD** |
| PANSS-G12 | Lack of judgement & insight | 2, positive symptoms and behaviors | affective symptoms | 27.7 | FEP > CHR > MD |
| PANSS-G14 | Poor impulse control | 2, positive symptoms and behaviors | affective symptoms | 37.5 | FEP > CHR = MD |
| SIPS-N1 | Social anhedonia or withdrawal | 3, negative and anxious-depressive symptoms | negative symptoms | 73.7 | FEP > CHR > MD |
| SIPS-N2 | Avolition | 3, negative and anxious-depressive symptoms | negative symptoms | 76.1 | FEP > CHR > MD |
| SIPS-N3 | Decreased expression of emotion | 3, negative and anxious-depressive symptoms | negative symptoms | 48.6 | FEP > CHR > MD |
| SIPS-N4 | Decreased experience of emotions and self | 3, negative and anxious-depressive symptoms | negative symptoms | 49.6 | FEP > CHR > MD |
| SIPS-N5 | Decreased ideational richness | 3, negative and anxious-depressive symptoms | negative symptoms/cognitive-disorg. symptoms | 39.8 | FEP > CHR > MD |
| SIPS-N6 | Deterioration in role functioning | 3, negative and anxious-depressive symptoms | negative symptoms | 65.6 | FEP > CHR > MD |
| SIPS-D4 | Impairment in personal hygiene/social attentiveness | 3, negative and anxious-depressive symptoms | negative symptoms/cognitive-disorg. symptoms | 36.4 | FEP > CHR = MD |
| SIPS-G1 | Sleep disturbance | 3, negative and anxious-depressive symptoms | negative symptoms | 67.8 | FEP > CHR > MD |
| SIPS-G2 | Dysphoric mood | 3, negative and anxious-depressive symptoms | affective symptoms | 83.3 | FEP > CHR > MD |
| SIPS-G3 | Motor disturbances | 3, negative and anxious-depressive symptoms | negative symptoms | 26.6 | FEP > CHR > MD |
| SIPS-G4 | Impaired tolerance to normal stress | 3, negative and anxious-depressive symptoms | negative symptoms | 62.2 | FEP > CHR > MD |

(*continued on next page*)

**Table 2** (*continued*)

| Item number | Symptom name | Empirical cluster, number and name | Inspection-based subgroup[a] | % present[a] | Subgroup differences[a] |
|---|---|---|---|---|---|
| PANSS-N1 | Blunted affect | 3, negative and anxious-depressive symptoms | negative symptoms | 46.4 | FEP > CHR > MD |
| PANSS-N2 | Emotional withdrawal | 3, negative and anxious-depressive symptoms | negative symptoms | 49.4 | FEP > CHR > MD |
| PANSS-N3 | Poor rapport | 3, negative and anxious-depressive symptoms | negative symptoms | 46.1 | FEP > CHR > MD |
| PANSS-N4 | Passive-apathetic social withdrawal | 3, negative and anxious-depressive symptoms | negative symptoms | 68.9 | FEP > CHR > MD |
| PANSS-N6 | Lack of spontaneity & flow of conversation | 3, negative and anxious-depressive symptoms | negative symptoms | 40.0 | FEP > CHR > MD |
| PANSS-N7 | Stereotyped thinking | 3, negative and anxious-depressive symptoms | negative symptoms | 41.6 | FEP > CHR > MD |
| PANSS-G1 | Somatic concern | 3, negative and anxious-depressive symptoms | affective symptoms | 45.0 | FEP > CHR > MD |
| PANSS-G2 | Anxiety | 3, negative and anxious-depressive symptoms | affective symptoms | 59.8 | FEP > CHR > MD |
| PANSS-G3 | Guilt feelings | 3, negative and anxious-depressive symptoms | affective symptoms | 37.8 | FEP > CHR = MD |
| PANSS-G6 | Depression | 3, negative and anxious-depressive symptoms | affective symptoms | 80.8 | FEP > CHR = MD |
| PANSS-G7 | Motor retardation | 3, negative and anxious-depressive symptoms | negative symptoms | 42.7 | FEP > CHR = MD |
| PANSS-G13 | Disturbance of volition | 3, negative and anxious-depressive symptoms | negative symptoms | 28.8 | FEP > CHR > MD |
| PANSS-G15 | Preoccupation | 3, negative and anxious-depressive symptoms | affective symptoms | 45.7 | FEP > CHR > MD |
| PANSS-G16 | Active social avoidance | 3, negative and anxious-depressive symptoms | negative symptoms | 53.9 | FEP > CHR > MD |

[a] According to Jimeno et al. (2020). Subgroup comparison of item frequency (% of SIPS or SPI-A item ≥1 and PANSS-item ≥2, resp.) between first-episode psychosis (FEP), clinical high risk (CHR) and major depression (MD) was done using Kruskal- Wallis *H*-test and post-hoc Mann-Whitney *U* test (two-tailed *alpha* > 0.05).
[b] Cells given in bold indicate cluster membership that completely differs from the earlier assumed inspection-based subgroup membership.

completely based on observed manifestations during the course of interview. Subjective awareness and insight might also play a role in the unexpected placement of the two hallucination items of SIPS (P4) and PANSS (P3) that were scored at a level of frank psychotic hallucinations (Fig. 1) in only 17.6% (SIPS-P4 score of '6') and 18.8% (PANSS-P3 score of '4' or higher) of the sample, respectively. Thus, the majority of abnormal perceptions in the total sample (48.2% and 40.3%, resp.) were at the levels of basic or attenuated psychotic symptoms (Fig. 1) that indicate the maintenance of at least some insight into their abnormal nature and, thus, their immediate or deferred self-perception as disturbances (see 4.2 for further discussion of the significance of hallucinatory experiences).

As regards the other five symptoms whose placement into one of the five inspection-based subgroups had not been entirely clear (Jimeno et al., 2020), the placement into one of the considered groups became also clearer (Table 2). Disorganized communication (SIPS-P5, PANSS-P2), "decreased ideational richness" (SIPS-N5), and "impairments in personal hygiene and social attentiveness" (SIPS-D4) might be better understood as positive and negative symptoms, respectively, rather than cognitive-disorganized symptoms. In case of "difficulty in abstract thinking" (PANSS-N5) that had been considered either as a negative (Kay et al., 1987) or a cognitive-disorganized symptom (Vignapiano et al., 2019; Wallwork et al., 2012), with PS&B, a completely different cluster was suggested. This placement, however, is in line with the close connection between difficulty in abstract thinking and disorganization of the PANSS reported for male patients with schizophrenia-spectrum disorders (van Rooijen et al., 2018), the close association between disorganized and cognitive-perceptual symptoms in a study of schizotypal personality traits in the general population (Dodell-Feder et al., 2019) and between PANSS positive and disorganization total scores in first-episode psychosis and schizophrenia (Chang et al., 2019; Galderisi et al., 2020). However, its placement is challenged by a recent network analysis including neurocognitive and PANSS measures (Moura et al., 2021) in which "difficulty in abstract thinking" (PANSS-N5) was the only PANSS item integrated in the neurocognitive domain.

### 4.2. Clinical significance of (attenuated) hallucinations

The clinical and diagnostic significance of perceptual aberrations, in particular of hallucinatory experiences, for psychosis has been challenged by their association with age and developmental stage in both clinical and community samples (Maijer et al., 2019; Brink et al., 2020; Schimmelmann et al., 2015; Schultze-Lutter and Schmidt, 2016; Schultze-Lutter et al., 2017, 2020a, 2020b; Walger et al., 2020), their occurrence in a broad range of other mental and somatic disorders (Carota and Bogousslavsky, 2019; Coerver and Subramanian, 2020; Jean et al., 2020; Thakur and Gupta, 2020; Waters and Fernyhough, 2017) and their unclear psychosis-predictive value (Zhang et al., 2020; Niles et al., 2019; Marshall et al., 2019). It was suggested that hallucinations might better be regarded as a common endpoint of multiple processes and that, by assessing hallucinations in different modalities together as one, as done in SIPS and PANSS, meaningful differences in etiology and phenomenology may be ignored (Pienkos et al., 2019). These differences in perceptual aberrations do not only involve differences in affected sensory modalities or in stages on one common dimension, such as suggested by the severity ratings of SIPS and PANSS ranging from changes in perceptual sensitivity via perceptual distortions and pseudo- or attenuated hallucinations to frank psychotic hallucinations (Fig. 2). Rather, next to variations in genetic and neurophysiological processes, differences in accompanying cognitions and appraisals, in characteristics of the experience such as loudness in auditory hallucinations, in insight and in environmental factors (such as adversity and trauma) seem to result in truly different perceptual experiences with likely different levels of need for care, whose complexity should better be assessed differentially (Pienkos et al., 2019; Ben-Zeev et al., 2020). The view of multi- rather than one-dimensionality is supported by early studies on basic symptoms that failed to show a particular association between early perceptive basic symptoms and subsequent hallucinations (Klosterkötter, 1992; Klosterkötter et al., 2001). Rather, both cognitive and perceptive, mainly visual basic symptoms were predictive of positive symptoms – delusions, formal

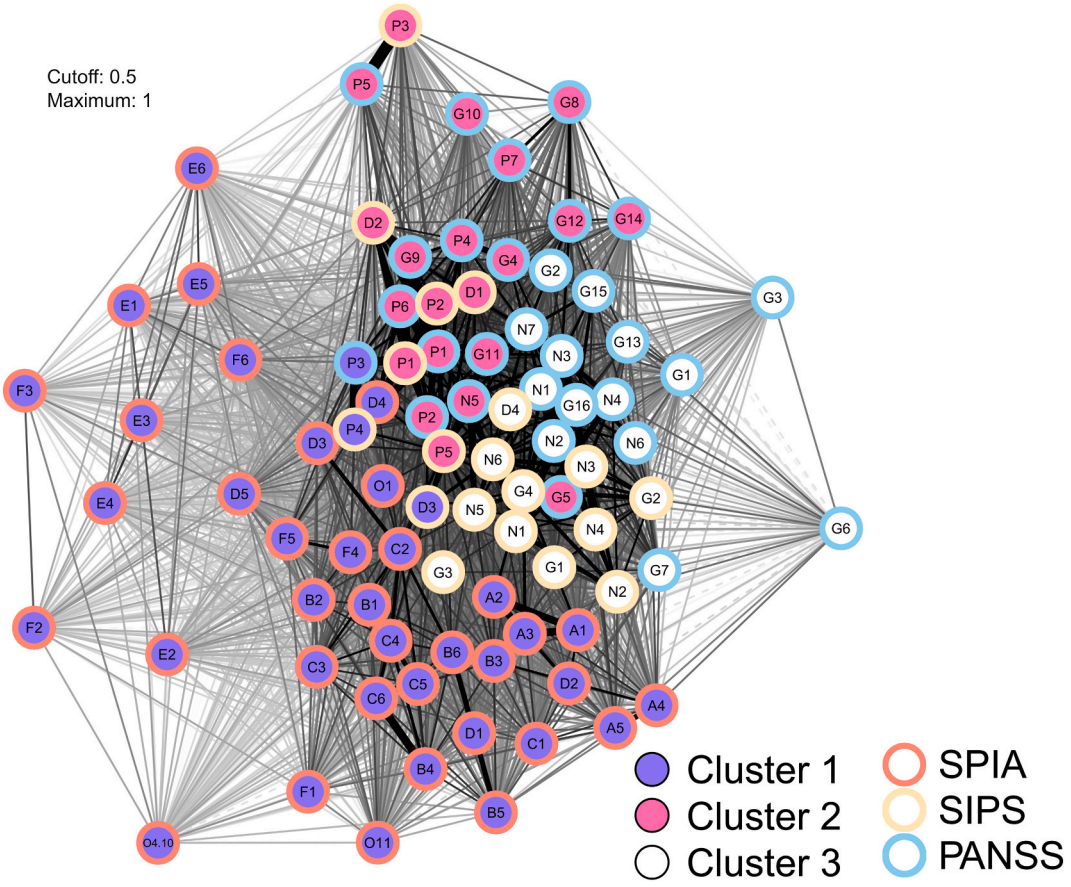


**Fig. 2.** Modularity analysis of the network with SPI-A, SIPS, and PANSS items as nodes, i.e., of basic, attenuated psychotic and frank psychotic symptoms respectively ($N = 460$).

Border color of nodes represent scale membership: SPI-A items (red border), SIPS items (yellow border), and PANSS items (blue border), with numbers in nodes indicating item number in the respective scale (see also Table 2). Fill color of nodes indicate cluster membership: cluster 1 (purple filling), cluster 2 (pink filling), and cluster 3 (white filling). The lines' type represents the direction of correlation between two nodes with continuous line indicating positive and dotted lines indicating negative correlations. The lines' thickness represents the correlation between the two connected nodes with thicker line indicating higher correlation. The correlation matrix, on which this figure is based on, can be inspected at http://www.gib.tel.uva.es/NetworkAnalysis-SchRes/Network_Clusters_wBorders_600dpis.png (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

thought disorder and hallucinations alike (Klosterkötter, 1992; Klosterkötter et al., 2001). This is supported in our network by the proximity of (attenuated) hallucinations to both cognitive and perceptive basic symptoms (especially, "thought interference", SPI-A-C2; "thought pressure", SPI-A-D3; "unstable ideas of reference", SPI-A-D4; "hypersensitivity to sounds/noise", SPI-A-F4; "changed intensity/quality of acoustic stimuli", SPI-A-F5; and "thought perseveration", SPI-A-O1).

Loss of insight is not explicitly stated in the definition of psychotic hallucinations in DSM-5 that briefly, defines them as vivid and clear perception-like experiences that, in the context of a clear sensorium, occur without voluntary control and an external stimulus but with the full force and impact of normal perceptions, although the latter implies complete loss of insight. Yet, oftentimes, formed hallucinations, in particular hearing voices, are considered already as "psychotic" when some insight is still maintained, e.g., in the transition criteria of the Comprehensive Assessment of At-Risk Mental States (CAARMS, Yung et al., 2006), an alternative instrument for the assessment of UHR criteria. The CAARMS regards hallucinations that can still be questioned, though "with effort", already as "true hallucinations" at a "psychotic but not severe" level (p. 6; Yung et al., 2006) and, indicative of conversion to psychosis if they occur with the required frequency and duration. This preference of the phenomenon over the related loss of insight into its abnormal nature is out of line with the evaluation of unusual thought contents, in which loss of insight "(no doubt)" is the leading criterion for a rating as "psychotic" (p.2 and 4; Yung et al., 2006). The placement of the mostly attenuated hallucinations together with clearly non-psychotic, subthreshold basic symptoms in our network model now further supports the outlined doubts about the clinical and diagnostic significance of hallucinatory experiences for psychosis and questions the CAARMS's use of still attenuated hallucinations in the definition of a conversion to psychosis. As stated above, most of the hallucinations were still in an attenuated form with at least some insight maintained (McGlashan et al., 2010). A recent metanalysis on insight as assessed by the Beck Cognitive Insight Scale (BCIS; Beck et al., 2004) in UHR samples, mainly by attenuated psychotic symptoms (Dondé et al., 2021) confirmed the assumed definition-inherent widely maintained insight in attenuated positive symptoms. It found that, in comparison to healthy controls, UHR subjects did not display significantly abnormal self-reflectiveness (i.e., a widely maintained ability to re-evaluate unusual perceptual experiences and correct erroneous inference) or deficits in overall cognitive insight abilities (i.e., a largely maintained general ability to question and reconsider own beliefs and judgements) but only a significantly abnormal self-certainty (i.e., a higher tendency to be overconfident about own judgements, which is more relevant to delusional beliefs). Thus, emphasizing the role of insight/subjectivism in the clinical significance of hallucinatory experiences (Pienkos et al., 2019), future studies should distinguish between hallucinations with and without some insight that should also be specifically assessed, e.g., with the BCIS, and examine whether frankly psychotic hallucinations link to other psychotic symptoms and behaviors, while attenuated

hallucinations link to subjective disturbances such as basic symptoms. In case of this, hallucinations experienced with some insight should not be rated and treated as a symptom of frank psychosis but rather as a potential risk symptom, even when formed and distressing.

Furthermore, acoustic, in particular verbal hallucinations are considered most common in schizophrenia and related disorders (American Psychiatric Association, 2013). A potential more central role of acoustic abnormalities is supported by the more central role of acoustic basic symptoms ("hypersensitivity to sounds/noise", SPI-A-F4; "changed intensity/quality of acoustic stimuli", SPI-A-F5) compared to visual and proprioceptive basic symptoms in our network. Whether a similar distinction is also present at the level of attenuated and frank hallucinations should also be examined in studies using a more differentiated assessment of these. Furthermore, the effect of age should be considered in these studies to account for the higher prevalence but lesser clinical significance of (attenuated) hallucinations in children and adolescents, and the lesser dominance of auditory hallucinations in early-onset psychosis (Driver et al., 2020; Maijer et al., 2019; Schultze-Lutter and Schmidt, 2016).

### 4.3. Strengths and limitations

To the best of our knowledge, this is the first study on clusters of a comprehensive set of symptoms relevant to early psychosis using modularity analysis in a large transdiagnostic patient sample attending an early detection and intervention service. Thereby, the use of the SPI-A allowed for the differential assessment of perceptual abnormalities of different modalities, while (attenuated) hallucinations were only assessed in a single item of each SIPS and PANSS. Next to its reported strengths, our study has some limitations: One is the high amount of missing data for eight criteria-relevant perceptive basic symptoms that, therefore, could not be included in the analysis. Yet, earlier studies on basic symptom dimensions consistently linked these to the other perceptive basic symptoms (Klosterkotter et al., 1996; Schultze-Lutter et al., 2012, 2008). Based on the very good results of previous stability analyses (see Jimeno et al., 2020 for details) and the cut-off value selected for the network edges (i.e., 0.5), we are fairly confident that their inclusion would likely not have altered the global network structure and, therefore, the clusters reported here should be similar in another population or with a similar set of items. The second limitation is the cross-sectional design of the study that does not allow to draw causal conclusion with regard to symptom development, in particular in the CHR group (Sandini et al., 2021), or changes related to treatment (Esfahlani et al., 2017). These should be studied in future longitudinal studies using a similarly broad range of symptom measures.

## 5. Conclusions

Modularity analysis of 86 basic, attenuated and frank psychotic symptoms in patients of an early recognition and intervention for psychosis service revealed three different clusters: "subjective disturbances", "positive symptoms and behaviors", and "negative and anxious-depressive symptoms". Thereby, the predominately attenuated hallucinations were associated with the basic symptoms in "subjective disturbances" rather than with other positive psychotic symptoms and related affects and behaviors. For the symptom-inherent differences in insight, this finding may underline the importance of insight in separating true, frank psychotic hallucinations from other hallucinatory experiences that, albeit being phenomenologically almost equal are still experienced with at least some insight. We conclude that, strictly, hallucinations held with any degree of insight should not be used to diagnose transition to or presence of frank psychoses and, relatedly, to justify antipsychotic medication. A detailed assessment of perceptual aberrations with regard not only to insight but also to sensory modality is essential in both research and the clinic.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.schres.2022.02.018.

## Role of funding sources

This work was supported by independent grants from the Deutsche Forschungsgemeinschaft (grant IDs KL970/3-1 and KL970/3-2 to JKl and FSL), and from the Koeln Fortune Program/Faculty of Medicine of the University of Cologne (project IDs 8/2005 and 27/2006 to FSL). It was also supported by the Spanish Ministerio de Ciencia, Innovacion y Universidades and Fondo Europeo de Desarrollo Regional (FEDER) (project IDs PGC2018-098214-A-I00 to JP and DPI2017-84280-R to RH). JKa received funding by the European Union under the 7th Framework Program (grant agreement n° 602152), the German Research Foundation (DFG, grant number KA 4413/1-1) and received honoraria by Otsuka, Lundbeck and Janssen.

The funding sources were not involved in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the article for publication.

## CRediT authorship contribution statement

JKl and FSL obtained funding. NJ and FSL conceived of the study. JGP, JP, and RH analyzed the data. NJ, FSL, KV, EM, TKL, JKa, and MR interpreted the data analyses. NJ wrote the first draft of the manuscript, revised by FSL, KV, JGP, JP and RH. All authors approved of the submission version.

## Declaration of competing interest

The authors confirm that they do not have any conflicts of interest that could inappropriately bias their work.

## Acknowledgments

None.

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