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Contrasting Monosymptomatic Patients with Hallucinations and Delusions in First-Episode Psychosis Patients: A Five-Year Longitudinal Follow-Up Study

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Key Words
Hallucinations · Delusions · Psychotic symptoms · Suicide

Abstract
Background: The main aim of this study was to identify subgroups of patients characterized by having hallucinations only or delusions only and to examine whether these groups differed with regard to demographic characteristics, clinical characteristics and outcome factors, including suicidality. ***Methods:*** Out of 301 consecutively admitted patients with first-episode psychosis, individuals with delusions only (D) and hallucinations only (H) were identified based on Positive and Negative Syndrome Scale (PANSS) items P1 (delusions) and P3 (hallucinations) scores at baseline and through 4 follow-up interviews over 5 years. The subgroups were compared with regard to demographic data, premorbid functioning, duration of untreated psychosis, clinical variables, time to remission and suicidality. ***Results:*** Two groups of patients were identified; H (n = 16) and D (n = 106). 179 patients experienced both hallucinations and delusions (dual symptom group). The H group was significantly younger, had a longer duration of untreated psychosis, poorer premorbid function and better insight than the D group. Notably, the H group scored higher on measures of suicidality, and at 5 years follow-up a significantly higher proportion of patients was lost to suicide in this group. The dual symptom group was closer to the D group on significant parameters, including suicidality and suicide rate. ***Conclusions:*** Patients with hallucinations only can be separated from patients with delusions only and the subgroups differ with regard to demographical data, clinical variables and notably with regard to suicidality. These findings suggest distinctions in the underlying biological and psychological processes involved in hallucinations and in delusions.

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Introduction

Lately, there has been a revival of the debate on how to best describe and define the psychotic illnesses [1, 2]. These illnesses have proven to be heterogeneous with regard to clinical features and etiology. Categorically based diagnoses have proven insufficient in the search for genetic correlates and specific brain morphology [3, 4]. Consequently studying more homogenous subgroups of psychotic illnesses based on individual symptoms and a dimensional approach might further our understanding of psychotic illnesses.

Delusions and hallucinations comprise the main features of the reality distortion component of psychotic illnesses, and have in many studies been described together as the positive symptom component. Though commonly described together, these symptoms often occur separately and possibly contribute to different outcomes including suicidality.

Little has been done to disentangle subgroups of positive symptom sufferers. Clinical studies of patients who experience delusional ideation without also suffering from hallucinosis, usually focus on delusional disorder [5, 6], and this diagnosis generally infers better outcome [7]. Other samples of patients who experience delusions only have not received specific attention.

Contrasting groups that experience hallucinations but not delusions have received limited attention in the literature. It has been described in nonclinical samples, e.g. in a study comparing a group of voice hearers without additional psychopathology to a normal (non-voice-hearing) control group. This study found the voice-hearing group to have poorer global functioning [8]. Another study comparing a similar group of voice hearers to a schizophrenia patient group found that while the form of hallucinations was similar between patient and nonpatient groups, other differences existed between the groups in terms of hallucinatory content, emotional quality and locus of control of the voices [9]. Recently, a patient group with a clinical picture dominated by hallucinations rather than delusions has been described [10, 11]. The group was labeled hallucinatory disorder and found to be of older age, to have higher academic achievement, to score better on insight measures and to have higher suicidality compared to a traditional schizophrenia patient group. The study lent evidence to hallucinatory disorder as a separate disease entity.

A number of studies have recorded the presence of both hallucinations and delusions in patient samples over time and related individual symptoms to associated symptoms and outcome factors [12, 13]. Furthermore, several studies have related the presence of delusions and of hallucinations to suicidality. A study investigating the relationship between delusions and suicidality found no evidence of a significant correlation between delusions at admission, and a history of suicidal ideation or suicide attempts [14]. The association between hallucinosis and suicidality is unclear, with a limited number of studies showing hallucinations as a risk factor for suicidality [15, 16]. Lately, the OPUS study found that hallucinations at 2 years of follow-up predicted suicidality (plans and attempts) in first-episode psychosis [17]. These studies, however, looked at data cross-sectionally and recorded the number of patients suffering from any one symptom at a particular time rather than showing longitudinal symptom profiles and their separate correlates.

Our aim in this study was to examine to what extent monopositively symptomatic first-episode psychosis (FEP) patients differ with regard to demography, premorbid function, duration of untreated psychosis (DUP), time to remission, associated symptomatology and suicidality. We wanted to follow the longitudinal trajectory of patients with FEP with hallucinations only or delusions only. Such subgroups are not very common and rarely examined. However, given our large first-episode sample, meaningful comparisons between the 2 groups could be made. By studying symptoms in subgroups not based on the traditional DSM subtypes, we wanted to shed light on whether different pathological mechanisms were involved in delusions and hallucinations. More specifically we wanted to answer the following research questions:

(1) Is it possible to identify subgroups of patients during a 5-year follow-up period who have suffered either from hallucinations only or delusions only, and can these groups be differentiated on demographic characteristics, DUP, premorbid functioning [Premorbid Assessment of Functioning Scale (PAS)] and time to remission?
(2) To what extent do the 2 groups differ clinically, i.e. in PANSS scores, including insight (G12), in the follow-up period?
(3) Are hallucinations related to suicidality (ideation, plans and attempts) and completed suicides to a greater extent than delusions?

Methods

The Early Treatment and Identification of Psychosis Study

The Early Treatment and Identification of Psychosis study is a large, cross-sectional and longitudinal study of consecutively admitted FEP patients [18, 19]. The study was designed to identify

and follow up clinical, epidemiologic samples of FEP patients from 4 Scandinavian catchment areas. All patients were evaluated reliably with an extensive clinical assessment battery at baseline, and re-evaluated after 3 months, 1 year, 2 years and 5 years [20].

Study Subjects

The study was carried out within the specialist psychiatric healthcare services of 4 Scandinavian health care sectors (North and South Sector, Rogaland County, Norway, Ullevaal Sector, Oslo, Norway, and Fjorden Midsector, Roskilde, Denmark).

The criteria for inclusion were:

(1) A first episode of a nonaffective psychosis.
(2) Living in the catchment area.
(3) Age 18–65 years (15–65 years in Rogaland).
(4) IQ >70.

The exclusion criteria were receiving adequate prior antipsychotic treatment and an organic/substance-induced psychosis.

Written informed consent was obtained from all subjects, and the study was approved by the regional ethics research committees. Altogether 301 patients were included from 1997 through 2000.

The current study looked at 2 groups of patients taken from the above sample.

(1) Patients experiencing hallucinations only (H). This group experienced hallucinations (rated as PANSS score item P3, hallucinations, of ≥4) but not delusions (PANSS score P1, delusions, of ≤3) (n = 16).

Patients who were found to experience delusions (PANSS score P1, delusions, of ≥4) on follow-up interviews, up to and including 5 years, were removed from the group (n = 9).

(2) Patients experiencing delusions only (D). This group experienced delusions (rated as PANSS score item P1, delusions, of ≥4), but not hallucinations (PANSS score P3, hallucinations, of ≤3) (n = 106).

Patients who were found to experience hallucinations (PANSS score P3, hallucinations, of ≥4) on follow-up interviews, up to and including 5 years, were removed from the group (n = 19).

This study aimed to explore monosymptomatic positive symptom groups. The patients experiencing both hallucinations and delusions (n = 179) were not the focus of the present study.

Instruments and Measures

The structured clinical interview for the DSM-IV (SCID) was used for diagnostic purposes [21]. Symptom levels were measured by the Positive and Negative Syndrome Scale Score (PANSS) [22], and symptom domains were represented by the corresponding PANSS components (positive, negative, excitative, cognitive and depressive) [23]. The patients were further described by individual PANSS items P1 (delusions), P3 (hallucinations) and G12 (insight). Global functioning was measured by the Global Assessment of Functioning Scale (GAF) [24]. Social functioning (number of friends and work functioning) at baseline was measured with the Strauss-Carpenter scale [25]. Quality of life was evaluated by Lehman's Quality of Life Interview [26]. In this study we used the item 'satisfaction with life in general'. The DUP was measured as the time in weeks from the first positive psychotic symptoms (PANSS score of ≥4 on positive scale items 1, 3, 5 or 6 or general scale item 9) to the start of the first adequate treatment of psychosis (i.e. admission to the study). Remission was defined as a period of at least 1 week without positive psychotic symptoms corresponding to a PANSS score ≤3 on positive subscale items 1, 3, 5 and 6 and on general subscale 9. Time to remission was defined as the time to adequate treatment was initiated to remission of symptoms as described above. Premorbid functioning was measured by the PAS, which describes 4 premorbid periods in life: childhood (up to 11 years), early adolescence (12–15 years), late adolescence (16–18 years) and adulthood (19 years and beyond). A previous analysis identified 2 premorbid dimensions: *social* consisting of PAS items social isolation and peer relationships and *academic,* which comprises school performance and school adaptation [27]. Suicidality was assessed by asking the patients at index diagnostic interview whether they had experienced any suicidal thoughts, plans or attempts in the preceding month (suicidality at baseline) or whether they had experienced any suicidal thoughts, plans or attempts earlier in their lifetime (suicidality before baseline). The questions were repeated in the follow-up interviews.

All raters were trained in the use of the study instruments by rating previously prepared case notes and audiotapes/videotapes before entering the study assessment teams. The assessment teams consisted of the same raters throughout the study. Good reliability for all major variables (PANSS, DUP and diagnosis) was achieved [28].

Statistical Analysis

The analysis was performed with the SPSS Statistical Program (version 16: SPSS Inc., Chicago, Ill., USA). Means and standard deviations are reported for continuous variables and percentages for categorical variables. DUP had a markedly left-skewed distribution and was transformed to its natural logarithm, which is normally distributed, before the t test was performed.

The clinical data were statistically analyzed using conventional descriptive methods and t tests. For nonparametric data and data of skewed distribution χ^2 and Mann-Whitney tests were performed. In situations where ≥1 expected cell frequencies were <5, Fisher's exact test was used.

Results

At baseline a total of 25 patients experienced hallucinations without also experiencing delusions. Nine of these patients later developed delusions, reported in follow-up interviews, leaving a total of 16 patients (H group) who experienced hallucinations without ever scoring >3 on delusions (PANSS P1) in the follow-up period. Baseline data further revealed a group of 125 patients whose presentation was that of delusions without concurrent hallucinations. Of these, 19 patients reported hallucinations in follow-up interviews, leaving a total of 106 delusional patients (D group) who never scored >3 on hallucinations (PANSS P3) in the follow-up period. Consequently, this study showed that it was possible to separate out 2 different subgroups of patients from a sample of patients with FEP on the basis of specific symptomatology.

As displayed in table 1, the H group was younger, had fewer completed years of education at baseline and a lon-

ger DUP compared to the D group. The diagnostic distribution in the H group was as follows: schizophrenia = 7 (44%), schizoaffective disorder = 4 (24%), mood disorder with mood-incongruent psychotic features = 3 (19%), brief psychotic disorder = 1 (6%) and psychosis not otherwise specified = 1 (6%). The diagnostic distribution in the D group was: schizophrenia = 24 (22%), schizophreniform disorder = 19 (18%), schizoaffective disorder = 7 (7%), delusional disorder = 12 (11%), mood disorder with mood-incongruent psychotic features = 16 (15%), brief psychotic disorder = 10 (9%) and psychosis not otherwise specified = 20 (19%). These diagnostic differences were expected based on the differential weight of the different symptoms in DSM IV.

Data describing premorbid functioning are displayed in table 2. The D group reported better premorbid functioning on all measures.

Table 3 shows PANSS component scores, insight scores (G12) and scores for delusions item (P1) and hallucinations item (P3) as well as GAF scores at baseline and through 5 years of follow-up for the 2 groups. Most notably, the H group showed better cognitive functioning at all points (statistically significant at 2 and 5 years) and better insight at all points (statistically significant at baseline and 5 years). No statistically significant difference was found in the PANSS depression component. With regards to the positive component the H group scored consistently lower than the D group (statistically significant difference at baseline). As expected there were significant differences between the groups on measures of delusions (item P1) and hallucinations (item P3).

No significant differences between the groups were found on satisfaction with life in general (Lehman's Quality of Life Interview) or social functioning (Strauss-Carpenter scale).

Regarding the use of antipsychotic medication, this study included a fixed regimen for the first 2 years of the study (for details [29]). In years 3, 4 and 5 a larger proportion of the D group were prescribed medication (no statistically significant differences). Furthermore, the D group used consistently higher doses on all points of measure (no statistically significant differences).

Table 4 addresses the group differences in suicidality. Suicidality before admission was significantly higher in the H than the D group. At the 5-year interview a total of 4 patients from the H group were dead. In the 5-fold larger D group, 5 patients were dead. In the H group 3 people were dead by suicide and 1 from overdose. In the D group 2 patients were dead by suicide, 1 from overdose and 2 from unclear cause. Statistical analyses of the numbers of patients dead by suicide showed a significantly higher

Table 1. Patient characteristics at baseline and time to remission

Groups	Hallucinations (n = 16)	Delusions (n = 106)
Age, years	23.1 ± 7.36*	29.2 ± 9.78*
Males, %	68.8	58.5
Years of education	11.2 ± 1.30*	12.5 ± 2.70*
SZP spectrum disorders, %	68.8	46.2
DUP, weeks		
Median	26*	7.5*
Range	0–450	0–415
Weeks to remission	13.5 ± 20.37	16.6 ± 28.53

Figures are means ± SD unless otherwise indicated. t test after log transformation of DUP. SZP spectrum disorders equal a diagnosis of schizophrenia, schizophreniform disorder or schizoaffective disorder. * $p < 0.05$.

Table 2. Premorbid function (PAS)

Groups	Hallucinations (n = 16)	Delusions (n = 106)		
	mean ± SD	mean ± SD	MWUz	p
PAS social level childhood	1.34 ± 0.94	0.74 ± 0.88	–2.53	0.011
PAS social level last score	2.63 ± 1.53	1.66 ± 1.43	–2.43	0.015
PAS academic level childhood	2.03 ± 1.23	1.49 ± 1.11	–1.73	0.083
PAS academic level last score	3.03 ± 1.42	2.16 ± 1.17	–2.35	0.019

MWUz = Mann-Whitney U z Value.

Table 3. PANSS scores including 4 components, insight item (G12), delusions item (P1), hallucinations item (P3) and GAF scores from baseline to 5-year follow-up

Groups	Baseline	3 months	1 year	2 years	5 years
Pos. comp.					
H	10.88 ± 3.12*	7.88 ± 3.76	6.25 ± 2.00	6.08 ± 1.61	5.67 ± 1.63
D	14.10 ± 3.86*	8.16 ± 3.42	7.71 ± 3.69	7.69 ± 3.52	6.97 ± 2.76
Neg. comp.					
H	22.69 ± 9.76	19.44 ± 9.28	15.58 ± 6.75	12.77 ± 3.49*	13.33 ± 2.07
D	19.37 ± 8.37	16.65 ± 6.76	16.02 ± 6.08	15.63 ± 6.57*	14.58 ± 6.91
Depr. comp.					
H	12.69 ± 3.89	10.00 ± 4.23	8.17 ± 2.17	8.54 ± 3.69	7.83 ± 3.82
D	12.10 ± 4.01	9.25 ± 3.55	8.37 ± 3.03	8.44 ± 3.15	7.58 ± 2.81
Cogn. comp.					
H	6.25 ± 3.22	4.44 ± 2.37	3.83 ± 1.12	3.23 ± 0.60*	3.00 ± 0.00*
D	6.89 ± 3.15	4.76 ± 2.13	4.54 ± 1.76	4.44 ± 1.88*	4.20 ± 1.98*
Insight G12					
H	1.69 ± 1.45*	1.69 ± 1.25	1.42 ± 0.79	1.31 ± 1.11	1.00 ± 0.00*
D	2.73 ± 1.52*	1.73 ± 2.11	1.62 ± 1.08	1.53 ± 0.95	1.43 ± 0.98*
Del. P1					
H	1.75 ± 0.93*	1.50 ± 0.89*	1.00 ± 0.00*	1.31 ± 0.63*	1.00 ± 0.00*
D	4.65 ± 0.81*	2.27 ± 1.34*	2.08 ± 1.34*	2.10 ± 0.94*	1.78 ± 1.11*
Hall. P3					
H	4.44 ± 0.63*	2.25 ± 1.61*	1.25 ± 0.87	1.38 ± 0.96	1.33 ± 0.82
D	1.90 ± 0.94*	1.21 ± 0.56*	1.10 ± 0.43	1.21 ± 0.57	1.14 ± 0.46
GAFs					
H	34.62 ± 5.62*	48.50 ± 13.56	53.77 ± 10.73	60.54 ± 12.47	63.50 ± 12.72
D	29.86 ± 6.61*	50.02 ± 12.88	55.33 ± 13.56	56.98 ± 15.77	61.25 ± 14.63
GAFf					
H	37.38 ± 8.80	48.62 ± 13.12	50.85 ± 12.06	57.46 ± 12.98	62.00 ± 9.30*
D	32.94 ± 11.27	50.70 ± 13.63	55.04 ± 14.27	55.43 ± 15.70	58.06 ± 16.10*

Figures are means ± SD.

Numbers at baseline: H = 16, D = 106; 3 months: H = 16, D = 99; 1 year H = 12, D = 90; 2 years: H = 13, D = 81; 5 years: H = 6 D = 65. * $p < 0.05$.

Table 4. Suicidality (ideations, plans and attempts, not completed suicides) from baseline to 5-year follow-up

Groups	Hallucinations (mean ± SD)	Delusions (mean ± SD)	MWUz	p
Suicidality before baseline	2.25 ± 1.00	1.56 ± 0.84	–3.121	0.020
Suicidality at baseline	1.75 ± 0.58	1.58 ± 0.92	–1.798	0.072
Y1 suicidality	1.33 ± 0.49	1.37 ± 0.55	–0.980	0.922
Y2 suicidality	1.77 ± 1.01	1.46 ± 0.80	–1.414	0.254
Y5 suicidality	1.33 ± 0.82	1.37 ± 0.55	–0.595	0.552

Numbers at baseline H = 16, D = 105; 1 year H = 12, D = 93; 2 years H = 13, D = 82; 5 years H = 6, D = 62.

rate of completed suicides in the hallucination only group (Fisher exact test; $p = 0.016$).

A total of 179 patients showed a disposition to both hallucinations and delusions when initially ill or in relapse. As expected, this dual symptom group proved more symptom burdened (PANSS) and with poorer global functioning (GAF) than both the H and the D groups (significant differences, $p < 0.05$, between D and dual symptom group on GAFs and GAFf and PANSS positive symptoms scores, and between H and the dual symptom group on PANSS positive symptoms, on all assessments). With regard to PANSS insight (G12) and cognitive component the dual symptom group scored consistently poorer than the monosymptomatic groups at all points of measure (statistically significant differences between the dual and H groups at baseline and 5 years for insight and 1, 2 and 5 years for cognition, and between the D and dual groups at 3 months, 1 year and 5 years for insight and at 1, 2 and 5 years for cognition).

There were no statistically significant differences in suicidality between the dual symptom group and the D group at any point of measure. After 5 years of follow-up 6 patients in the dual symptom group had passed away, 3 by suicide. Analysis showed no statistically significant difference in suicide rate between the dual symptom group and the D group. Between the mixed group and the H group, however, the difference was significant (Fisher's exact test; $p = 0.009$).

Discussion

This study demonstrated that it is possible to identify 2 subgroups of monopositively symptomatic FEP patients from a longitudinal symptom perspective. We found that the patients with a clinical picture dominated by hallucinations were of a younger age and had completed fewer years of education. This contrasted with results from a previous study by Mauri et al. [11], who found the group of patients dominated by hallucinations to be older at the time of onset and with higher academic achievement. On the other hand our findings are similar to previously mentioned studies of nonclinical voice hearers that reported the group experiencing hallucinations to be younger at the age of onset compared to a schizophrenia patient group [9]. The main reason for the divergent findings is likely because different patient populations were involved, i.e. Mauri et al. [11] examined patients with chronic psychosis, whereas our patients were in their first episode.

We additionally found that the H group scored poorer on both social and academic premorbid variables. To our knowledge no other study has examined this relationship, or found this difference that appears to be present even before the onset of psychosis.

The most notable finding of this study is the apparent relationship between symptomatology and suicidality. The difference in suicidality between the 2 groups was statistically significant at baseline but appeared to level out at later times. This could be due to attrition of the most highly suicidal patients in the H group, where 25% of the patients were deceased at the 5-year follow-up. This contrasts with the D group, where the mortality rate was much lower (1 fifth), and fewer patients were lost to suicide.

It may be that the increased suicidality in the H group could be related to the clinical picture itself, insofar as hallucinations tend to be experienced as frightening, intrusive and imperative, and might lead to suicidal thoughts and acts more easily. A recent review of schizophrenia and suicidality reported on 5 empirical studies of command hallucinations and their relationship to suicidality [30]. The results were conflicting, with 3 of the studies finding that command hallucinations did not correlate significantly with suicidal ideation and attempts.

Our data indicate that suicidality is more tightly linked to hallucinations than delusions. A potential mediator between hallucinations and suicidality could be insight. A substantial body of data supports insight as a risk factor for suicidality in schizophrenia [31–33]. As previously mentioned by Mauri et al. [10], better insight might be linked with hallucinations. More recently a study found that patients with hallucinations without concurrent delusions had better cognitive insight than patients with delusions only [34]. Our study assesses insight using the PANSS G12 item. This measure has shown good correlation with measures of insight in more specialized insight scales such as the Beck Cognitive Insight Scale, the Birchwood Self Rating Scale and the Schedule of Assessment of Insight – expanded version [35, 36]. Our results show that the more suicidal H group displayed better insight on all assessments. Furthermore, they scored consistently better than the D group on the cognitive component of the PANSS. Two recent meta-analyses have found that cognitive deficits and poor insight may be linked [37, 38].

Compared to the monosymptomatic patients, who are the focus of this paper, the patients who experienced both hallucinations and delusions were found to be more symptom burdened and have poorer global functioning. Notably, the dual symptom group scored closer to the D

group with respect to suicidality and suicide rate. Furthermore, this dual symptom group had poorer insight scores than the single symptom groups at baseline and on all follow-ups. On the basis of these findings we could hypothesize that delusions could have a protective effect on suicidality, and that this possibly could be mediated by reduced insight associated with delusions. Overall, we feel our findings suggest a further link between hallucinations and suicidality that ought to be explored.

Other potential mediators of suicidality could be DUP and premorbid function. Previous literature has found poor premorbid function to be both a risk factor [39] and a protective factor [29, 38] for suicidality. Long DUP has been related to suicidality in FEP [40, 41], while other FEP studies have failed to find this association [17, 42]. While longer DUP could explain some of the differences in suicidality between the groups before baseline, it is less certain how much it might contribute to the higher suicide rate in the H group at 5 years of follow-up.

This study is limited by the small sample of patients in the hallucinations only group. In fact such a clinical picture is not commonly seen. A related limitation is the small number, particularly in our H group, after the 2-year follow-up (n = 13 at the 2-year follow-up), when a significant number of patients in this group had been lost to suicide. As a consequence of the small sample size in the H group, advanced multivariate statistics were not performed. A further limitation of the present study is the lack of a standardized measure of suicide risk. The assessment tool provided has, however, formed the basis of indepth investigations of suicidality in FEP [43].

In conclusion, this study contributes to a growing corpus of data that encourages a return to the study of individual symptoms and dimensions as important determinants of course in psychotic illnesses. A similar division of symptom groups could potentially aid further research into the genotypes and endophenotypes of schizophrenia spectrum disorders, and aid us in furthering our understanding of the various processes that drives psychosis manifest. This study also highlights a potential link between hallucinations and suicidality, with insight as a possible mediator. The subgroup of patients with a clinical picture dominated by hallucinations is particularly interesting, and its relation to suicidality needs to be further explored.

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