

NIH Public Access

Author Manuscript

Compr Psychiatry. Author manuscript; available in PMC 2013 August 01.

Published in final edited form as:

Compr Psychiatry. 2012 August ; 53(6): 718–726. doi:10.1016/j.comppsych.2011.11.003.

Auditory Hallucinations in a Cross-Diagnostic Sample of Psychotic Disorder Patients: A Descriptive, Cross-Sectional Study

Ann K. Shinn, Danielle Pfaff, Sarah Young, Kathryn E. Lewandowski, Bruce M. Cohen, and Dost Öngür

Schizophrenia and Bipolar Disorder Program, McLean Hospital and Harvard Medical School Department of Psychiatry, USA

Abstract

Background—Auditory hallucinations (AH) are a cardinal feature of schizophrenia spectrum disorders. They are not disease specific, however, and can occur in other conditions, including affective psychoses.

Methods—In this descriptive, cross-sectional study, we examined AH in relation to other psychotic symptoms, mood symptoms, illness severity, and functional status in 569 patients with psychosis (n=172 schizophrenia, n=153 schizoaffective disorder, n=244 bipolar disorder with psychotic features).

Results—323 (56.7%) patients reported a lifetime history of AH (75.6% of patients with schizophrenia, 71.9% schizoaffective disorder, and 34.0% bipolar disorder). The mean score for the hallucinations item (P3) of the Positive and Negative Syndrome Scale (PANSS) in the AH group was 3.66 ± 1.79 , indicating mild to moderate state hallucinations severity. AH were strongly associated with hallucinations in other sensory modalities and with the first-rank symptoms of delusions of control, thought insertion, and thought broadcasting. Multivariate analysis showed that AH were associated with lower education even after controlling for diagnosis, age, and gender. There was no association between AH and functional status as measured by the Multnomah Community Ability Scale (MCAS).

Conclusions—AH are associated with specific clinical features across the continuum of both schizophrenic and affective psychoses independent of DSM-IV diagnosis.

Keywords

Hallucinations, auditory; Psychotic disorders; Schizophrenia; Bipolar disorder

Introduction

Auditory hallucinations (AH) are a cardinal feature of schizophrenia and other psychotic disorders. Though AH are most common in schizophrenia (1), they are not disease specific

^{© 2011} Elsevier Inc. All rights reserved

Corresponding author: Ann K. Shinn, MD, MPH 115 Mill Street Belmont, MA 02478 Tel: 617-855-3053 Fax: 617-855-2895 akshinn@partners.org.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

and can occur in affective psychosis (2), non-psychotic psychiatric conditions like borderline personality disorder and post-traumatic stress disorder (3), substance intoxication (4) and withdrawal (5), neurological disease (6), and even in healthy individuals (7-10). The current version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) (11) reflects the dichotomous categorization of psychotic illness into schizophrenic and affective psychoses stemming from the Kraepelinian tradition. While such a categorical system has improved diagnostic reliability, the validity of such diagnostic constructs has been questioned (12). The clinical overlap in symptoms such as AH, along with a growing body of epidemiological, genetic, and neuroscience research, suggests that schizophrenia and affective psychoses may not be biologically discrete disease entities (13–15), but rather syndromes on a continuum (16). Such evidence challenges the DSM-IV nosology and suggests that research should focus on dimensional measures of psychopathology, some of which traverse diagnostic categories (17). The dimensional approach aligns well with the goals of the National Institute of Mental Health (NIMH), which recently launched the Research Domain Criteria project to find new ways of classifying psychopathology based on dimensions of observable behavior and neurobiological measures, cutting across disorders as traditionally defined (18).

The phenomenology of AH in schizophrenia-spectrum disorders has been well-described (19–29). Several theories have been proposed for both the cognitive and biological bases of AH, but after much research it is still not clear why some patients hallucinate and others do not. It is also not clear whether AH are independently associated with a broad range of clinical outcomes across psychotic disorder diagnoses.

In this descriptive, cross-sectional study, we focused on the symptom dimension of AH rather than on psychotic disorder diagnoses (schizophrenia, schizoaffective disorder, and bipolar disorder). We explored the characteristics of AH in relation to other psychotic symptoms, mood symptoms, substance use disorders, and anxiety disorders in a large cross-diagnostic sample of patients. In addition, we examined whether AH is associated with functional status and illness severity after controlling for diagnosis and demographic factors such as age, gender, and age of onset. We predicted that AH would be associated with poorer outcomes across diagnostic categories.

Materials and Methods

Subjects

Subjects were recruited for a genotype-phenotype association study of psychotic and mood disorders. The study was approved by the McLean Hospital Institutional Review Board. All subjects provided informed consent. More than 4,000 consecutive admissions to the Mclean Hospital Psychotic Disorders inpatient units and 300 outpatients from the hospital community were screened over a four year period. We reviewed the medical records of inpatients on these units daily, and approached individuals who met eligibility criteria. Subjects were included if they were 18–89 years in age, carried a diagnosis of schizophrenia, bipolar disorder, or other psychotic or mood disorder, and had legal and mental competency to provide informed consent. Individuals with psychotic or mood disorders attributable to a general medical condition, a neurological illness, or substance intoxication or withdrawal were excluded. Due to the large number of patients screened each day, our recruitment strategy did not necessarily capture all inpatients meeting eligibility criteria. Outpatients were recruited through advertisements posted at McLean Hospital and surrounding areas, and screened for eligibility using a telephone questionnaire.

At the time of this analysis, the database consisted of 651 subjects with diagnoses of schizophrenia (n=172), schizoaffective disorder (n=153), bipolar I disorder (n=302), and

major depressive disorder with psychotic features (n=24). Fifty-eight subjects with bipolar I disorder without psychotic symptoms were excluded from the analysis. We also excluded the 24 subjects with psychotic depression, given the group's small sample size. The final study sample consisted of a total of 569 patients: n=172 with schizophrenia, n=153 with schizoaffective disorder, and n=244 with bipolar I disorder with psychotic features.

Assessments

Patients underwent a comprehensive clinical research evaluation. The Structured Clinical Interview for DSM-IV (SCID) (30) was used to diagnose primary psychotic and mood disorders and co-occurring substance use and anxiety disorders. The SCID evaluation, including the assessment of hallucinations, was based on all available information, including hospital records and, with patient consent, information from family and outpatient treaters. The SCID takes into account both current and previous history of psychiatric disorders. The SCID does not systematically evaluate of history of suicide attempts or treatment with electroconvulsive therapy (ECT); questions about these items were added. Assessment also included the Positive and Negative Syndrome Scale (PANSS) (31), the Young Mania Rating Scale (YMRS) (32), and the Montgomery-Asberg Depression Rating Scale (MADRS) (33) to assess the severity of current psychotic and mood symptoms. The Multnomah Community Ability Scale (MCAS) (34, 35) was administered to evaluate level of functioning in the community. The MCAS is a 17-item scale (rated from 1, or impaired, to 5, or normal) that asks about behavior such as ability to cope with stress and anxiety, manage money successfully, independently complete activities of daily living, and utilize effective social skills. MCAS items 2-4 (intellectual functioning, thought process, mood abnormality), 14 (medication compliance), and 16-17 (alcohol/drug abuse, impulse control) were removed because these aspects of psychopathology are already measured by other administered scales. Thus, the abbreviated version of the MCAS used in this study consisted of 11 items for a maximum possible score of 55. MCAS data were available on 265 of the 569 studied subjects (46.6%). For the four scales (PANSS, YMRS, MADRS, and MCAS), patients were asked to focus on the most severe symptoms experienced in the current episode or within the previous month.

Patients were assessed by trained research staff. We carried out monthly reliability exercises where a study subject was interviewed in the presence of the research team. Each rater assessed the subject independently. Reliability was measured by the fraction of raters who showed perfect agreement on a specific measure. Rates of agreement were perfect (1.0) for SCID diagnoses, near-perfect for current mood episodes (1.0 for major depression, 0.93 for mania), and excellent for specific psychotic symptoms (0.80 for persecutory delusions, 0.85 for AH).

We performed all statistical analyses using SPSS (PASW) version 18. We used the chisquare test to assess for independence among categorical variables, and t-tests to test for differences between continuous variables. SCID item B16, which asks about lifetime AH ("Did you ever hear things that other people couldn't, such as noises, or the voices of people whispering or talking?"), was used to group patients, and formed the basis of the current analysis. This item was coded into a binary measure: subjects with a score of 3 (threshold or true) were categorized as having AH, while those with scores of 1 (absent or false), 2 (subthreshold), or 4 (inadequate information) were coded as non-auditory hallucinators (NAH). All other individual SCID items were coded similarly, with the exception of items for thought insertion, thought withdrawal, olfactory hallucinations, and gustatory hallucinations, which are already in binary format in the SCID.

To estimate the severity of AH, we used PANSS item 3 which asks about hallucinatory behavior using a scale from 1 (absent) to 7 (most severe). P3 assesses state severity of AH,

while the SCID item B16 assesses lifetime AH. While PANSS P3 is not specific to AH, these were the most common subtype in this sample. Thus, we used P3 as a proxy for AH severity in individuals who scored 3 on SCID item B16. To assess the degree to which hallucinations in sensory modalities other than audition contribute to the P3 score, we also examined P3 in patients with visual, olfactory, gustatory, or tactile hallucinations (VOGTH). VOGTH was analyzed as a binary variable; patients with a lifetime history of hallucinations in one or more non-auditory modalities were coded as having VOGTH. To determine whether the addition of VOGTH impacts the P3 score in patients with AH, we compared patients with pure-AH to patients with AH plus VOGTH. To assess whether VOGTH experiences are similar in severity to AH experiences, we compared the pure-AH group to patients with VOGTH-only.

Medication information was recorded from the discharge medication list for inpatients, and self-reported for outpatients. Medication data were missing in 30 patients. In the 539 patients with complete medication data, the chlorpromazine (CPZ) equivalent dose was calculated. The CPZ equivalent, or the standardized dose of antipsychotic medications that a patient required at the time of study participation, was regarded to be a marker of illness severity, and thus was treated as an outcome variable. For typical antipsychotics, we calculated CPZ equivalents using the Schizophrenia Patient Outcomes Research Team (PORT) treatment recommendations (36). For most atypical antipsychotics, we used the CPZ equivalent doses published by Woods (37). For the newer antipsychotic paliperidone, we used the dosing guidelines by Gardner and colleagues (38); to preserve the relationship between risperidone and paliperidone (the active metabolite of risperidone), we also turned to Gardner et al for the dosing equivalent of risperidone.

We performed multivariate analyses to investigate whether the relationships observed with chi-square tests and t-tests would persist after controlling for diagnosis, age, and gender. For binary outcomes, we performed forward stepwise conditional logistic regressions, with 20 iterations, entering diagnosis into the first block, age and gender into the second block, and AH into the third block. A p-value of less than 0.05 was used as the criterion for retention, while a p-value of 0.10 was the criterion for excluding variables at each block. For continuous outcomes, we performed forward stepwise multiple linear regressions using the same parameters for retention and exclusion of variables as the logistic regression model.

Results

Prevalence of Auditory Hallucinations by Diagnosis

Three hundred twenty-three of 569 subjects (56.8%) experienced lifetime AH, while 246 (43.2%) did not. Not surprisingly, diagnosis was strongly associated with AH (χ^2 =90.535, df=2, p=2.19 × 10⁻²⁰). Approximately three-quarters of patients with schizophrenia and schizoaffective disorder experienced AH (n=130, 75.6% and n=110, 71.9%, respectively) while approximately a third of patients with bipolar disorder with psychosis did (n=83, 34.0%).

Demographic Features

There were no significant differences between AH and NAH patients with respect to age, gender, handedness, age at illness onset, or proportion with family history of psychotic illness (Table 1).

Severity and Quality of Auditory Hallucinations

PANSS P3 data were available for 317 of the 323 AH patients and for 241 of the 246 NAH patients. The mean P3 score for the AH group was 3.66 ± 1.79 , which reflects hallucinations

of mild to moderate severity in the month prior to study participation. The P3 score for the AH group differed significantly from the P3 score of the NAH group ($p=9.591 \times 10^{-4}$). Notably, the mean P3 score for the NAH group (1.66 ± 1.06) was between "absent" (1) and "minimal-- questionable pathology; may be at the upper extreme of normal limits" (2), suggesting that the NAH group included some patients who may experience sub-threshold or questionable AH. Of the 317 AH patients with P3 data, 235 (74.1%) had P3 scores of 3 or greater, indicating unequivocally active AH in the month prior to study participation. The remaining 82 patients had no (n=71), or only questionable (n=11), AH in the preceding month despite a history of AH in their lifetimes.

The difference in P3 scores between the pure-AH (n=163) group and the AH plus VOGTH group (n=154) was statistically significant but relatively small in magnitude (3.42 ± 1.82 and 3.91 ± 1.73 , respectively; t=-2.438, p=0.015). VOGTH-only patients (n=59) had comparatively lower P3 scores (2.25 ± 1.48) than pure-AH patients; this difference was statistically significant (t=4.439, p= 1.429×10^{-5}).

Of the 323 patients with AH, 37.5% reported hearing a running commentary (SCID item B17), and 30.7% reported hearing two or more voices conversing with one another (SCID item B18). Among individuals who reported having AH, a greater proportion of schizophrenia and schizoaffective disorder patients endorsed running commentary and voices conversing than patients with bipolar psychosis, but these were still common among patients with bipolar psychosis (Table 2).

Auditory Hallucinations and Other Psychotic and Mood Symptoms

We examined the relationship between AH and hallucinations in other sensory modalities (Table 3). A larger proportion of AH patients had experienced visual, tactile, and olfactory hallucinations compared to NAH patients. Interestingly, there was no association between AH and gustatory hallucinations. The latter represented the lowest frequency hallucinations of any modality in our sample.

Given the hypothesis that AH are a manifestation of a broader phenomenon in which patients misattribute self-generated stimuli as alien and externally imposed, we examined the association between AH and other Schneiderian first-rank passivity symptoms. AH was significantly associated with delusions of control, thought insertion, and thought broadcasting. There was also a trend for an association between AH and thought withdrawal (p=0.071).

A greater percentage of AH patients reported bizarre delusion content compared to NAH patients. There was a trend for an association between AH and delusions of reference (p=0.067). AH was not strongly associated with persecutory delusions, disorganized behavior, or disorganized speech.

The AH and NAH groups showed a statistically significant difference in manic symptoms in the month prior to study participation, with NAH patients showing higher average scores on the YMRS compared to AH. There was no significant association between AH and depressive symptoms within the prior month, as measured by the MADRS (Table 3).

Auditory Hallucinations and Functional Status

A significantly greater proportion of NAH patients compared to AH patients had attained higher levels of education. There were trend-level differences between AH and NAH groups in rates of employment (p=0.063) and type of residence (p=0.060). There were no differences between the two groups with respect to marital status or the proportion with

children (Table 4). Among the subset of 265 patients in whom the modified MCAS was completed, there was no significant difference between the AH and NAH groups.

Auditory Hallucinations and Indicators of Illness Severity

There was no difference between AH and NAH groups in the proportion of patients who were inpatient hospitalized at the time of study participation, suggesting that the two groups were relatively well-matched for acuity of illness. Significantly more patients with AH had co-occurring conditions (Table 4). Patients with AH had significantly lower rates of lifetime alcohol abuse compared with their NAH counterparts (18.3% AH vs. 28.0% NAH); they also had somewhat higher rates of lifetime alcohol dependence (19.2% AH vs. 14.6% NAH) although this difference was non-significant. When alcohol abuse and alcohol dependence were combined into a single alcohol use disorder category, there was no statistically significant difference between the AH and NAH groups. No differences were seen between groups with regard to lifetime drug abuse or dependence, or with lifetime anxiety disorders (Table 4).

There was a trend level difference in the proportion of patients with a history of attempted suicide, with the AH group having higher rates of suicide attempts than the NAH group (p=0.069), and no significant difference between in the proportion of patients who had suicide attempts severe enough to warrant a stay in a hospital intensive care unit.

With regard to treatments that suggest a history of treatment refractoriness, a significantly greater proportion of patients with AH compared to patients without AH were on clozapine at the time of study participation. In addition, AH patients required higher antipsychotic medication doses (mean chlorpromazine equivalent 545 ± 451 mg) than NAH patients (417mg \pm 340mg). Groups did not differ in terms of history of electroconvulsive therapy (ECT) (Table 4).

Multivariate Analyses

Functional Outcome—For categorical indicators of functional outcome, we performed a forward stepwise logistic regression procedure to determine whether AH could account for any variance in the data after controlling for diagnosis, age, and gender. The negative association between AH and college graduation persisted in this model. Patients with AH were less likely to have graduated from college compared to NAH patients, regardless of diagnosis, age, and gender. Age was the only predictor variable, other than AH, to be associated with college graduation; older individuals were more likely to have graduated from college (Table 5).

As already described, chi-square tests showed no association between AH and the functional outcome measures of independent living, marital status, and whether someone had children. This remained the case even after controlling for diagnosis, age, and gender with stepwise conditional logistic regression. Similarly, multivariate stepwise linear regression confirmed the lack of association between AH and MCAS scores in the subset of 261 individuals for whom MCAS data were available.

Illness Severity—The negative association between AH and lifetime alcohol abuse persisted after accounting for diagnosis, age, and gender ($\beta = -0.523$, p=0.024). Diagnosis had no association with lifetime alcohol abuse. Males and younger patients were more likely to have lifetime alcohol abuse. Again, however, the inverse relationship between AH and alcohol consumption did not persist when alcohol use disorders were combined into a single category.

Stepwise conditional multivariate analysis confirmed the lack of association between AH and the illness severity outcome variables of lifetime drug abuse, lifetime anxiety disorders, history of suicide attempt, and clozapine treatment (Table 5).

For continuous variables that indicate illness severity, we performed forward stepwise multiple linear regression analyses. CPZ equivalent dose was strongly associated with diagnosis ($\beta = 23.349$, p < 0.0001) and age ($\beta = 4.226$, p = 0.001). It had no association with gender and no association with AH. Duration of illness was also entered into a stepwise conditional linear regression as an outcome variable of interest, and was found to be associated with older age ($\beta = 0.796$, p < 0.0001). Diagnosis, gender, and AH had no association with duration of illness.

Discussion

In this study, we examined the association between AH and clinical variables in a crossdiagnostic sample of 569 patients with psychosis. The rate of AH clearly varies by diagnosis; we found that 75.6% of schizophrenia patients, 71.9% of schizoaffective patients, and 34.0% of patients with bipolar psychosis experienced AH at some time in their lives. These rates are similar to those of 75.9% in schizophrenia, 68.3% in schizoaffective disorder, and 27.4% in bipolar disorder previously reported in an overlapping sample by our group (39). The rates are also comparable with previously published rates. In the International Pilot Study on Schizophrenia, 74% of schizophrenia patients had AH (1). Baethge and colleagues found that 61% of schizophrenia patients, 23% of bipolar patients in a mixed episode, and 11% of bipolar patients in either manic or depressed episodes had AH (2).

When examining AH cross-diagnostically, we found that AH are strongly associated with hallucinations in other sensory modalities. We previously observed that visual, tactile, gustatory, and olfactory hallucinations were much more common than previously reported in the literature (39). Here, we found that patients with AH are more than twice as likely to experience visual, tactile, or olfactory hallucinations compared to patients without AH. Furthermore, only a small percentage of psychotic patients experience visual (15.9%), tactile (11.4%), olfactory (6.1%), or gustatory (1.6%) hallucinations in isolation, without AH. These findings suggest that while AH are the most common type of hallucination in psychosis patients, the pathophysiology underlying hallucinations likely involves abnormalities affecting multiple sensory modalities. The observed lack of association between AH and gustatory hallucinations in this sample. Future studies should investigate the mechanisms by which hallucinations occur in single vs. multiple modalities.

The DSM-IV distinguishes Schneiderian first-rank (40) hallucinations as qualitatively different from other hallucinations. Whereas non-first-rank hallucinations must be accompanied by at least one other criterion A symptom for a schizophrenia diagnosis to be made, hallucinations consisting of a running commentary on the person's behavior or thoughts, or two or more voices conversing with one another, are alone sufficient to diagnose schizophrenia. In our sample, 37.5% of AH patients reported hearing a running commentary, and 30.7% reported hearing two or more voices conversing. The rates we found in the schizophrenia group (47% with running commentary, 36% with voices conversing, 57% with either running commentary or voices conversing) are roughly similar to the published rates of 48% in a Danish sample of 388 first-episode schizophrenia patients (41) though somewhat lower than the rate of 64% in a smaller sample of 60 hospitalized patients with AH (24)'. The rates differed according to diagnosis, with higher proportions of schizophrenia and schizoaffective disorder patients than bipolar patients reporting such

experiences. Nonetheless, Schneiderian first-rank AH were not specific to schizophrenia or schizoaffective disorder; they were also prevalent among patients with bipolar psychosis. These results suggest that Scheiderian first-rank AH are not pathognomonic of schizophrenia, but are symptoms that are present across the spectrum of psychotic illness.

AH was strongly associated with other psychotic phenomena that have in common with AH the features of misattribution, ego permeability, and impairments in the perception and initiation of action (42). Specifically, AH was strongly associated with delusions of control, thought insertion, and thought broadcasting. In all of these "passivity" symptoms, patients misattribute self-generated thoughts or perceptions as being alien, and there is a breakdown in the boundary between self and not self. The DSM-IV criteria for schizophrenia consist of a checklist of disparate symptoms without a core unifying theme or experience that defines the phenomenological experience of patients with psychosis. Such "passivity" concepts as ego disintegration, invasion, and other disturbances of minimal or basic self (43, 44) may better reflect the essence of psychotic illness.

In bivariate analyses, AH was associated with lower education. This relationship remained even after controlling for diagnosis, age, and gender in a multivariate logistic regression analysis. This finding is consistent with that of Baethge and colleagues (2) showing that affective disorder patients with hallucinations are less well-educated than affective disorder patients without hallucinations. A potential explanation is that the presence of AH may interrupt schooling. Alternatively, there may be shared brain abnormalities that give rise to both poor academic performance and vulnerability to AH. Bivariate analyses also showed AH to be significantly associated with higher medication requirements, as measured by CPZ equivalent doses, as well as with more aggressive treatment with clozapine. In addition, bivariate analysis demonstrated trends of AH being associated with lower rates of employment and higher rates of suicide. However, with the exception of education level, the relationships between AH and these outcome variables did not survive once diagnosis, age, and gender were controlled for in a multivariate analysis. These data suggest that while AH is associated with lower functioning.

Contrary to expectation, we did not find any differences between the AH and NAH groups in MCAS scores. This lack of difference may be related to the particular methods employed in this study; here, the MCAS may reflect illness acuity at the time of study participation more than true functional status. The majority of patients were inpatients at a tertiary care psychiatric hospital at the time of study participation. They were asked to answer MCAS questions based on their experiences within the previous month, especially focusing on the current episode. Assessments of baseline community functioning, over a longer period than the month preceding hospital admission, might have provided a more informative point of comparison between patients who do and do not have a history of AH.

Both bivariate and multivariate analyses showed a statistically significant inverse relationship between AH and alcohol abuse. However, when alcohol abuse and dependence were combined into a single alcohol use disorder category (45–48), the relationship did not persist. The lack of association between AH and lifetime history of anxiety disorders in our sample is unexpected, as difficulties with emotion regulation, particularly anxiety, have been implicated in triggering and maintaining hallucinations (49). Rumination has been shown to be significantly correlated with AH-related distress in schizophrenia patients (50), and a history of trauma has been demonstrated to be associated with hallucinations in the general population (9, 51). There was similarly no difference in our study between individuals with and without AH on depressive symptoms. While many patients with AH hear voices as disturbing and unpleasant, there are a sizeable minority for whom the voices are either

neutral or pleasant (52), and sometimes even functionally adaptive (53). The affective impact of AH appears to be determined by how integrated AH are with the patient's experience (52). In this study, we do not have data on the form, content, or mood congruency of patients' AH. Furthermore, the MADRS depression ratings reflect mood in the previous month while classification into AH and non-AH groups occurred on the basis of whether patients reported ever experiencing lifetime AH. Thus, we are limited in our

ability to make interpretations about the temporal association between AH and mood.

This study has several limitations. First, these data were not acquired for the purpose of investigating AH. Thus, we do not have detailed information about phenomenological characteristics of hallucinatory experiences such as frequency, duration, location, content, and reality of patients' hallucinations. We used PANSS item 3 as a proxy for AH severity, even though the item states that hallucinations may occur in the auditory, visual, olfactory, or somatic realms. Though we cannot rule out the possibility that non-auditory hallucinations are driving the P3 scores in patients with AH plus VOGTH, it is reassuring that the pure-AH group's mean P3 score is much higher than that of the VOGTH-only group. Second, the data are cross-sectional, and thus limit our ability to make inferences about causality. Third, we had MCAS data on a limited subset of patients. Furthermore, asking about baseline community functioning, rather than community functioning during the immediate period preceding acute illness and hospitalization, may have been more informative. Fourth, the majority of the patients in our study were acutely ill patients hospitalized in a tertiary care facility, thus limiting the generalizability of our findings to less severely ill patients.

Overall, the findings in our study contribute to the understanding of AH from the perspective of a symptom dimension across three diagnostic categories, encompassing schizophrenia, schizoaffective disorder, and bipolar psychosis. We show that while Schneiderian first-rank AH are most common in patients with schizophrenia or schizoaffective disorder, they are also prevalent among patients with bipolar psychosis. AH are strongly associated with other modality hallucinations as well as with symptoms of "passivity" and ego disintegration. With regard to measures of functional outcome, patients with AH are less likely to graduate from college even after controlling for diagnosis, age, and gender. In combination, the findings suggest that AH is a dimension that is complex; it does not unequivocally predict worse functional outcome or severity. Clinicians are encouraged to inquire about a patient's AH in the context of that person's specific course and life circumstances. The main limitation of the current study is the lack of phenomenological details associated with patients' experience of AH. Future studies should look at how the form and content of AH are associated with both neural substrates and clinical outcomes in a cross-diagnostic sample, such as ours, which includes both schizophrenic and affective psychoses.

Acknowledgments

Funding from Shervert Frazier Research Institute to BMC and NIMH (K23MH079982) to DO. Salary for AKS from unrestricted educational grants [Harvard Psychiatry Dupont Warren Fellowship; Harvard-MIT/Beth Israel Deaconess Medical Center (BIDMC) Clinical Investigator Training Program, in collaboration with Merck & Co. and Pfizer Inc.]. We are grateful to all the patients who participated in this study.

References

[1]. Wing, JKCJ.; Sartorius, N. Measurement and Classification of Psychiatric Symptoms. Cambridge University Press; Cambridge, UK: 1974.

Page 9

- [2]. Baethge C, Baldessarini RJ, Freudenthal K, Streeruwitz A, Bauer M, Bschor T. Hallucinations in bipolar disorder: characteristics and comparison to unipolar depression and schizophrenia. Bipolar Disord. Apr; 2005 7(2):136–45. [PubMed: 15762854]
- [3]. Pierre JM. Hallucinations in nonpsychotic disorders: toward a differential diagnosis of "hearing voices". Harv Rev Psychiatry. 2010; 18(1):22–35. [PubMed: 20047459]
- [4]. Johanson E. Auditory hallucinosis, paranoic reactions and schizophreniform psychoses in alcoholic patients. Acta Soc Med Ups. 1961; 66:105–28. [PubMed: 14451952]
- [5]. Saravay SM, Pardes H. Auditory elementary hallucinations in alcohol withdrawal psychosis. Arch Gen Psychiatry. Jun; 1967 16(6):652–8. [PubMed: 6027363]
- [6]. Korsnes MS, Hugdahl K, Nygard M, Bjornaes H. An fMRI study of auditory hallucinations in patients with epilepsy. Epilepsia. Apr; 2009 51(4):610–7. [PubMed: 19817808]
- [7]. Tien AY. Distributions of hallucinations in the population. Social Psychiatry & Psychiatric Epidemiology. 1991; 26(6):287–92. [PubMed: 1792560]
- [8]. Johns LC. Hallucinations in the general population. Curr Psychiatry Rep. Jun; 2005 7(3):162–7. [PubMed: 15935129]
- [9]. Sommer IE, Daalman K, Rietkerk T, Diederen KM, Bakker S, Wijkstra J, et al. Healthy Individuals With Auditory Verbal Hallucinations; Who Are They? Psychiatric Assessments of a Selected Sample of 103 Subjects. Schizophr Bull. May; 2010 36(3):633–41. [PubMed: 18849293]
- [10]. Lawrence C, Jones J, Cooper M. Hearing voices in a non-psychiatric population. Behav Cogn Psychother. May; 2010 38(3):363–73. [PubMed: 20441666]
- [11]. APA. Diagnostic and Statistical Manual of Mental Disorders. Revised. 4th ed.. Author; Washington, DC: 2000.
- [12]. Andreasen NC. DSM and the death of phenomenology in america: an example of unintended consequences. Schizophr Bull. Jan; 2007 33(1):108–12. [PubMed: 17158191]
- [13]. Craddock N, Owen MJ. Rethinking psychosis: the disadvantages of a dichotomous classification now outweigh the advantages. World Psychiatry. Jun; 2007 6(2):84–91. [PubMed: 18235858]
- [14]. Purcell SM, Wray NR, Stone JL, Visscher PM, O'Donovan MC, Sullivan PF, et al. Common polygenic variation contributes to risk of schizophrenia and bipolar disorder. Nature. Aug 6; 2009 460(7256):748–52. [PubMed: 19571811]
- [15]. Ivleva EI, Morris DW, Moates AF, Suppes T, Thaker GK, Tamminga CA. Genetics and intermediate phenotypes of the schizophrenia--bipolar disorder boundary. Neurosci Biobehav Rev. May; 2010 34(6):897–921. [PubMed: 19954751]
- [16]. van Os J. Is there a continuum of psychotic experiences in the general population? Epidemiol Psichiatr Soc. Oct-Dec;2003 12(4):242–52. [PubMed: 14968483]
- [17]. Heckers S. Making progress in schizophrenia research. Schizophr Bull. Jul; 2008 34(4):591–4.[PubMed: 18492660]
- [18]. Insel T, Cuthbert B, Garvey M, Heinssen R, Pine DS, Quinn K, et al. Research domain criteria (RDoC): toward a new classification framework for research on mental disorders. Am J Psychiatry. Jul; 2010 167(7):748–51. [PubMed: 20595427]
- [19]. Strauss JS. Hallucinations and delusions as points on continua function. Rating scale evidence. Arch Gen Psychiatry. Nov; 1969 21(5):581–6. [PubMed: 5823480]
- [20]. Aggernaes A. The experienced reality of hallucinations and other psychological phenomena. An empirical analysis. Acta Psychiatr Scand. 1972; 48(3):220–38. [PubMed: 4680572]
- [21]. Lowe GR. The phenomenology of hallucinations as an aid to differential diagnosis. Br J Psychiatry. Dec; 1973 123(577):621–33. [PubMed: 4772302]
- [22]. Larkin AR. The form and content of schizophrenic hallucinations. Am J Psychiatry. Jul; 1979 136(7):940–3. [PubMed: 36765]
- [23]. Junginger J, Frame CL. Self-report of the frequency and phenomenology of verbal hallucinations. J Nerv Ment Dis. Mar; 1985 173(3):149–55. [PubMed: 3973575]
- [24]. Oulis PG, Mavreas VG, Mamounas JM, Stefanis CN. Clinical characteristics of auditory hallucinations. Acta Psychiatr Scand. Aug; 1995 92(2):97–102. [PubMed: 7572267]

- [25]. Nayani TH, David AS. The auditory hallucination: a phenomenological survey. Psychol Med. Jan; 1996 26(1):177–89. [PubMed: 8643757]
- [26]. Singh G, Sharan P, Kulhara P. Phenomenology of hallucinations: a factor analytic approach. Psychiatry Clin Neurosci. Jun; 2003 57(3):333–6. [PubMed: 12753575]
- [27]. Stephane M, Thuras P, Nasrallah H, Georgopoulos AP. The internal structure of the phenomenology of auditory verbal hallucinations. Schizophr Res. Jun 1; 2003 61(2–3):185–93.
 [PubMed: 12729870]
- [28]. Hayashi N, Igarashi Y, Suda K, Nakagawa S. Phenomenological features of auditory hallucinations and their symptomatological relevance. Psychiatry Clin Neurosci. Dec; 2004 58(6):651–9. [PubMed: 15601391]
- [29]. Oulis P, Gournellis R, Konstantakopoulos G, Matsoukas T, Michalopoulou PG, Soldatos C, et al. Clinical dimensions of auditory hallucinations in schizophrenic disorders. Compr Psychiatry. Jul-Aug;2007 48(4):337–42. [PubMed: 17560954]
- [30]. First, MB.; Spitzer, RL.; Gibbon, M.; Williams, JBW. Structured clinical interview for DSM-IV Axis I Disorders. New York State Psychiatric Institute, Biometrics Research; New York: 1995.
- [31]. Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophrenia Bulletin. 1987; 13:261–76. [PubMed: 3616518]
- [32]. Young RC, Biggs JT, Ziegler VE, Meyer DA. A rating scale for mania: reliability, validity and sensitivity. Br J Psychiatry. Nov.1978 133:429–35. [PubMed: 728692]
- [33]. Montgomery S, Asberg M. A new depression scale designed to be sensitive to change. British Journal of Psychiatry. 1979; 134:382–9. [PubMed: 444788]
- [34]. Barker S, Barron N, McFarland BH, Bigelow DA. A community ability scale for chronically mentally ill consumers: Part I. Reliability and validity. Community Ment Health J. Aug; 1994 30(4):363–83. [PubMed: 7956112]
- [35]. Barker S, Barron N, McFarland BH, Bigelow DA, Carnahan T. A community ability scale for chronically mentally ill consumers: Part II. Applications. Community Ment Health J. Oct; 1994 30(5):459–72. [PubMed: 7851100]
- [36]. Lehman AF, Steinwachs DM. Translating research into practice: the Schizophrenia Patient Outcomes Research Team (PORT) treatment recommendations. Schizophr Bull. 1998; 24(1):1– 10. [PubMed: 9502542]
- [37]. Woods SW. Chlorpromazine equivalent doses for the newer atypical antipsychotics. Journal of Clinical Psychiatry. Jun; 2003 64(6):663–7. [PubMed: 12823080]
- [38]. Gardner DM, Murphy AL, O'Donnell H, Centorrino F, Baldessarini RJ. International consensus study of antipsychotic dosing. Am J Psychiatry. Jun; 2010 167(6):686–93. [PubMed: 20360319]
- [39]. Lewandowski KE, DePaola J, Camsari GB, Cohen BM, Ongur D. Tactile, olfactory, and gustatory hallucinations in psychotic disorders: a descriptive study. Ann Acad Med Singapore. May; 2009 38(5):383–5. [PubMed: 19521636]
- [40]. Schneider, K. Clinical psychopathology. Grune & Stratton; New York: 1959.
- [41]. Thorup A, Petersen L, Jeppesen P, Nordentoft M. Frequency and predictive values of first rank symptoms at baseline among 362 young adult patients with first-episode schizophrenia Results from the Danish OPUS study. Schizophr Res. Dec; 2007 97(1–3):60–7. [PubMed: 17698323]
- [42]. Frith CD. The positive and negative symptoms of schizophrenia reflect impairments in the perception and initiation of action. Psychol Med. Aug; 1987 17(3):631–48. [PubMed: 3628624]
- [43]. Ebel H, Gross G, Klosterkotter J, Huber G. Basic symptoms in schizophrenic and affective psychoses. Psychopathology. 1989; 22(4):224–32. [PubMed: 2798714]
- [44]. Parnas J, Moller P, Kircher T, Thalbitzer J, Jansson L, Handest P, et al. EASE: Examination of Anomalous Self-Experience. Psychopathology. Sep-Oct;2005 38(5):236–58. [PubMed: 16179811]
- [45]. Saha TD, Chou SP, Grant BF. Toward an alcohol use disorder continuum using item response theory: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Psychol Med. Jul; 2006 36(7):931–41. [PubMed: 16563205]
- [46]. Saha TD, Stinson FS, Grant BF. The role of alcohol consumption in future classifications of alcohol use disorders. Drug Alcohol Depend. Jun 15; 2007 89(1):82–92. [PubMed: 17240085]

- [47]. Borges G, Ye Y, Bond J, Cherpitel CJ, Cremonte M, Moskalewicz J, et al. The dimensionality of alcohol use disorders and alcohol consumption in a cross-national perspective. Addiction. Feb; 2010 105(2):240–54. [PubMed: 20078482]
- [48]. Mewton L, Slade T, McBride O, Grove R, Teesson M. An evaluation of the proposed DSM-5 alcohol use disorder criteria using Australian national data. Addiction. May; 2011 106(5):941– 50. [PubMed: 21205055]
- [49]. Freeman D, Garety PA. Connecting neurosis and psychosis: the direct influence of emotion on delusions and hallucinations. Behav Res Ther. Aug; 2003 41(8):923–47. [PubMed: 12880647]
- [50]. Badcock JC, Paulik G, Maybery MT. The role of emotion regulation in auditory hallucinations. Psychiatry Res. Feb 28; 185(3):303–8. [PubMed: 20678808]
- [51]. Freeman D, Fowler D. Routes to psychotic symptoms: trauma, anxiety and psychosis-like experiences. Psychiatry Res. Sep 30; 2009 169(2):107–12. [PubMed: 19700201]
- [52]. Copolov DL, Mackinnon A, Trauer T. Correlates of the affective impact of auditory hallucinations in psychotic disorders. Schizophr Bull. 2004; 30(1):163–71. [PubMed: 15176770]
- [53]. Miller LJ, O'Connor E, DiPasquale T. Patients' attitudes toward hallucinations. Am J Psychiatry. Apr; 1993 150(4):584–8. [PubMed: 8465874]

Demographic Features Based on Auditory Hallucinations Status.

Total N=569	AH (n=323)	NAH (n=246)	Statistical C	Comparison
Age (years)	38.4 ± 12.3	36.8 ± 13.4	t = -1.472	p = 0.141
Age at onset (years)	21.2 ± 7.0	22.0 ± 8.3	t = 0.733	p = 0.464
Female gender	152 (47.1%)	107 (43.5%)	$\chi^2 = 0.715$	p = 0.398
Family history of psychosis	113 (35.0%)	101 (41.1%)	$\chi^2 = 2.194$	p = 0.139

Breakdown of First-Rank Auditory Hallucinations Symptoms by Diagnosis.

Total N=323	SZ (n=130)	SZ (n=130) SZA (n=110) BP (n=83) Statistical Comparison	BP (n=83)	Statistical Co	mparison
Running Commentary	61 (46.9%) 43 (39.1%)	43 (39.1%)	17 (20.5%)	$\chi^2 = 15.306$	17 (20.5%) $\chi^2 = 15.306$ $\mathbf{p} = 4.746 \times 10^{-4}$
Voices Conversing	47 (36.2%)	47 (36.2%) 36 (32.7%)	16 (19.3%)	16 (19.3%) $\chi^2 = 7.127$	p = 0.028
At Least One First-Rank AH 74 (56.9%) 60 (54.5%)	74 (56.9%)	60 (54.5%)	26 (31.3%)	26 (31.3%) $\chi^2 = 14.953$ p = 0.001	p = 0.001

Association of Auditory Hallucinations with Other Symptoms.

Total N=569	AH (n=323)	NAH (n=246)	Statistical Co	omparison
Psychotic Symptoms				
Hallucinations in Other Sens	sory Modalities			
Visual hallucinations	109 (33.7%)	39 (15.9%)	$\chi^2 = 23.230$	$p = 1.437 \times 10^{-10}$
Tactile hallucinations	92 (28.5%)	28 (11.4%)	$\chi^2 = 24.539$	$p = 7.282 \times 10^{-10}$
Gustatory hallucinations	10 (3.1%)	4 (1.6%)	$\chi^2 = 1.257$	p = 0.262
Olfactory hallucinations	51 (15.8%)	15 (6.1%)	$\chi^2 = 12.793$	$p = 3.480 \times 10^{-4}$
First-Rank Symptoms				
Delusions of control	94 (29.1%)	40 (16.3%)	$\chi^2 = 12.792$	$p = 3.482 \times 10^{-10}$
Thought insertion	79 (24.5%)	35 (14.2%)	$\chi^2 = 9.123$	p = 0.003
Thought withdrawal	25 (7.7%)	10 (4.1%)	$\chi^2 = 3.267$	p = 0.071
Thought broadcasting	118 (36.5%)	53 (21.5%)	$\chi^2 = 14.923$	$p = 1.120 \times 10^{-1}$
Other Psychotic Symptoms				
Persecutory delusions	211 (65.3%)	144 (58.5%)	$\chi^2 = 2.743$	p = 0.098
Delusions of reference	243 (75.2%)	168 (68.3%)	$\chi^2 = 3.353$	p = 0.067
Bizarre content	47 (14.6%)	19 (7.7%)	$\chi^2 = 6.348$	p = 0.012
Disorganized behavior	44 (13.6%)	29 (11.8%)	$\chi^{2} = 0.420$	p = 0.517
Disorganized speech	63 (19.5%)	34 (13.8%)	$\chi^2 = 3.190$	p = 0.074
Mood Symptoms				
YMRS	16.0 ± 11.7	22.0 ± 14.0	t = 5.54	$p = 4.5 \times 10^{-6}$
MADRS	15.9 ± 10.4	14.5 ± 9.4	t = -1.55	p = 0.122

Association of Auditory Hallucinations with Indicators of Functional Status and Illness Severity.

Total N=569	AH (n=323)	NAH (n=246)	Statistical Co	omparison
Indicators of Functional Status				
Education			$\chi^2 = 10.524$	p = 0.005
Did not graduate HS	31 (9.6%)	11 (4.5%)		
Graduated HS	201 (62.2%)	140 (56.9%)		
Graduated college	88 (27.2%)	93 (37.8%)		
Employed	117 (36.2%)	108 (43.9%)	$\chi^2 = 3.445$	p = 0.063
Living situation			$\chi^2 = 7.391$	p = 0.060
Independent	130 (40.2%)	88 (35.8%)		
With family	138 (42.7%)	130 (52.8%)		
Residential	40 (12.4%)	18 (7.3%)		
Other	15 (4.6%)	10 (4.1%)		
Marital Status ^a			$\chi^2 {=} 0.414$	p = 0.937
Never married	225 (69.7%)	170 (69.1%)		
Separated/divorced	52 (16.1%)	37 (15.0%)		
Widowed	1 (0.3%)	1 (0.4%)		
Married	42 (13.0%)	36 (14.6%)		
Has Children	76 (23.5%)	59 (24.0%)	$\chi^2 {=} 0.016$	p = 0.900
Modified MCAS ^b	41.0 ± 8.5	42.7 ± 8.4	t = 1.601	p = 0.111
Indicators of Illness Severity				
Inpatient Hospitalized	247 (76.5%)	199 (80.9%)	$\chi^2 = 1.613$	p = 0.204
Co-occurring conditions	103 (31.9%)	57 (23.2%)	$\chi^2 = 5.358$	p = 0.021
Lifetime anxiety disorders	81 (25.1%)	47 (19.1%)	$\chi^2 = 2.856$	p = 0.091
Lifetime alcohol abuse	59 (18.3%)	69 (28.0%)	$\chi^2 = 7.665$	p = 0.006
Lifetime alcohol dependence	62 (19.2%)	36 (14.6%)	$\chi^2 = 2.038$	p = 0.153
Lifetime alcohol use disorder c	121 (37.7%)	105 (43.2%)	$\chi^2 = 1.752$	p = 0.186
Lifetime drug abuse	71 (22.0%)	59 (24.0%)	$\chi^2 = 0.318$	p = 0.573
Lifetime drug dependence	72 (22.3%)	42 (17.1%)	$\chi^2 = 2.373$	p = 0.123
History of Suicide Attempt	104 (32.2%)	62 (25.2%)	$\chi^2 = 3.307$	p = 0.069
ICU Stay Due to Suicide Attempt	33 (10.2%)	24 (9.8%)	$\chi^2 = 0.033$	p = 0.856
Chlorpromazine Equivalent (mg) ^d	545 +/- 451	417 +/- 340	t = -3.639	$p = 3.0 \times 10^{-4}$
Clozapine Treatment	60 (18.6%)	18 (7.3%)	$\chi^2 = 14.964$	$p = 1.096 \times 10^{-4}$
Electroconvulsive Therapy (ECT)	42 (13.0%)	23 (9.3%)	$\chi^2 = 1.842$	p = 0.175

 a Marital status data are missing for n=5 (3 AH, 2 NAH) participants.

 b MCAS data are unavailable for n=304 (174 AH, 130 NAH) participants.

^cAlcohol abuse and dependence combined into a single category. Alcohol use disorder data are missing for n=5 (2 AH, 3 NAH) participants.

NIH-PA Author Manuscript

Shinn et al.

Table 5

,	
Ś	2
	000
	1
F	
	-
	$\overline{\mathbf{x}}$
•	Z
	5
	a
	ä
	∢
	2
	Б
•	Ξ
	ŝ
	ല
	ы
	vegr
۴	Y
	\overline{c}
	St
•	Ě
	2
	3
	g
	Ξ
•	Ξ
-	Ξ
	Я
	5
τ	Ũ
	т П
	š
•	⋝
	5
	Ð
č	5
	6
	Ĕ
	52
	g
	>
	Ξ
	F
1	⋝
	-

Outcome	Dx (BP)	Dx (BP) Dx1 (SZ vs. BP)	Dx2 (SZA vs. BP)	Age (Continuous)	Gender $(F = 1, M = 0)$ AH $(AH=1, NAH=0)$	AH (AH=1, NAH=0)
Functional Status						
College graduate	p = 0.181	$p=0.181 \qquad P=-0.437, \ p=0.068 \qquad P=-0.258, \ p=0.280 \qquad P=0.034, \ p<0.0001$	P = -0.258, p = 0.280	P = 0.034, p < 0.0001		$\beta = -0.413, p = 0.042$
Living independently			-	$\beta = 0.024, p = 0.001$		
Never married	p <0.0001	$\beta = 1.142, p <\! 0.0001$	$\beta = 0.819, p = 0.002$	$\beta = -0.089$, $p < 0.0001$ $\beta = -0.627$, $p = 0.003$	$\beta = -0.627, p = 0.003$	
Has children	p <0.0001	$p < 0.0001 \beta = -0.891, \\ p = 0.001 \beta = -1.017, \\ p < 0.0001 P = 0.084, \\ p < 0.0001 P = 0.857, \\ p < 0.0001 P = 0.084, \\ p < 0.0001 P = 0.857, \\ p < 0.0001 P = 0.0001 P $	$\beta = -1.017, p <\! 0.0001$	P = 0.084, p < 0.0001	P = 0.857, p < 0.0001	
Illness Severity						
Lifetime alcohol abuse				$\beta = -0.015, p = 0.071$	$\beta = -0.626, p = 0.003$	$\beta = -0.523, p = 0.011$
Lifetime alcohol use dis *	p = 0.016			$\beta = 0.003, p = 0.613$	$\beta = -0.803, p <\! 0.0001$	
Lifetime drug abuse		-	-		$\beta = -0.500, p = 0.015$	
Lifetime anxiety disord.	p = 0.017	$\beta = -0.314, p = 0.221 \qquad \beta = 0.438, p = 0.062$	$\beta = 0.438, p = 0.062$			
History suicide attempt	p <0.0001	$\beta = 0.044, p = 0.848$	$\beta = 0.813, p <\! 0.0001$		-	
Clozapine treatment	p <0.0001	$p < \! 0.0001 \beta = -1.933, p < \! 0.0001 \beta = -1.971, p < \! 0.0001$	$\beta = -1.971$, p <0.0001			

alegory. Ϋ́