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## Twenty year multi-follow-up of different types of hallucinations in schizophrenia, schizoaffective disorder, bipolar disorder, and depression

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### ABSTRACT

Hallucinations are a salient feature of both psychotic and mood disorders. Currently there is a call for more research on the phenomenology of different forms of hallucinations, in a broader array of disorders, to further both theoretical knowledge and clinical utility. We investigated auditory, visual, and olfactory hallucinations at index hospitalization and auditory and visual hallucinations prospectively for 20 years in 150 young patients, namely 51 schizophrenia, 25 schizoaffective, 28 bipolar, and 79 unipolar depression. For the index hospitalization, the data showed schizophrenia and schizoaffective patients had a greater rate of auditory and visual hallucinations than bipolar and depression patients. However, over the longitudinal trajectory of their illness, a greater percentage of schizophrenia patients had auditory and visual hallucinations than schizoaffective patients, as well as bipolar and depression patients. Also, in contrast to the initial period, schizoaffective patients did not differentiate themselves over the follow-up period from bipolar patients. Bipolar and depression patients did not significantly differ at index hospitalization or at follow-up. We found visual hallucinations differentiated the groups to a greater degree over the 20 year course than did auditory hallucinations. These findings suggest the longitudinal course is more important for differentiating schizophrenia and schizoaffective disorder, whereas the initial years may be more useful to differentiate schizoaffective disorder from bipolar disorder. Furthermore, we found that the early presence of auditory hallucinations was associated with a reduced likelihood for a future period of recovery. No olfactory hallucinations were present at the index hospitalization in any patients. Over the course of 20 years, a minority of schizophrenia patients presented with olfactory hallucinations, and very few schizoaffective and bipolar patients presented with olfactory hallucinations. This study underscores the importance of the longitudinal course of symptoms to understand the relationship between related disorders and recovery.

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### 1. Introduction

Hallucinations are a core feature of psychotic disorders and also present frequently in mood disorders (APA, 2013). Despite the diagnostic value of hallucinations, there is currently limited information on different forms of hallucinations and their prominence in different psychotic and mood disorders. Furthermore, the longitudinal course of different forms of hallucinations is largely unavailable. As hallucinations are one of the most commonly endorsed psychotic symptom and can be reliably assessed, a more fulsome understanding of the presence and persistence of different types of hallucination in common psychotic and mood disorders would provide necessary information on course

and differentiation. Given that hallucinations are endorsed by patients with a variety of diagnoses, misdiagnosis is common, which can have serious implications for treatment planning. Also, much of our theoretical knowledge of schizophrenia and the categorization of psychosis and mood disorders comes from the longitudinal understanding of course (Kraepelin, 1907). Therefore, this information has implications for our understanding of diagnostic boundaries, differential diagnosis, and treatment planning. To this end, our goal was to present information on different forms of hallucinations prospectively over 20 years and to relate index hallucinatory status to recovery in patients with schizophrenia, schizoaffective disorder, bipolar disorder, and unipolar depression.

Underscoring the importance of research in this area, the International Consortium on Hallucinations, focusing on auditory hallucinations, in its top 16 goals, listed understanding the phenomenology of hallucinations in different clinical groups as a core goal (Waters et al.,

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2012). Also, the proliferation of the Hearing Voices Movement and related networks has highlighted the number of patients and nonpatients affected (Corstens et al., 2014). Given that there is even less information on non-auditory forms of hallucinations, we extend the call to better understanding all forms of hallucinations, and also better understanding the relationship between symptom presentation and outcome.

Focusing more broadly on symptoms and functioning in schizophrenia and other disorders, research has shown that schizophrenia is a more chronic disorder that tends to be more severe, as schizophrenia patients have poorer outcomes than schizoaffective, bipolar, and unipolar affective patients (reviewed in Mcglashan, 1988). Furthermore, longitudinal studies have demonstrated that the early phase of schizophrenia (first 5–10 years) is where the greatest loss of recovery takes place (Mcglashan, 1988). Last, studies have demonstrated that outcome is heterogeneous in schizophrenia (Mcglashan, 1988).

More specific examination of symptom dimensions longitudinally over 10 years, by Eaton et al. (1995), demonstrated that positive and negative symptoms decline in the year following first hospitalization and then remained largely stable. This study also showed that the positive and negative symptom clusters were largely independent at baseline and over the 10 year follow-up; however, over time a single factor including both positive and negative symptoms became more prominent. In contrast, Mancevski et al. (2007), focusing on chronically institutionalized schizophrenia patients and following patients from onset to death, found that there were significant decreases in positive symptoms and increases in negative symptoms with time. Research generally has demonstrated that positive symptoms tend to decrease over the lifespan of schizophrenia patients (Goghari et al., 2013; Gur et al., 1996; Harrow and Jobe, 2010; Pfohl and Winokur, 1982; Schultz et al., 1997).

In our previously published study from this dataset (Goghari et al., 2013), we investigated the longitudinal course of all forms of hallucinations collapsed, based on diagnoses at their index hospitalization, for patients with schizophrenia, schizoaffective disorder, bipolar disorder with psychosis, and depression without psychosis prospectively over 20 years. Our data showed that schizophrenia, schizoaffective, and bipolar with psychosis patients all had significantly less hallucinations after the early years. Some of this reduction was due to the high level of psychopathology that was present during the early years for many patients. Of significance, our data highlighted that there were a substantial number of patients who continued to show hallucinations after their index hospitalization. Forty-four percent of schizophrenia patients and 20% of schizoaffective patients showed frequent or chronic hallucinations over the 20 year course of the study. Additionally, we found the longitudinal course of hallucinations differentiated between disorders. The pattern clearly differentiated between schizophrenia and bipolar disorder with psychosis patients, and suggested some diagnostic similarities between schizophrenia and schizoaffective patients, and between bipolar disorder and schizoaffective disorder with depression patients.

In that study, we also investigated the relationship between hallucinations and outcome (Goghari et al., 2013). We found the early presence of hallucinations predicted the lack of a future period of recovery in all patients, and increased hallucinatory activity was associated with reduced work attainment in all patients. Previous reviews have proposed recovery is most predicted by cognition, and to a lesser degree, by negative symptoms, with positive symptoms playing a modest role (Green, 1996; Green et al., 2000). However, other studies from our group have provided supports that positive symptoms, such as delusions, are associated with lower work recovery (Harrow et al., 2004; Harrow and Jobe, 2010; Racenstein et al., 2002). These results advocate for further study of the association between different forms of hallucinations and recovery.

Most studies have focused on hallucinations or positive symptoms in general. However, the prevalence and trajectory of individual forms of hallucinations has not received substantial attention, and less is known about the association with different forms of hallucinations

and recovery. Knowing the longitudinal trajectory of the frequency of different forms of hallucination in common psychotic and mood disorders is necessary to increase our clinical knowledge. To further advance the area of phenomenology of different forms of hallucinations, including visual, auditory, and olfactory, in psychiatric disorders, our objectives were to document (1) the longitudinal course of different forms of hallucinations, (2) determine whether hallucinations differentiated patients with different psychotic and mood disorders, and (3) determine whether the presence of hallucinations during the early years was associated with the presence or absence of a later period of recovery.

## 2. Material and methods

### 2.1. Participants and measures

As described in detail previously (Goghari et al., 2013; Harrow et al., 2004; Harrow and Jobe, 2005), the current investigation is based on data from the Chicago Follow-up Study, a prospectively designed, longitudinal, multi-follow-up research program studying psychopathology and recovery in psychiatric disorders. Institutional Review Board approval was obtained from the University of Chicago and University of Illinois-Chicago. Signed informed consent was obtained from all participants. All participants were given ample time to read the consent form and ask any questions. Additionally, the study personnel highlighted key information for the participants. The sample for this investigation consisted of 183 patients, who were studied prospectively at an index phase of hospitalization and at six follow-up periods over 20 years. In this study, we included patients who attended five or six follow-up assessments (out of a possible six). Diagnostic groups did not differ in percentage of follow-ups attended ( $X^2(3) = 1.34, p = 0.71$ ).

Using the Research Diagnostic Criteria (Spitzer et al., 1978), four major patient groups were studied - 51 schizophrenia, 25 schizoaffective (23 schizoaffective-depressed and 2 schizoaffective-manic), 28 bipolar, and 79 unipolar depression patients. These categorizations were based on research diagnoses at the index hospitalization. The schizophrenia and schizoaffective sample are the same as in our previous paper on hallucinations (Goghari et al., 2013). Twenty-five of the bipolar patients and 11 of the unipolar depression patients had psychotic features at the index hospitalization. The research diagnoses were based on at least one of two structured interviews: (1) the Schedule for Affective Disorders and Schizophrenia (SADS; Endicott and Spitzer, 1978) and/or (2) the Schizophrenic State Inventory (Grinker and Harrow, 1987). Satisfactory inter-rater reliability was established for diagnosis (e.g., a kappa of 0.88 for schizophrenia).

The patients were then reassessed, individually, at six subsequent follow-ups over a 20 year period. The follow-ups occurred at approximately 2, 4.5, 7.5, 10, 15, and 20 years after index hospitalization. Information for the 20 year follow-up was available for 73% of the original sample assessed. There were no notable differences in attrition for the different diagnostic groups. The sample assessed at the 20 year follow-up did not differ significantly on major demographic variables from the sub-samples that were assessed at index hospitalization and 2 year follow-up, but not assessed at the 20 year follow-up. The primary reason for dropouts was participants relocating and our inability to contact them.

The follow-up evaluations involved structured interviews on symptoms and recovery. These interviews were conducted by trained raters who were blind to the diagnosis and to the data from previous follow-ups for a patient. Hallucinations at index hospitalization and at each follow-up were assessed with the SADS for the past month (Endicott and Spitzer, 1978). This included auditory hallucinations, such as audible thoughts, voices commenting, voices conversing, voices arguing; visual hallucinations; and olfactory hallucinations. Hallucinations were rated on a 3-point scale as follows: 1 = Hallucination Absent; 2 = Weak or

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