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Are UHR patients who present with hallucinations alone at lower risk of transition to psychosis?

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ABSTRACT

The aim of this study was to investigate whether Ultra High Risk for psychosis (UHR) patients who present with hallucinations alone at identification as UHR are at lower risk of transition to psychosis than UHR patients who present with symptoms other than hallucinations or hallucinations plus other symptoms.

Our primary dataset was a retrospective "case-control" study of UHR patients ($N=118$). The second, independent dataset was a long-term longitudinal follow up study of UHR patients ($N=416$). We performed a survival analysis using Log-rank test and Cox regression to investigate the relationship between symptom variables and transition to a psychotic disorder.

Hallucinations alone at baseline were not significantly associated with a reduced risk of transition to psychosis. In the case control study the presence of hallucinations when found in the absence of any thought disorder and visual hallucinations in the absence of substance misuse was associated with a reduced risk of transition to psychosis. In the longitudinal follow-up dataset perceptual disturbance found in the absence of a disorder of affect or emotion was associated with an increased risk of transition to psychosis.

1. Introduction

Hallucinations are sensory experiences that take place in the absence of corresponding external stimulation of the relevant sensory organ, in the awake state and with sufficient sense of reality that the individual attributes the event to being outside of their control (David, 2004). Hallucinations have traditionally been defined by the sensory modality in which they are perceived i.e. auditory, visual, gustatory, olfactory, somatic or tactile (Aleman and Laroi, 2008). Aleman and Laroi (2008) suggest that the hypotheses proposed to explain the underlying mechanism of hallucinations can be loosely divided into three categories (1) hallucinations as a disturbance in cognitive-perceptual processes (Slade and Bentall, 1988), (2) hallucinations as a disturbance of metacognitive processes (Frith, 1992; Bentall., 1990; Morrison et al., 1995) and (3) hallucinations as a disturbance of brain biochemistry and/or structure (David 1994; Woodruff et al., 1997; Allen et al., 2012). While evidence exists to support many of these hypotheses, the field is yet to reach scientific consensus (Aleman and Laroi, 2008; Blom and Sommer, 2011).

Hallucinations are a primary symptom of psychotic disorders such as schizophrenia in both ICD-10 and DSM-5 (World Health Organisation, 1992; American Psychiatric Association, 2013). 70% of patients with schizophrenia experience hallucinations, most commonly in the auditory modality, followed by visual hallucinations (Mueser et al., 1990). Hallucinations are reported in current psychiatry textbooks as key psychotic symptoms (Kraepelin, 1899; Jaspers, 1963; Saddock et al., 2009; Gelder et al., 2009). Hallucinations also appear in screening tools to detect psychotic disorders (Bebbington and Nayani, 1995; Konings et al., 2006).

The "Ultra High Risk" group (UHR), also referred to as the At Risk Mental State' (ARMS) or "clinical high risk" (CHR) group, are a

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group of help seeking adolescents or young adults identified using reliable measurement tools and clinical criteria as being at very high risk of developing a psychotic illness in the near future (Yung et al., 2003; Miller et al., 2003). This clinically defined population was found, in initial studies, to have a rate of "transition" to a frank psychotic disorder of around 40% in the first 12 months after presentation (Yung et al., 2003; Phillips et al., 2000). However, more recently a reduction in the transition rates has been reported in the literature, with authors reporting transition rates as low as 12% in 12 months (Morrison et al., 2012). A meta-analysis by Fusar-Poli et al. (2012) found consistent transition rates of 22% after 1 year, 29% after 2 years, and 36% after 3 years. These rates are 200–300 times higher than would be expected in a general population sample. The PACE 400 dataset is the first long-term follow-up of a UHR cohort, and this has estimated that the overall rate of transition was 34.9% over a 10-year period (95% CI, 28.7–40.6%). The highest risk of transition was in the first 2 years of entry into the service (Nelson et al., 2013). Factors which have been associated with an increased risk of transition to psychosis in UHR samples include long duration of symptoms before treatment (Yung et al., 2003), basic and negative symptoms (Mason et al., 2004; Simon et al., 2006; Haroun et al., 2006; Yung et al., 2005), schizotypal disorder (Ruhrmann et al., 2010) sleep disturbances (Ruhrmann et al., 2010) and substance abuse (Cannon et al., 2008). Three factors of particular interest are subthreshold positive symptoms, (Yung et al., 2003, 2005; Mason et al., 2004; Ruhrmann et al., 2010) poor functioning, (Yung et al., 2003; Mason et al., 2004; Ruhrmann et al., 2010; Yung et al., 2006) and having genetic risk with functional decline. These three factors were found to be significant predictors in the large North American Prodrome Longitudinal Study (Cannon et al., 2008) and replicated in an independent sample (Thompson et al., 2011). Hallucinations are included in the UHR (ARMS/ CHR) criteria in either sub-threshold or infrequent forms as indicating high and imminent risk for psychosis (Yung et al., 2003).

However, more recently general population studies have shown that psychotic symptoms and subclinical psychotic symptoms [or "psychotic like experiences" (PLEs)], are common in the general population (van Os et al., 2001). These PLE's include hallucinations, delusions, thought disorder and negative symptoms. Most general population studies of PLEs have tended to focus on PLEs in general, without distinguishing between different types of PLE. However, hallucinations do appear to be the most prevalent PLE in general population samples (Horwood et al., 2008; Kelleher et al., 2012). Epidemiological studies estimate the prevalence of hallucinations to be between 5% and 15% in the general population (Tien, 1991; Johns et al., 2004). In adolescent and young adult (university) samples these estimates are higher with rates of between 6% and 37% reported in the literature (Dhossche et al., 2002; Altman et al., 1997; Barrett and Etheridge, 1992). However, Johns et al. (2002) found that only 25% of adults reporting hallucinations met diagnostic criteria for a psychotic disorder. Hallucinations in adolescent populations often appear to be common but transitory phenomena that do not persist into adulthood (De Loore et al., 2011).

Numerous studies have also found that there is a non-clinical population (i.e. people who have never been clinically referred or have never received a psychiatric or neurological diagnosis) who hear voices, which they experience as benign and are not associated with psychological distress, functional decline or psychiatric illness (Romme and Escher, 1989; Daalman et al., 2011). These voice hearers do not seek help from clinical services.

Hallucinations are also common in many non-psychotic psychiatric disorders and in a number of organic disorders. These include mood disorders where they are considered a marker of disorder severity (Choong et al., 2007) and borderline personality disorder where they are mostly auditory, distressing and tend to have a critical quality (Slotema et al., 2012).

As such, hallucinations, which were once considered a classic psychotic symptom, now appear to be common in general population samples, not necessarily associated with distress or help seeking and frequently occur in non-psychotic illnesses. It is in this context that we felt it timely to re-examine the clinical significance in the UHR population of hallucinations if they and they alone are the reason for assessing someone as being at UHR. Only one, relatively small, study has reported that presence of auditory hallucinations at entry to the clinic was predictive of transition to psychosis (Mason et al., 2004), but this finding has not been replicated in larger cohorts (Ruhrmann et al., 2010; Woods et al., 2009; Nelson et al., 2013).

This exploration is particularly pertinent as it has been proposed that in a given individual, PLEs, like hallucinations might either be: (i) an expression of an underlying neurological/psychological vulnerability to a psychotic disorder; (ii) an "incidental" attenuated psychotic symptom which is not necessarily associated with risk of psychosis but is associated with a non-psychotic illness that will remit once treated; or (iii) present in non-clinical normal individuals, and not associated with distress or disability or increased vulnerability to psychotic disorder (Yung et al., 2009). A possible analogy, which encapsulates (i) and (ii) is to consider a hallucination as being like a fever. Both a hallucination and a fever are common non-specific symptoms that exist on a continuum with normal, are associated with some distress and indicate some underlying pathology. However, this underlying illness may be relatively benign and short-lived or something more serious and enduring.

Much attention has been focused on the identification of clinical signs, symptoms or factors, which alone or in combination could enrich the identification of those at highest risk within the UHR population. However, little has been reported on the identification of clinical factors that alone or in combination may indicate a reduced risk of transition within the UHR population. In other areas of medical practise it is common for the presence of one symptom to be considered more or less significant when found in the absence of other symptoms or signs. An example would be a cough found in the absence of crepitations being considered less clinically concerning than when found with crepitations. In the UHR field, little consideration has been given to the clinical relevance of the presence of one particular symptom while in the absence of other specific symptoms, signs or clinical factors. This is important because "relevant negatives" may offer additional insight into the clinical trajectory of UHR patients (Yung et al., 2012).

Historically the presence of visual hallucinations in the absence of other psychotic symptoms raised a query about organicity/ substance use (Teeple et al., 2009). However, possible disparities in transition rates associated with different forms of perceptual disturbance, in the UHR population, is an under researched area.

1.1. Aims of this study

The primary aim of this study was to investigate if the presence of hallucinations alone at baseline in UHR individuals is associated with a reduced risk of transition to psychosis compared to those who present with symptoms other than hallucinations. The secondary aims were twofold (a) to examine if hallucinations with/ without specific other symptoms e.g. hallucinations with or in the absence of thought disorder, were more or less likely to transition to psychosis (b) certain forms of hallucinations e.g. visual, tactile, olfactory are associated with an even lower level of risk of transition.