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Perceptual abnormalities in clinical high risk youth and the role of trauma, cannabis use and anxiety

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Abstract

Recent research suggests that perceptual abnormalities are a group of diverse experiences, which have been associated with trauma, cannabis use, and anxiety. Of the attenuated psychotic symptoms that are present in youth at clinical high risk (CHR) of psychosis, perceptual abnormalities tend to be one of the most frequently endorsed symptoms. However, very few

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studies have explored perceptual abnormalities and their relationships with the above environmental and affective factors in a CHR sample. Four hundred and forty one CHR individuals who met criteria for attenuated psychotic symptom syndrome (APSS) determined by the Structured Interview for Psychosis-risk Syndromes (SIPS) were assessed on the content of their perceptual abnormalities, early traumatic experience, cannabis use and self-reported anxiety. Logistic regression analyses suggested that both simple auditory and simple visual perceptual abnormalities were more likely to be reported by CHR who had early traumatic experiences, who are current cannabis users, and who have higher levels of anxiety. Multiple regression analysis revealed that only trauma and anxiety were independent predictors of both simple auditory and simple visual perceptual abnormalities. It is possible that examining subtypes of perceptual abnormalities in CHR leads to an improved understanding of the prevalence of such symptoms.

Keywords

Clinical high risk; Attenuated psychotic symptoms; Perceptual abnormalities; Hallucinations

1. Introduction

Hallucinations have been long considered as an important psychotic symptom (Saddock, 2009) and are one of the key symptoms for a diagnosis of schizophrenia in DSM-5 (American Psychiatric Association, 2013). They have been defined as "...a false sensory experience that has the compelling sense of reality despite the absence of an external stimulus" (VandenBos, 2007)(p110). Hallucinations are a group of heterogeneous experiences and involve multiple sensory modalities, including auditory, visual, olfactory, gustatory and somatosensory/tactile (Jardri et al., 2014). In addition to categorizing hallucinations based on the sensory modalities, existing classification methods use the content of perceptual abnormalities and further distinguish between complex (or formed) and simple (or unformed) perceptual abnormalities (Blom and Sommer, 2011) within each modality. In the auditory modality, complex perceptual abnormalities typically take the form of well-articulated speech and simple perceptual abnormalities commonly take the form of distinct or indistinct noises, such as clicking sounds and doorbell ringing. In the visual modality, complex perceptual abnormalities typically take the shape of a person, a face, an animal, a landscape or a scene, while simple perceptual abnormalities may take the form of flashes, shapes, geometric patterns, or shadows (Blom, 2010; Ffytche and Wible, 2014). Despite the documentation of the diversity of hallucinatory experiences, current research on hallucinations in psychiatric populations has mainly focused on auditory verbal hallucinations while hallucinations in other modalities or subtypes of hallucinations are less well understood (Langdon et al., 2011; Waters et al., 2014).

The experience of hallucinations has been associated with environmental factors, such as trauma and cannabis use, and affective factors, in particular anxiety. A large body of evidence has suggested a link between exposure to early traumatic experiences and the development of hallucinatory experiences in individuals with psychotic disorders (Daalman et al., 2012) as well as in the general population (Bentall et al., 2012; Read et al., 2005). Recent cannabis use has been associated with a greater risk of developing hallucinatory

experience in adolescent general populations (Hides et al., 2009; Scott et al., 2009), in particular, visual hallucinations (Caton et al., 2005). In addition, anxiety has been considered as one of the antecedents that may lead to the onset of hallucinations in schizophrenia patients (Delespaul et al., 2002), in both the adult general population (Allen et al., 2005), and in the adolescent general population (Escher et al., 2002). Theoretical papers have suggested that anxiety is specifically associated with simple hallucinations (Dodgson and Gordon, 2009; Wilkinson, 2014). However, this hypothesis remains to be tested. Furthermore, younger age and being female were associated with increased experiences of hallucinations (Kelleher et al., 2012b; McGrath et al., 2015).

In the schizophrenia field, there has been a growing interest in the identification of individuals who are at clinical high risk (CHR) for developing psychosis. Individuals can be identified as being at CHR based on well-established clinical criteria (McGlashan et al., 2010). Perceptual abnormalities are one of the attenuated psychotic symptoms that can be used to determine CHR status. Perceptual abnormalities in CHR differ from full-blown hallucinations by their limited frequency, duration, severity, and the relative intact ability of the individual to question the reality of hallucinatory experience (McGlashan et al., 2010). As in psychotic disorders, perceptual abnormalities are one of the most frequently endorsed attenuated psychotic symptoms in CHR populations (Addington et al., 2015).

Although the associations between hallucinations and early traumatic experiences, cannabis use and anxiety have been documented in psychotic patients and the general population, few studies have addressed these relationships in CHR. One study reported higher severity of perceptual abnormalities among CHR individuals who reported a history of traumatic experiences (Velthorst et al., 2013), while other studies have failed to detect such a relationship (Stowkowy et al., 2016; Thompson et al., 2009). Furthermore, the presence of visual, but not auditory perceptual abnormalities was associated with traumatic experience in CHR (Velthorst et al., 2013). Cannabis use was reported to be temporally associated with the severity of perceptual abnormalities in CHR individuals, when controlling for concurrent exposures to other substance use (Corcoran et al., 2008). In addition, cannabis use in CHR has been linked to the visual perceptual symptom "photopsia" (Korver et al., 2010), which refers to a perceptual abnormality in the form of flashes, flames or geometric shapes (Klosterkotter et al., 2001). Anxiety has reportedly been associated with the overall severity of attenuated psychotic symptoms in CHR (McAusland et al., 2015), but the association between anxiety and perceptual abnormalities in CHR has not been examined. One of the limitations of the above studies is the lack of evaluations of the subtypes of perceptual abnormalities.

Since the findings from previous literature suggest that perceptual abnormalities are a group of diverse experiences in schizophrenia patients and the general population, it may be help our understanding of perceptual abnormalities to explore the content and subtypes of the symptom in CHR. The first aim of this exploratory study was to examine the prevalence of different subtypes of perceptual abnormalities in a large sample of CHR individuals. The second aim was to examine the associations between different subtypes of perceptual abnormalities and early traumatic experiences, cannabis use and anxiety. Our primary

hypothesis is that different subtypes of perceptual abnormalities have different relationships with trauma, cannabis use and anxiety.

2. Methods

2.1 Sample

All participants were recruited as part of the North American Prodrome Longitudinal Study 2 (NAPLS-2). Specific details of ascertainment and recruitment have been described elsewhere (Addington et al., 2012). All CHR participants met the Criteria of Psychosis-risk Syndromes (COPS) using the Structured Interview for Psychosis-risk Syndromes (SIPS) (McGlashan et al., 2010). The COPS includes diagnosis of three CHR syndromes including: brief intermittent psychotic symptoms syndrome (BIPS), genetic risk and deterioration syndrome (GRD), and attenuated psychotic symptoms syndrome (APSS). Participants were excluded if they met criteria for any current or lifetime axis I psychotic disorder, IQ<70 or past or current history of a clinically significant central nervous system disorder, DSM-IV criteria for a current substance dependence disorder or the diagnostic prodromal symptoms were clearly caused by an Axis I disorder or were clearly under the direct influence of substance use. Only participants who met APSS or APSS plus another COPS criteria were included in the current study. A total of 556 participants across the eight NAPLS 2 sites had been recruited from February 2009 until December 2011. Four hundred and forty one participants met eligibility for inclusion in the current study based on meeting APSS.

2.2 Measures

2.2.1 Clinical rating scales—APSS criteria were evaluated using the SIPS. The severity of perceptual abnormalities was assessed using the P4- perceptual abnormalities severity rating from the Scale of Prodromal Symptoms (SOPS; McGlashan et al., 2010). The SOPS measures attenuated psychotic symptom severity on a range of 0–6, where 0 is absent, 1 is questionably present, 2 is mild, 3 is moderate, 4 is moderately severe, 5 is severe but not psychotic and 6 is severe and psychotic. The psychosis-risk range includes scores 3, 4, and 5.

Anxiety was assessed with the Self-Rating Anxiety Scale (SAS) (Zung, 1971). The scale is a self-report questionnaire with 20 items that assess general and somatic symptoms of anxiety that are rated on a 4-point Likert scale from 1 (none or little of the time to 4 (most or all of the time).

Based on commonly used measures and interview questions in the literature (Arseneault et al., 2002), a cannabis scale was used to record the history of cannabis use. Participants were asked about total usage in their lifetime, past or current use, the age of first usage and the frequency of usage.

Childhood Trauma and Abuse scale (Janssen et al., 2004), was used to assess the experience of traumatic experiences that occurred prior to the age of 16 are recorded. Traumatic events included emotional neglect, physical abuse, psychological abuse or sexual abuse. Trauma was coded as either present (1) or absent (0). Trauma was considered as present if it had been recorded that the participant had experienced one or more traumatic events.

2.2.2. Case vignettes—Vignettes were written for each participant at baseline based on the SIPS and were used on the NAPLS multi-site consensus diagnostic call to determine entry criteria to the NAPLS 2 project. Each vignette was generated to contain detailed and content-rich descriptions of each of the five attenuated psychotic symptoms from the SOPS, including unusual thought content, suspicious ideas, grandiose ideas, perceptual abnormalities, and disorganized communication. The descriptions of the symptoms for this project were taken from these comprehensive vignettes.

2.2.3. Content of Attenuated Positive Symptoms Codebook—The Content of Attenuated Positive Symptoms (CAPS) (Marshall et al., 2011) codebook was used to code the content of perceptual abnormalities in CHR. Descriptions of symptoms were taken from vignettes (described above) written for each participant based on the SOPS assessment. Each symptom content item of the CAPS is presented with a definition and several examples. CAPS codebook items are assigned a numeric code with items dichotomously coded as 0 (absent in the vignette) or 1 (present in the vignette). Using this coding scheme, a prior interrater reliability analysis (Marshall et al., 2014) reported higher than 'acceptable' (>70%) (Krippendorff, 2012) reliabilities for the majority (83.33%) of the CAPS items.

2.3 Procedures

All diagnostic instruments and clinical rating scales were administered at baseline. Raters were experienced research clinicians who demonstrated adequate measure-specific reliability at routine reliability checks. "Gold standard" ratings were established for the SOPS items and interclass correlations were used to compare raters' agreement with this standard, which ranged from 0.92 to 0.96 for the SOPS positive symptoms(Addington et al., 2012). Each vignette was presented and reviewed on a diagnosis consensus call chaired by JA and attended by experienced clinical raters who all met strict reliability standards from each of the NAPLS-2 sites. The NAPLS-2 protocols and informed consents were reviewed and approved by the ethical review boards of all study sites. Figure 1 describes the procedures for assessing the different variables in the study.

2.3.1. Symptom coding and classification of perceptual abnormalities—

Symptom coding of case vignettes was completed by two raters, each of whom was trained on the CAPS codebook (Marshall et al., 2014). The content items of perceptual abnormalities were then used to generate the subtypes. For the present study, six subtypes of perceptual abnormalities were generated per previous literature: simple auditory, complex auditory, simple visual, complex visual, tactile and olfactory. The content items of perceptual abnormalities that are considered to have similar features were grouped together to form these subtypes based on previous literature (Blom and Sommer, 2011; Ffytche and Wible, 2014) (See Table 2). The subtypes of perceptual abnormalities were coded as either present (1) or absent (0). A subtype was considered present if one or more of the symptoms content items under the subtype were presented. Coded subtypes were then used for further analysis.

2.3.2 Statistical analysis—The prevalence of the subtypes of perceptual abnormalities was calculated for the total CHR participants (N=441). The subtypes were only coded for

those CHR participants who had a severity rating of P4 in the psychosis-risk range (P4=3–5 on the SOPS). Mann-Whitney U-tests were used to analyze gender differences in P4 severity. Spearman correlations were used to evaluate the relationship between age and P4 severity. Chi-square and t tests were used to compare gender and age differences between CHR with certain subtypes of perceptual abnormalities and those without. Univariate logistic regression analyses were used to assess the associations of the subtypes of perceptual abnormalities (dependent variable) with trauma, cannabis use and anxiety. Multiple logistic regression analyses were then used to identify independent predictors of the presence of the subtypes of perceptual abnormalities. Data were screened for missing values and outliers. Studentized residual values greater than 2.5 were examined for exclusion from the analyses. Age and gender were entered as covariates in all logistic regression analyses.

3. Results

3.1 Sample characteristics

The study sample consisted of 441 CHR (255 males, 186 females) with a mean age of 18.7 years. The majority of the participants were male, Caucasian and enrolled as students. Demographic details are presented in Table 1. The majority of participants met APSS criteria alone (90%). The remainder met APSS in combination with GRD (6%), or BIPS (2%) or both (2%).

3.2 Prevalence of the subtypes of perceptual abnormalities

The mean severity rating for perceptual abnormalities at baseline as measured by the P4 severity rating, was 3.19. The most frequently endorsed subtypes of perceptual abnormalities were simple auditory and simple visual. Complex auditory, complex visual, tactile and olfactory were less frequent (see Table 2).

3.3 Associations between severity ratings, subtypes, age and gender

Among the CHR participants who endorsed perceptual abnormalities, CHR with complex auditory perceptual abnormalities compared to those with simple auditory perceptual abnormalities compared to those with simple auditory perceptual abnormalities had a significantly higher P4 severity rating (4.19±0.69 vs. 3.25 ± 1.06 , p<0.001). Similarly, CHR who endorsed complex visual perceptual abnormalities compared to those with simple visual perceptual abnormalities also had a significantly higher P4 rating (4.06 ± 0.73 vs. 3.39 ± 0.91 , p=0.002). Females had a significantly higher P4 severity rating than males (3.38 ± 1.33 vs. 3.05 ± 1.39 , p=0.009). Females compared to males, presented with more frequent simple visual perceptual abnormalities (61.3% vs. 49.4%, p=0.013). There were no gender differences detected with other subtypes of perceptual abnormalities. Younger age was significantly correlated with higher P4 severity rating ($r_s=-0.13$, p=0.005). CHR with complex auditory perceptual abnormalities compared to those without were significantly younger (17.59 ± 3.63 vs. 19.13 ± 4.27 , p<0.001). No age differences were observed with other subtypes of perceptual abnormalities.

3.4.1 Perceptual abnormalities and early traumatic experiences—In the study sample, 385 out of 441 CHR completed the trauma scale. Almost half (47.8%) of the CHR participants in this study reported experiencing at least one type of trauma. Females were more likely to have experienced trauma than males (65.5% vs. 46.8%; $\chi 2=13.22$, p<0.001). CHR participants who reported traumatic experiences were significantly older than those who did not (19.29±4.24 vs. 18.24±4.14, p=0.015). No group differences on P4 severity rating were detected between CHR with and without traumatic experiences (3.30±1.30 vs. 3.03±1.49, *p*=0.165). Logistic regression analyses demonstrated that, after controlling for age and gender, both simple auditory and simple visual were more likely to be reported by CHR participants who had traumatic experiences. Neither age nor gender was a significant predictor in the model. Complex auditory, complex visual, tactile and olfactory perceptual abnormalities were not associated with traumatic experiences. There were no differences on P4 severity rating or prevalence of any subtypes of perceptual abnormalities between those who completed the trauma scale and those who did not. These results are presented in Table 3.

3.4.2 Perceptual abnormalities and cannabis use—In the study sample, 438 out of 441 CHR completed the cannabis scale. At baseline, 42.2% of the CHR participants in this study reported having never used cannabis, 35.6% of the CHR reported having used cannabis sometime in the past but not currently using, and 21.5% of the CHR were current cannabis users. CHR participants were divided into three groups: (1) those who had never used cannabis, (2) those who had used cannabis in the past but were not currently using, and (3) those who were currently using cannabis. No difference in P4 severity rating was detected between these three cannabis use groups (3.13 ± 1.44 vs. 3.19 ± 1.44 vs. 3.26 ± 1.12 , *p*=0.148). The never-used group was coded as the reference group for the logistic regression. Compared to the never-used group, current-user group was more likely to report both simple auditory and simple visual perceptual abnormalities, controlling for age and gender. The past-user group did not differ from never-used group on the subtypes of perceptual abnormalities. These results are presented in Table 4.

3.4.3 Perceptual abnormalities and anxiety—In the study sample, 420 out of 441 CHR completed the SAS scale. Females had significantly higher SAS scores than males $(50.44\pm 12.45 \text{ vs.} 45.34\pm 12.80, \text{ p}<0.001)$. There was no significant relationship between age and SAS scores. A higher level of anxiety, as measured by SAS scores, was significantly correlated with higher P4 severity rating in the current CHR sample (r_s =0.16, p=0.001). Logistic regression analyses indicated that higher levels of anxiety were associated with a greater risk of simple auditory, simple visual, and tactile perceptual abnormalities, controlling for age and gender. Neither age nor gender was a significant predictor in the model. There were no significant associations between complex auditory, complex visual or olfactory perceptual abnormalities and SAS scores. These results are presented in Table 5.

3.4.4 Multiple logistic regression of simple auditory and simple visual perceptual abnormalities—Because both simple auditory and simple visual perceptual abnormalities were associated with trauma, cannabis use and anxiety, multiple logistic

regressions were used to model both types of perceptual abnormalities with the above factors as independent predictors. For the model of simple auditory perceptual abnormalities, there were four outliers with a studentized residual greater than 2.5. These cases were excluded in the analysis. The Nagelkerke pseudo R^2 indicated that the model accounted for approximately 17.4 % of the total variance. The Wald test indicated that only age, trauma and anxiety were statistically significant independent predictors. For the model of simple visual perceptual abnormalities, there was one outlier with a studentized residual greater than 2.5. This case was excluded in the analysis. The Nagelkerke pseudo R^2 indicated that the model accounted for approximately 12.3% of the total variance. The Wald test indicated that only trauma and anxiety were statistically significant independent predictors. Table 6 presents the Wald test, odds ratio and the 95% confidence intervals for each predictor. Explorative analyses were performed to examine whether there were interaction effects between trauma, cannabis use and anxiety. Standard logistic regression did not reveal any significant interaction effects.

4. Discussion

The current study examined the prevalence of different subtypes of perceptual abnormalities in a large CHR sample and further explored the relationships between these subtypes and trauma, anxiety and cannabis use. Simple auditory and simple visual perceptual abnormalities were found to be the most prevalent subtypes. Complex auditory, and complex visual perceptual abnormalities, although frequently reported, were less common compared to those reported in schizophrenia patients (Mueser et al., 1990).

Interestingly, younger age was correlated with more prevalent complex auditory perceptual abnormalities. It has been shown that perceptual abnormalities were more common in younger adolescence compared to middle adolescence and that the prevalence in adolescence was higher compared to the adult sample (Kelleher et al., 2012a), although longitudinal studies have shown that incidence of perceptual abnormalities declined in young people followed over time (Bartels-Velthuis et al., 2011; Mackie et al., 2011). It is possible that the more common occurrence of complex auditory perceptual abnormalities in younger adolescence might be part of normal development (Jardri et al., 2014). It might also be that complex auditory perceptual abnormalities are typically considered as more problematic, so that seeking help is prompted earlier than with other subtypes of perceptual abnormalities.

Furthermore, being female was associated with increased simple visual perceptual abnormalities. Females also reported more early traumatic experiences and higher level of anxiety. However, gender was not an independent predictor of simple visual PA when entered together with trauma and anxiety, suggesting that the higher prevalence of trauma and increased anxiety might play a role in the increased prevalence of simple visual perceptual abnormalities in females.

Consistent with previous studies (Stowkowy et al., 2016; Thompson et al., 2009), trauma was not related to the severity of perceptual abnormalities. However, CHR individuals who have had traumatic experience were more likely to report both simple auditory and simple

visual perceptual abnormalities compared to those without a history of trauma. This fits with a recent study in CHR that reported association between physical abuse and visual perceptual abnormalities (Velthorst et al., 2013), although, our results suggested that only simple visual but not complex visual perceptual abnormalities was associated with trauma. Furthermore, it was simple auditory but not complex auditory perceptual abnormalities that were associated with traumatic experience. This result contrasts with previous studies in the general population, reporting associations between trauma and hearing voices (Bentall et al., 2012; Daalman et al., 2012), although it has been suggested that complex auditory hallucinations, or hearing voices, are a group of heterogeneous experience and trauma might be only related to those voices with content that reflects traumatic memories (McCarthy-Jones et al., 2014).

Secondly, our results showed that cannabis users and non-users did not differ in the severity of perceptual abnormalities. However, CHR individuals who were current cannabis users were more likely to report simple visual perceptual abnormalities compared to those who have never used cannabis. This result is consistent with a previous study in CHR (Korver et al., 2010) reporting that cannabis use was related to symptoms of visual perceptual abnormalities in the form of flashes, flames or geometric shapes. This is also in line with a neuroimaging study showing that cannabis use could induce the activations of primary visual cortex, which is linked to simple visual hallucinations (Winton-Brown et al., 2011). Although cannabis use has been typically linked more to visual hallucination than auditory hallucinations (Caton et al., 2005), we also found that current cannabis use was associated with increased risk for simple auditory perceptual abnormalities. Also, it should be noted that only current cannabis use but not past cannabis use was related to the subtype of perceptual abnormalities. This is not surprising given that a previous study observed that cannabis use and symptoms of perceptual abnormalities covary over time (Corcoran et al., 2008).

Consistent with existing literature suggesting anxiety is linked to hallucinations (Allen et al., 2005; Hartley et al., 2013), a more severe level of anxiety was associated with more severe ratings on perceptual abnormalities. In terms of the subtypes, more severe anxiety was associated with the presence of simple auditory, simple visual and tactile perceptual abnormalities. Our results support current theoretical models suggesting anxiety is linked to simple hallucinations (Wilkinson, 2014). According to these theoretical accounts, a state of anxiety could enhance one's attention directed outward and increase perception sensitivity of the external stimuli. This would allow an individual to tolerate more false positive signals, i.e., detecting a signal when absent, which results in simple perceptual abnormalities, for instance, hearing footsteps or seeing shadows (Dodgson and Gordon, 2009). Complex auditory perceptual abnormalities were not found to be associated with anxiety. A possible explanation is that complex auditory hallucinations act as a response to reduce anxiety level before the onset of complex auditory hallucinations and decreased anxiety level afterwards was observed (Delespaul et al., 2002).

Finally, we examined the unique impact of traumatic experience, cannabis use, and anxiety on perceptual abnormalities. The results demonstrated that both trauma and anxiety were

significantly and independently associated with increased risk for both simple auditory and simple visual perceptual abnormalities. However, cannabis use was no longer a significant predictor of simple auditory or simple visual perceptual abnormalities, when controlling for trauma and anxiety. These findings might indicate that cannabis use could be a proxy for other factors to have influence on the symptoms of perceptual abnormalities. In other words, cannabis use among CHR individuals who reported simple auditory and simple visual perceptual abnormalities might be attributable to trauma and anxiety. Support for this idea could be found in a recent study suggesting that anxiety mediated the relationship between cannabis use and attenuated psychotic symptoms (Reeves et al., 2014). This idea is also in line with studies reporting a reduced and non-significant effect of cannabis use on prediction of psychosis, when trauma was included in the model (Houston et al., 2008; Houston et al., 2011).

Overall, we observed that simple auditory and simple visual perceptual abnormalities were associated with trauma, cannabis use and anxiety while neither complex auditory nor complex visual were related to these factors. Hence, it appears that simple perceptual abnormalities, regardless of whether they are auditory or visual, might share similar underlying psychopathology. Although simple hallucinations have been well studied with patients who have organic disorders, such as epilepsy and Charles Bonnet Syndrome (Ffytche and Wible, 2014), they have been rarely documented in psychiatric populations. Evidence from neuroimaging studies has lent support for the distinction between simple hallucinations and complex hallucinations. It has been suggested that simple hallucinations are directly related to the activation of corresponding primary sensory cortex, whereas complex hallucinations are related to a network of brain regions consisting of brain areas representing higher level sensory processing, language, social interaction, memory and self (Ffytche and Wible, 2014). Affective state, especially anxiety can influence perception by enhancing one's attention directed outward and activate primary sensory cortex with the absence of external stimuli, resulting simple hallucinations (Mohanty et al., 2005). Thus, simple perceptual abnormalities in CHR might represent a type of altered perception, which is caused by enhanced anxiety state and over activation of the sensory system.

Several limitations should be noted with the current study. The vignettes used for the analysis were not written specifically for coding the symptom content and it is possible that certain content was not documented. We are aware that classifying perceptual abnormalities into simple and complex might be too simplistic to accommodate many of the phenomenological features of the symptom. However, even with this simple classification, this paper has added new knowledge by considering these subtypes in addition to severity. A further limitation was that the frequency and severity of the traumatic experiences were not available. This might affect the results as previous findings suggested a dose dependent relationship between trauma and psychotic symptoms (Shevlin et al., 2007). Additionally, validity of self-report accounts of traumatic experience and anxiety needs to be considered when translating these results. Moreover, the cross-sectional nature of the current study did not allow us to explore how changes in trauma, cannabis and anxiety relate to changes in perceptual abnormalities. Finally, we did not take into account the subtypes of complex auditory perceptual abnormalities, such as inner speech voices and memory based voices. This might be relevant, as previous studies have reported possible different

psychopathologies underlying different subtypes of complex auditory hallucination (McCarthy-Jones et al., 2014). However, this was beyond the scope of the current study.

There are several implications of this study. First, future work could examine the role of complex versus simple perceptual abnormalities in later conversion to psychosis. Secondly, in further studies examining correlates of perceptual abnormalities, subtypes as well as severity could be examined. Thirdly, clinical implications include addressing trauma, cannabis use and anxiety as a means to perhaps reduce early signs of perceptual abnormalities.

References

- Addington J, Cadenhead KS, Cornblatt BA, Mathalon DH, McGlashan TH, Perkins DO, et al. North American Prodrome Longitudinal Study (NAPLS 2): overview and recruitment. Schizophr Res. 2012; 142:77–82. [PubMed: 23043872]
- Addington J, Liu L, Buchy L, Cadenhead KS, Cannon TD, Cornblatt BA, et al. North American Prodrome Longitudinal Study (NAPLS 2): The Prodromal Symptoms. J Nerv Ment Dis. 2015; 203(5):328–335. [PubMed: 25919383]
- Allen P, Freeman D, McGuire P, Garety P, Kuipers E, Fowler D, et al. The prediction of hallucinatory predisposition in non-clinical individuals: examining the contribution of emotion and reasoning. Br J Clin Psychol. 2005; 44:127–132. [PubMed: 15826349]
- American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5. American Psychiatric Publishing; Arlington, VA: 2013.
- Arseneault L, Cannon M, Poulton R, Murray R, Caspi A, Moffitt TE. Cannabis use in adolescence and risk for adult psychosis: longitudinal prospective study. BMJ. 2002; 325(7374):1212–1213. [PubMed: 12446537]
- Bartels-Velthuis AA, van de Willige G, Jenner JA, van Os J, Wiersma D. Course of auditory vocal hallucinations in childhood: 5-year follow-up study. Br J Psychiatry. 2011; 199(4):296–302. [PubMed: 21708881]
- Bentall RP, Wickham S, Shevlin M, Varese F. Do specific early-life adversities lead to specific symptoms of psychosis? A study from the 2007 the Adult Psychiatric Morbidity Survey. Schizophr Bull. 2012; 38(4):734–740. [PubMed: 22496540]
- Blom, J. A dictionary of hallucinations. NY: Springer, New York; 2010.
- Blom, J., Sommer, I. Research and practice. Springer-Verlag; New York Inc: 2011. Hallucinations.
- Caton CL, Drake RE, Hasin DS, Dominguez B, Shrout PE, Samet S, et al. Differences between earlyphase primary psychotic disorders with concurrent substance use and substance-induced psychoses. Arch Gen Psychiatry. 2005; 62(2):137–145. [PubMed: 15699290]
- Corcoran CM, Kimhy D, Stanford A, Khan S, Walsh J, Thompson J, et al. Temporal association of cannabis use with symptoms in individuals at clinical high risk for psychosis. Schizophr Res. 2008; 106(2–3):286–293. [PubMed: 18809298]
- Daalman K, Diederen KM, Derks EM, van Lutterveld R, Kahn RS, Sommer IE. Childhood trauma and auditory verbal hallucinations. Psychol Med. 2012; 42(12):2475–2484. [PubMed: 22716897]
- Delespaul P, deVries M, van Os J. Determinants of occurrence and recovery from hallucinations in daily life. Soc Psychiatry Psychiatr Epidemiol. 2002; 37(3):97–104. [PubMed: 11990012]
- Dodgson G, Gordon S. Avoiding false negatives: are some auditory hallucinations an evolved design flaw? Behav Cogn Psychother. 2009; 37(3):325–334. [PubMed: 19371459]
- Escher S, Romme M, Buiks A, Delespaul P, Van Os J. Independent course of childhood auditory hallucinations: a sequential 3-year follow-up study. Br J Psychiatry Suppl. 2002; 43:s10–18. [PubMed: 12271794]
- Ffytche DH, Wible CG. From tones in tinnitus to sensed social interaction in schizophrenia: how understanding cortical organization can inform the study of hallucinations and psychosis. Schizophr Bull. 2014; 40(Suppl 4):S305–316. [PubMed: 24936089]

- Hartley S, Barrowclough C, Haddock G. Anxiety and depression in psychosis: a systematic review of associations with positive psychotic symptoms. Acta Psychiatr Scand. 2013; 128(5):327–346. [PubMed: 23379898]
- Hides L, Lubman DI, Buckby J, Yuen HP, Cosgrave E, Baker K, et al. The association between early cannabis use and psychotic-like experiences in a community adolescent sample. Schizophr Res. 2009; 112(1–3):130–135. [PubMed: 19428219]
- Houston JE, Murphy J, Adamson G, Stringer M, Shevlin M. Childhood sexual abuse, early cannabis use, and psychosis: testing an interaction model based on the National Comorbidity Survey. Schizophr Bull. 2008; 34(3):580–585. [PubMed: 18024467]
- Houston JE, Murphy J, Shevlin M, Adamson G. Cannabis use and psychosis: re-visiting the role of childhood trauma. Psychol Med. 2011; 41(11):2339–2348. [PubMed: 21557896]
- Janssen I, Krabbendam L, Bak M, Hanssen M, Vollebergh W, de Graaf R, et al. Childhood abuse as a risk factor for psychotic experiences. Acta Psychiatr Scand. 2004; 109(1):38–45. [PubMed: 14674957]
- Jardri R, Bartels-Velthuis AA, Debbane M, Jenner JA, Kelleher I, Dauvilliers Y, et al. From phenomenology to neurophysiological understanding of hallucinations in children and adolescents. Schizophr Bull. 2014; 40(Suppl 4):S221–232. [PubMed: 24936083]
- Kelleher I, Connor D, Clarke MC, Devlin N, Harley M, Cannon M. Prevalence of psychotic symptoms in childhood and adolescence: a systematic review and meta-analysis of population-based studies. Psychol Med. 2012a; 42(9):1857–1863. [PubMed: 22225730]
- Kelleher I, Keeley H, Corcoran P, Lynch F, Fitzpatrick C, Devlin N, et al. Clinicopathological significance of psychotic experiences in non-psychotic young people: evidence from four population-based studies. Br J Psychiatry. 2012b; 201(1):26–32. [PubMed: 22500011]
- Klosterkotter J, Hellmich M, Steinmeyer EM, Schultze-Lutter F. Diagnosing schizophrenia in the initial prodromal phase. Arch Gen Psychiatry. 2001; 58(2):158–164. [PubMed: 11177117]
- Korver N, Nieman DH, Becker HE, van de Fliert JR, Dingemans PH, de Haan L, et al. Symptomatology and neuropsychological functioning in cannabis using subjects at ultra-high risk for developing psychosis and healthy controls. Aust N Z J Psychiatry. 2010; 44(3):230–236. [PubMed: 20180725]
- Krippendorff, K. Content analysis: An introduction to its methodology. Sage; 2012.
- Langdon R, McGuire J, Stevenson R, Catts SV. Clinical correlates of olfactory hallucinations in schizophrenia. Br J Clin Psychol. 2011; 50(2):145–163. [PubMed: 21545448]
- Mackie CJ, Castellanos-Ryan N, Conrod PJ. Developmental trajectories of psychotic-like experiences across adolescence: impact of victimization and substance use. Psychol Med. 2011; 41(1):47–58. [PubMed: 20346196]
- Marshall C, Denny E, Cadenhead KS, Cannon TD, Cornblatt BA, McGlashan TH, et al. The content of attenuated psychotic symptoms in those at clinical high risk for psychosis. Psychiatry Res. 2014; 219(3):506–512. [PubMed: 25048759]
- Marshall C, Falukozi E, Albertin M, Zhu H, Addington J. The development of the Content of Attenuated Positive Symptoms Codebook for those at clinical high risk of psychosis. Psychosis. 2011; 4(3):191–202. [PubMed: 26161138]
- McAusland L, Buchy L, Cadenhead KS, Cannon TD, Cornblatt BA, Heinssen R, et al. Anxiety in youth at clinical high risk for psychosis. Early Interv Psychiatry. 2015
- McCarthy-Jones S, Trauer T, Mackinnon A, Sims E, Thomas N, Copolov DL. A new phenomenological survey of auditory hallucinations: evidence for subtypes and implications for theory and practice. Schizophr Bull. 2014; 40(1):231–235. [PubMed: 23267192]
- McGlashan, T., Walsh, B., Woods, S. The Psychosis-Risk Syndrome: Handbook for Diagnosis and Follow-Up. Oxford University Press; 2010.
- McGrath JJ, Saha S, Al-Hamzawi A, Alonso J, Bromet EJ, Bruffaerts R, et al. Psychotic Experiences in the General Population: A Cross-National Analysis Based on 31,261 Respondents From 18 Countries. JAMA psychiatry. 2015; 72(7):697–705. [PubMed: 26018466]
- Mohanty A, Herrington JD, Koven NS, Fisher JE, Wenzel EA, Webb AG, et al. Neural mechanisms of affective interference in schizotypy. J Abnorm Psychol. 2005; 114(1):16–27. [PubMed: 15709808]

- Mueser KT, Bellack AS, Brady EU. Hallucinations in schizophrenia. Acta Psychiatr Scand. 1990; 82(1):26–29. [PubMed: 2399817]
- Read J, van Os J, Morrison AP, Ross CA. Childhood trauma, psychosis and schizophrenia: a literature review with theoretical and clinical implications. Acta Psychiatr Scand. 2005; 112(5):330–350. [PubMed: 16223421]
- Reeves LE, Anglin DM, Heimberg RG, Gibson LE, Fineberg AM, Maxwell SD, et al. Anxiety mediates the association between cannabis use and attenuated positive psychotic symptoms. Psychiatry Res. 2014; 218(1–2):180–186. [PubMed: 24745470]
- Saddock, BJ., Saddock, VA., Ruiz, P. Kaplan and Sadock's Comprehensive Textbook of Psychiatry. 9. Lippincott Williams & Wilkins; Philadelphia: 2009.
- Scott J, Martin G, Bor W, Sawyer M, Clark J, McGrath J. The prevalence and correlates of hallucinations in Australian adolescents: results from a national survey. Schizophr Res. 2009; 107(2–3):179–185. [PubMed: 19046858]
- Shevlin M, Dorahy M, Adamson G. Childhood traumas and hallucinations: an analysis of the National Comorbidity Survey. J Psychiatr Res. 2007; 41(3–4):222–228. [PubMed: 16643948]
- Stowkowy J, Liu L, Cadenhead KS, Cannon TD, Cornblatt BA, McGlashan TH, et al. Early traumatic experiences, perceived discrimination and conversion to psychosis in those at clinical high risk for psychosis. Soc Psychiatry Psychiatr Epidemiol. 2016; 51(4):497–503. [PubMed: 26851943]
- Thompson JL, Kelly M, Kimhy D, Harkavy-Friedman JM, Khan S, Messinger JW, et al. Childhood trauma and prodromal symptoms among individuals at clinical high risk for psychosis. Schizophr Res. 2009; 108(1–3):176–181. [PubMed: 19174322]
- VandenBos, GR. APS dictionary of psychology. American Psychological Association; Washington, DC: 2007.
- Velthorst E, Nelson B, O'Connor K, Mossaheb N, de Haan L, Bruxner A, et al. History of trauma and the association with baseline symptoms in an Ultra-High Risk for psychosis cohort. Psychiatry Res. 2013; 210(1):75–81. [PubMed: 23871168]
- Waters F, Collerton D, Ffytche DH, Jardri R, Pins D, Dudley R, et al. Visual hallucinations in the psychosis spectrum and comparative information from neurodegenerative disorders and eye disease. Schizophr Bull. 2014; 40(Suppl 4):S233–245. [PubMed: 24936084]
- Wilkinson S. Accounting for the phenomenology and varieties of auditory verbal hallucination within a predictive processing framework. Conscious Cogn. 2014; 30:142–155. [PubMed: 25286243]
- Winton-Brown TT, Allen P, Bhattacharyya S, Borgwardt SJ, Fusar-Poli P, Crippa JA, et al. Modulation of auditory and visual processing by delta-9-tetrahydrocannabinol and cannabidiol: an FMRI study. Neuropsychopharmacology. 2011; 36(7):1340–1348. [PubMed: 21412224]
- Zung WW. A rating instrument for anxiety disorders. Psychosomatics. 1971; 12(6):371–379. [PubMed: 5172928]

Paper Highlights

- Simple auditory and simple visual perceptual abnormalities were the most prevalent subtypes in Clinical High Risk (CHR) youth
- Complex auditory and complex visual perceptual abnormalities, were less common in CHR compared to those reported in schizophrenia patients
- Both simple auditory and simple visual perceptual abnormalities were more likely to be reported by CHR who had a history of traumatic experiences, who are current cannabis users, and who have higher levels of anxiety

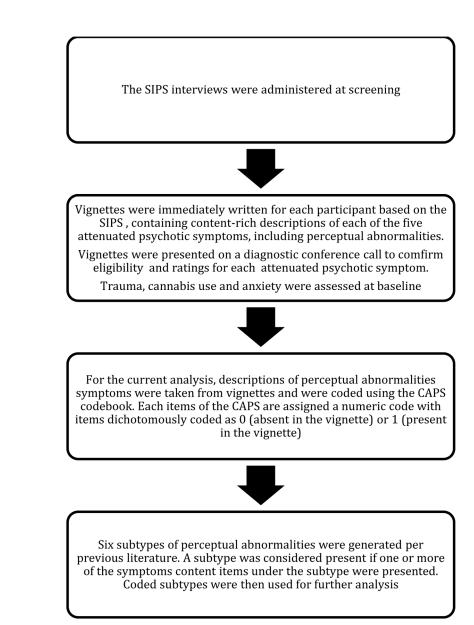


Figure 1. Procedure of symptom content coding

Demographics

Variable	CHR
variable	N=441
	Mean (SD)
Age in years	18.74 (4.17)
Years of education	11.46 (2.73)
	Number (%)
Gender	
Male	255 (57.8)
Female	186 (42.2)
Racial background	
Caucasian	254 (57.6)
Black	68 (15.4)
Asian	31(7.0)
Other	88 (20.0)
Marital status	
Single never married	421 (95.5)
Other	20 (4.5)
Currently enrolled as stu	dent
Yes	363 (82.3)
No	78 (17.7)
Currently working	
Yes	121 (27.4)
No	320 (72.6)

Frequencies of perceptual abnormalities content items and subtypes in CHR (N=441)

PA content items in CAPS	Frequencies n (%)	PA subtypes	Frequencies ^b n (%)
Indistinct noises	141 (32.0)	Simple auditory PA	264 (59.9)
Distinct noises	113 (25.6)		
Name being called	89 (20.2)		
Mumbling	23 (5.2)		
Auditory distortions	76 (17.2)		
Voices ^a	111 (25.2)	Complex auditory PA	111 (25.2)
Voices with negative content	64 (14.5)		
Voices with neutral content	51 (11.6)		
Voices with positive content	13 (2.9)		
Vague figures or shadows	206 (56.1)	Simple visual PA	240 (54.4)
Visual distortions	71 (20.5)		
Flashes of light	50 (11.3)		
Spots or floaters	22 (5.0)		
Geometric shapes	13 (2.9)		
Flames or fire	4 (1.0)		
Animals	72 (20.8)	Complex visual PA	93 (21.1)
Faces or people	93 (26.9)		
Numbness/Tingling	40 (11.6)	Tactile PA	118 (26.8)
Burn/Cold	17 (4.9)		
Ache/Pain	16 (4.6)		
Electricity/Vibrations	21 (6.1)		
Touching	44 (12.7)		
Bugs crawling	16 (4.6)		
Physical alterations	16 (4.6)		
Pleasant smells	18 (5.2)	Olfactory PA	39 (8.8)
Unpleasant smells	28 (8.1)		

PA, Perceptual Abnormalities; CAPS, Content of Attenuated Positive Symptoms.

^aAn individuals can present with more than one type of voice.

 b A PA subtype was considered present if anyone of the symptom content items under the PA subtype were present. An individual can present with more than one subtype of perceptual abnormalities.

Associations between the subtypes of perceptual abnormalities of and traumatic experiences in CHR (N=385)

PA subtypes	With Traumatic Experiences N=211 n (%)	Without Traumatic Experiences N=174 n (%)	OR (95%CI)
Simple Auditory PA	146 (69.2)	91 (52.3)	2.09 (1.35–3.11)**
Complex Auditory PA	56 (26.5)	41 (23.6)	1.39 (0.54–1.42)
Simple Visual PA	130 (61.6)	82 (47.1)	1.80 (1.18–2.73) **
Complex Visual PA	51 (24.2)	31 (17.8)	1.49 (0.89–2.49)
Tactile PA	63 (29.9)	49 (28.2)	1.16 (0.74–1.83)
Olfactory PA	19 (9.0)	17 (9.8)	0.95 (0.47–1.93)

PA, Perceptual Abnormalities; OR, odds ratio; CI, confidence interval.

* p<0.05,

** p<0.01

Table 4

Associations between the subtypes of perceptual abnormalities and cannabis use in CHR (N=438)

PA subtypes	Never used N=186		Past users N=157		Current users N=95	sers
	n, (%)	OR (95%CI) n (%)	(%) u	OR (95%CI) n (%)	(%) u	OR (95%CI)
Simple Auditory PA	104 (55.9) Ref.	Ref.	95 (60.5)	1.57 (0.97–2.54)	63 (66.3)	95 (60.5) 1.57 (0.97–2.54) 63 (66.3) 2.03 (1.17–3.51) [*]
Complex Auditory PA 48 (25.8)	48 (25.8)	Ref.	41 (26.3)	41 (26.3) 1.54 (0.90–2.65) 21 (22.1) 1.14 (0.61–2.13)	21 (22.1)	1.14 (0.61–2.13)
Simple Visual PA	94 (50.5)	Ref.	81 (51.9)	81 (51.9) 1.39 (0.87–2.24) 62 (65.3)	62 (65.3)	2.48 (1.43–4.31)**
Complex Visual PA	43 (23.1)	Ref.	29 (18.6)	29 (18.6) 0.90 (0.51–1.60) 19 (20.0) 0.97 (0.51–1.85)	19 (20.0)	0.97 (0.51–1.85)
Tactile PA	56 (30.1)	Ref.	35 (22.4)	35 (22.4) 0.81 (0.48–1.37) 37 (38.9) 1.69 (0.97–2.93)	37 (38.9)	1.69 (0.97–2.93)
Olfactory PA	21 (11.3) Ref.	Ref.	12 (7.7)	0.82 (0.36, 1.85) 6 (6.3)	6 (6.3)	0.66 (0.25–1.77)

ŝ b

 $p_{p<0.01}^{*}$, recept

Association between the subtypes of perceptual abnormalities and Self-Rating Anxiety Scales scores in CHR (N=420)

PA subtypes	B (SE)	Wald	OR (95%CI)
Simple Auditory PA	0.046 (0.009)	24.14	1.05 (1.03–1.07)****
Complex Auditory PA	0.006 (0.009)	0.48	1.01 (0.99–1.03)
Simple Visual PA	0.045 (0.009)	25.93	1.05 (1.03–1.07)****
Complex Visual PA	0.008 (0.009)	0.74	1.01 (0.99–1.03)
Tactile PA	0.018 (0.013)	8.97	1.03 (1.01–1.04)**
Olfactory PA	0.025 (0.008)	1.89	1.02 (0.99–1.05)

PA, Perceptual Abnormalities; OR, odds ratio; CI, confidence interval.

* p<0.05,

** p<0.01,

*** p<0.001

Page 21

Table 6

Multiple logistic regressions of simple auditory and simple visual perceptual abnormalities

Variable	Simple Auditory PA		Simple Visual PA	
	Wald	OR (95%CI)	Wald	OR (95%CI)
Age	7.20	0.92 (0.87, 0.98)**	0.95	0.95 (0.90, 1.00)
Gender	0.71	1.07 (0.66, 1.72)	0.45	1.17 (0.74, 1.83)
Trauma	8.10	1.97 (1.23, 3.14)***	4.62	1.61 (1.04, 2.52)*
Cannabis current use	0.84	1.14 (0.72, 2.50)	0.82	1.13 (0.87, 1.48)
Self-Rating Anxiety Scale score	24.58	1.06 (1.03, 1.08) ***	18.47	1.04 (1.02, 1.06) ***

PA, Perceptual Abnormalities; OR, odds ratio; CI, confidence interval.

** p<0.05,

** p<0.01,

*** p<0.001