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Perceptual abnormalities in an Ultra High Risk for psychosis population- relationship to trauma and co-morbid disorder

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Abstract

Aims: The aims of this study were three-fold. We wished to investigate whether at baseline entry to an Ultra High Risk clinic whether: (1) perceptual abnormalities are more prevalent in those young people with co-morbid psychiatric diagnoses, (2) perceptual abnormalities are more prevalent in those young people with histories of childhood adversity (childhood trauma, bullying) and (3) perceptual abnormality type is associated with co-morbid psychiatric diagnoses or histories of childhood adversity.

Methods: In a sample of 118 UHR patients we investigated the relationship between perceptual abnormalities and non-psychotic diagnoses and adverse life events at entry to a UHR clinic.

Results: Depressive disorder at baseline was associated with increased odds of experiencing perceptual abnormalities (OR 3.59, p=0.004), particularly visual perceptual abnormalities (OR 2.36, p=0.02). Borderline personality disorder at baseline was associated with increased odds of any auditory perceptual abnormalities (OR 3.44, p=0.04) and specifically second person perceptual abnormalities (OR 2.69, p=0.04). A history of childhood trauma and childhood bullying were both associated with increased odds of experiencing perceptual abnormalities at baseline (trauma OR 6.30, p<0.001; bullying OR 5.00, p=0.01).

Conclusions: Our findings suggest that in the UHR population certain types of perceptual abnormalities index risk for co-morbid non-psychotic disorder and indicate prior experience of childhood trauma. The use of detailed phenomenology of psychotic symptoms can help to shape our understanding of risk in UHR patients.

Background

Hallucinations are primary symptoms of psychotic disorders such as schizophrenia in both DSM-5 and ICD-10 (American Psychiatric Association. & American Psychiatric Association. DSM-5 Task Force., 2013; Organization, 1992). Hallucinations can be defined as a perceptual abnormality 'which occurs in the absence of corresponding external stimulation of the relevant sensory organ, has sufficient sense of reality to resemble a veridical perception, over which the subject does not feel s/he has direct and voluntary control, and which occurs in the awake state' (David, 2004).

The Ultra High Risk (UHR) population are a group of help-seeking young people who are identified using reliable measurement tools and clinical criteria as being at high risk of developing a psychotic illness in the near future (Phillips, Yung, & McGorry, 2000; Yung et al., 2003). The UHR criteria are summarised in Figure 1. Perceptual abnormalities are included in the UHR criteria as signifying high and impending risk for psychosis. These are either in a sub-threshold form (most commonly) or full/true hallucinations occurring at a frequency below that signifying a psychotic disorder. Perceptual abnormalities are one of the most prevalent attenuated symptoms in the UHR population (Cannon et al., 2008; Mason et al., 2004; Nelson et al., 2013; Ruhrmann et al., 2010; Walker et al., 2009). Our group previously examined the relationship between baseline perceptual abnormalities and subsequent risk of transition to a psychotic disorder in a UHR sample and found no significant relationship (O'Connor et al., 2016).

[Insert Figure 1 about here]

High rates of psychiatric co-morbidity have been reported in UHR populations (Woods et al., 2009; Yung & McGorry, 1996). A meta-analysis conducted by Fusar-Poli et al. (2014) reported rates of co-morbid depression of 40% and anxiety disorder of 15% in the available UHR studies. The possible role played by comorbid disorders in altering risk of transition to psychosis has been investigated in a number of studies (Fusar-Poli, Nelson, Valmaggia, Yung, & McGuire, 2014; Salokangas et al., 2012; A. Thompson et al., 2012; Yung et al., 2003), with evidence suggesting that co-morbid psychiatric disorders at baseline entry to a UHR clinic are not associated with a higher risk of transition to psychosis in the UHR population. However, given that a number of the cognitive theories proposed to explain the development of perceptual abnormalities identify a role for anxiety and low mood in the aetiology and persistence of hallucinations (Bentall & Slade, 1985; Morrison, Frame, & Larkin, 2003; Morrison, Haddock, & Tarrier, 1995; Myin-Germeys & van Os, 2007; van Os, Linscott, Myin-Germeys, Delespaul, & Krabbendam, 2009), it is surprising that little attention has to date been paid to the relationship between perceptual abnormalities specifically and comorbid disorders at baseline in the UHR population.

In recent years an area of particular research interest has been the role that childhood adversity (trauma, bullying) potentially play in the development of perceptual abnormalities and other psychotic symptoms. A relationship between childhood trauma and psychosis is well established (P. Bebbington et al., 2011; P. E. Bebbington et al., 2004; Bechdolf et al., 2010; Daalman et al., 2012; Harley et al., 2010; Kelleher et al., 2008; Shevlin, Dorahy, & Adamson, 2007; A. Thompson et al., 2010). Furthermore, a recent meta-analysis found that childhood trauma is highly prevalent among UHR subjects (Kraan, Velthorst, Smit, de Haan, & van der Gaag, 2015). To our knowledge, only four studies have reported on the association between childhood

trauma and perceptual abnormalities in UHR samples (Falukozi & Addington, 2012; A. Thompson et al., 2010; J. L. Thompson et al., 2009; Velthorst et al., 2013). Velthorst and colleagues (2013) reported that the intensity of perceptual abnormalities as rated on the Comprehensive Assessment of At Risk Mental States (CAARMS) was higher in young people who reported a history of physical abuse or 'other' abuse e.g. verbal, domestic abuse at entry to a UHR clinic. Thompson and colleagues (2010) reported that sexual abuse in childhood was associated with sexual content in attenuated psychotic symptoms and an association between childhood trauma and positive symptoms was reported by Thompson et al. 2009. Falukozi & Addington (2012) reported that trauma was associated with a hearing non negative voices. There is evidence from epidemiological and prospective studies suggesting that childhood bullying may be associated with an increased risk of later psychosis (Arseneault et al., 2011; Schreier et al., 2009). To our knowledge, a possible association between bullying and perceptual abnormalities has not been investigated in the UHR population.

The aims of this study were three-fold. We wished to investigate whether at baseline entry to a UHR clinic whether: (a) perceptual abnormalities are more prevalent in those young people with co-morbid psychiatric diagnoses, (b) perceptual abnormalities are more prevalent in those young people with histories of childhood adversity (childhood trauma, bullying) and (c) perceptual abnormality type is associated with co-morbid psychiatric diagnoses or histories of childhood adversity.

We hypothesised that (a) perceptual abnormalities would be more prevalent at baseline entry to the UHR clinic in young people with specific co-morbid psychiatric diagnoses particularly co-morbid depressive disorder, (b) that a history of childhood

adverse events (trauma or bullying) would be more common in those young people who present with perceptual abnormalities compared to those presenting with other psychotic symptoms and (c) that childhood adversity (trauma, bullying) would be associated with abusive auditory perceptual abnormalities.

Methods

Participants

The sample was taken from a specialist UHR clinic that treats young people ages 15 and 25 and meeting UHR criteria as assessed by the CAARMS (Yung et al., 2005). See Figure 1 for UHR criteria. All individuals accepted into the UHR clinic between 30/6/2003 and 31/10/2008 inclusively were included in the sample; there were no exclusions. All referrals to the clinic in this period were recorded in a central database. There were 605 individuals seen at the clinic during this period (O'Connor et al., 2016; A. Thompson et al., 2013; Velthorst et al., 2009). The study sample consisted of 'cases' and 'controls' from within the overall 605 individuals:

Transitioned 'cases'

All subjects that were known to have 'transitioned' to a full threshold psychotic disorder at 31/1/2010 (N= 65) were identified as 'cases'. The majority of these 'transition' cases were identified during their time attending the clinic. Some were identified from other sources including follow-up research interviews. The Victorian Public Mental Health Client Information Management System (CMI), an electronic database which documents all contact with public mental health services in the state of Victoria was searched to identify any other potential cases. This was done for the entire 605 individuals and identified three additional cases (N=3).

Transition to psychosis in the clinic is determined using the CAARMS criteria (Yung et al., 2003; Yung, Phillips, Yuen, & McGorry, 2004). This operationalised definition of transition to first episode psychosis consists of daily frank positive psychotic symptoms for longer than one week (Yung et al., 2005). For the 3 cases that were identified by the clinical database, transition was identified by the presence of a DSM-IV-TR psychotic disorder that fulfilled the above definition. Of the 65 subjects who were known to have developed a psychotic disorder, six were identified from the UHR clinic database to have already been psychotic at the time of their first appointment with a clinician. They were therefore excluded from the sample. The median time to transition was 1.5 years with a range of 0.1 years to 6.5 years.

Non transitioned 'controls'

A random sample of subjects who were known to have not transitioned on 31/01/2010 were the control group; 'non transition' status was established through a combination of known clinical contact with the UHR clinic, using details from our central database which included follow-up research assessments and searching electronic records in the Victorian public mental health client information management system. The search was conducted on 31/1/2010; it gave no indication that any of the subjects in this random sample had developed a psychotic disorder. Therefore, it was assumed that all these subjects remained free from transition up to the date of search. A total of 539 potential controls were identified. Fifty-nine of these subjects were randomly selected using random number generation to exactly match the number of transitioned cases. Thus cases and controls were not individually matched, but there was group 'matching' on period of recruitment. This is important as year of recruitment is known to be a strong predictor of development of a psychotic disorder (Nelson et al., 2013;

Yung et al., 2007). There was one control per case. The time to follow-up ranged from 1.2 to 6.5 years with a median of 4.5 years.

Symptom measures

An auditing tool was used to gather information on perceptual abnormalities and other psychotic symptoms as recorded in the clinical file (Appendix 1). A trained research assistant gathered the data. Training on the audit tool and on OPCRIT was delivered by BN and AT. The accuracy of the ratings of the presence/absence of the symptoms by the research assistant was regularly checked by one of the investigators (BN).

For the assessment of psychotic symptoms we included all symptoms assessed in the Operational Criteria for Psychotic Illness (OPCRIT) tool (McGuffin, Farmer, & Harvey, 1991). We supplemented this with additional symptom items related to symptom content that were not adequately covered by the OPCRIT tool, including details on the content of perceptual abnormalities (for example whether they were second person, third person, abusive or command in nature). A perceptual abnormality was considered present if it was rated 3 or greater on this CAARMS subscale. This threshold was selected as a rating of 3 or greater on the perceptual abnormalities subscale of the CAARMS could meet threshold for UHR status, if occurring with sufficient frequency. A rating of less than 3 on the perceptual abnormalities subscale alone would not be sufficient to meet UHR criteria threshold.

All initial assessments at the UHR clinic include a standardised comprehensive clinical interview with a clinical psychologist using a standardised assessment form, followed by a review by a psychiatrist and completion of the CAARMS instrument. Childhood

adversity would routinely be enquired about during an initial assessment at the UHR clinic and is included in the standardised assessment template.

Details of co-morbid diagnoses were obtained from the clinical files. Borderline personality disorder was considered present if 5 or more traits were documented in the clinical assessment or a pre-existing diagnosis was documented in the clinical file. 'Childhood trauma' was considered present if it had been recorded in the clinical file that the young person had experienced one or more traumatic events e.g. sexual abuse, emotional abuse, physical abuse (yes/no) up until the age of 18. 'Childhood bullying' was considered present if it had been recorded in the clinical file that the young person had been a victim of bullying (yes/no) up until the age of 18.

Procedure

Data from the date of first contact with a clinician at the UHR clinic until four weeks after first contact was used as recorded in the clinical file. All patients accepted into the UHR clinic receive a thorough and structured initial assessment by a clinical psychologist, which includes the CAARMS, and a full assessment of clinical symptoms, followed by an assessment by a psychiatrist. When the clinical files did not include any record of perceptual abnormalities, co-morbid diagnoses or adverse events these were considered to be absent.

Data Analysis

The dependent variables for analysis were all perceptual abnormalities, auditory perceptual abnormalities, visual perceptual abnormalities and 'other' perceptual abnormalities. A group of 'other' perceptual abnormalities symptoms comprising of

olfactory, gustatory, somatic and tactile perceptual abnormalities was formed, as the numbers in each of the individual groups were less than 10. In addition dependent variables based on the content of auditory verbal perceptual abnormalities were also formed; abusive, second person, third person and command perceptual abnormalities. In cases where perceptual abnormalities met criteria for two variable categories, for example were both abusive and second person, they were counted in both variables. The independent variables for the analysis were comorbid diagnoses, childhood bullying and childhood trauma.

Differences in socio-demographic characteristics in the study were examined with t-tests (age, Global Assessment of Functioning (GAF) and the chi-squared test (gender, comorbid diagnoses, history of adversity). Logistic regression analysis was used to assess the association between co-morbid diagnosis or an adverse event and perceptual disturbances. All analyses were additionally adjusted for age and gender.

Results

Demographics

There were 605 individuals seen at the UHR clinic between 30/6/2003 and 31/10/2008 inclusively. The sample included in this study was 118 subjects of the 605 individuals. The 118 subjects included all 59 cases and 59 randomly selected controls. The mean age of the sample was 18.3 years and 58.5% (n=67) were female.
There were no significant differences on age, gender, education level, occupation, duration of symptoms or history of substance use between the cases and the controls

(See Table 1). There was a trend for more of the cases to be living with their parents at baseline (p= 0.06*)*.

[Insert Table 1 here]

UHR patients who reported perceptual abnormalities at baseline were significantly more likely to be female (p<0.001), have a co-morbid diagnosis of depression (p=0.004) and to be in employment (p<0.001) (See Table 2). The majority of UHR subjects reported perceptual abnormalities at baseline entry to the clinic (65.2%, n=77). Auditory perceptual abnormalities were the most common type (50.8%, n=60), while visual perceptual abnormalities were also common and reported by 46.6% (n=55) of the subjects. At baseline, 46.6% (n=55) had a depressive disorder, 18.6% (n=22) had an anxiety disorder, 13.6% (n=16) had borderline personality disorder and 6.8% (n=8) had a substance dependence disorder (See Table 2).

[Insert Table 2 here]

Participants who reported perceptual abnormalities at baseline had significantly higher GAF scores than those presenting with other attenuated symptoms or meeting criteria based on trait criteria (GAF 51.0 SD=9 versus GAF 45.9 SD=9.3, p<0.001). This was still the case when those meeting criteria based on trait criteria alone were excluded from the sample (by definition these people need to have a drop in functioning of at least 30% in the previous month), (p=0.01).

Sub-threshold delusional beliefs were the most common attenuated psychotic symptom in the total sample (n=84, 72%), 35% of the sample were found to have at

least one negative symptom (n=41) and at least one symptom of thought disorder was present in 29% of the sample (n=34).

Relationship between psychiatric diagnoses and perceptual abnormalities at baseline

A diagnosis of depressive disorder was associated with a significantly increased odds of reporting any hallucination and particularly visual perceptual abnormalities at entry to the UHR clinic (any hallucination OR 3.59, p=0.004; visual perceptual abnormalities OR 2.36, p=0.02). These findings remained significant when all other co-morbid diagnoses were controlled for. A diagnosis of borderline personality disorder was associated with a significantly increased odds of experiencing auditory perceptual abnormalities at baseline entry to the UHR clinic (OR 3.44, p=0.04). This finding remained significant when all other diagnoses were controlled for. Table 3 shows the associations between psychiatric diagnoses and perceptual abnormalities at baseline.

[Insert Table 3 here]

Relationship between history of childhood adversity and the prevalence of perceptual abnormalities at baseline

A history of childhood trauma was associated with increased odds of experiencing any hallucination (OR 6.30, p=0.000), an auditory perceptual abnormalities (OR 2.57, p=0.02) and visual perceptual abnormalities (OR 2.66, p=0.01) at entry to the UHR clinic (See Table 4). These results remained significant when other perceptual abnormalities were controlled for (OR 2.33, p=0.04; OR 3.00, p=0.01). A history of

childhood bullying was associated with significantly increased odds of reporting any hallucination at baseline (OR 5.00, p=0.01). The finding that childhood bullying was associated with more than a five-fold increased odds of experiencing any hallucination at baseline (OR 5.00, p=0.01; cases n=25, controls n=3) theses results remained significant when we controlled for each hallucinatory type separately i.e. auditory, visual, other (OR 6.94, p=0.01; OR 8.17, p=0.004; OR 5.11, p=0.02).

[Insert Table 4 here]

Relationship between psychiatric diagnoses and content of perceptual abnormalities at baseline entry to UHR clinic

A diagnosis of borderline personality disorder at baseline entry to the UHR clinic was associated with an increased odds of experiencing second person auditory perceptual abnormalities (OR 2.69, p=0.04). (See Table 5)

[Insert Table 5 here]

Relationship between a history of adversity and content of perceptual abnormalities

No association was found between a childhood history of trauma or bullying and hallucinatory content. Nor was an association found between experiencing a psychosocial stressor in the three months prior to onset of attenuated symptoms and the content of auditory perceptual abnormalities (See Table 6).

[Insert Table 6 here]

Conclusions

Principal Findings

Young people meeting criteria for UHR who reported perceptual abnormalities at entry to the UHR clinic differed in several ways from those who did not. They were more likely to be female, to be in employment and to be functioning at a higher level as rated on the GAF. Consistent with our first hypothesis we found that those presenting with perceptual abnormalities at baseline were more likely to have a diagnosis of depressive disorder. Consistent with our second hypothesis those presenting with perceptual abnormalities at baseline were also more likely to have a history of trauma or a history of bullying. Our third hypothesis was not supported as no association was found between trauma and specific hallucinatory content.

Comparison with previous research

Demographics and functioning

The finding that perceptual abnormalities are more common in females is consistent with findings by Sharma et al. (40) in patients with schizophrenia and also with findings by Maric et al. (41) in general population samples (Maric, Krabbendam, Vollebergh, de Graaf, & van Os, 2003; Sharma, Dowd, & Janicak, 1999). The finding that those young people presenting with perceptual abnormalities at entry to the clinic were functioning at a higher level than those meeting UHR criteria in the absence of perceptual abnormalities was initially surprising. However, given the literature on the prevalence of perceptual abnormalities in non help seeking general populations samples, it may be that sub-threshold perceptual abnormalities in a UHR sample are less debilitating than other attenuated psychotic symptoms (Daalman et al., 2011).

Perceptual abnormalities and co-morbid psychiatric diagnosis

The finding that visual perceptual abnormalities were significantly more common in those UHR participants who had a depressive disorder underlies the importance of clinicians enquiring about all forms of perceptual abnormalities at assessment. Traditionally visual perceptual abnormalities have been associated with organic illness (Oyebode, 2014), and while there have been some reports that visual perceptual abnormalities are prevalent in first episode samples (Rajapakse, Garcia-Rosales, Weerawardene, Cotton, & Fraser, 2011), visual perceptual abnormalities remain understudied in clinical and non clinical populations (Sullivan et al., 2014).

The finding that second person auditory perceptual abnormalities were more common in UHR subjects who also had a diagnosis of borderline personality disorder was not unexpected. Auditory perceptual abnormalities in borderline personality disorder appear to be prevalent and phenomenologically similar to those seen in schizophrenia (Slotema et al., 2012).

Perceptual abnormalities and a history of childhood trauma

The percentage of those presenting to the UHR clinic with a history of childhood adversity was high in this study (55.1% reported a history of trauma, 23.1% reported a history of bullying). These rates were consistent with those previously reported from another UHR sample from the same UHR clinic (Bechdolf et al., 2010). The findings that those who reported perceptual abnormalities were higher functioning and female and that those with a history of trauma were more likely to report perceptual abnormalities was difficult to reconcile. However, it may be that these are not entirely

overlapping groups. Not all hallucinations are related to trauma and discriminating between different subgroups is likely to benefit understanding and treatment approaches. Furthermore, not all trauma types are the same. Some types of trauma may be more likely to lead to poorer functioning than others (Yung et al., 2015). However, in this sample we were unable to explore trauma type but further exploration would be warranted.

We found an association between childhood bullying and perceptual abnormalities at baseline in this UHR sample. This is consistent with previous work in non-clinical adolescent population samples that reported a dose-response relationship between childhood bullying and psychotic symptoms (Kelleher et al., 2013).

The finding that a history of childhood adverse events was not found to be associated with specific hallucinatory content was somewhat surprising as previous authors have found a relationship between trauma and content of hallucinatory experiences (A. Thompson et al., 2010; Velthorst et al., 2009). However, the numbers of subjects in some of the subgroups was small and it may be that the study was insufficiently powered to demonstrate a difference between the various content groups.

Strengths and Limitations

The strengths of this study are that it includes a relatively large UHR sample and includes detailed data on the form and content of perceptual abnormalities extracted from comprehensive clinical assessments completed face to face over a number of weeks. However, retrospective studies are associated with particular limitations. All initial assessments at the UHR clinic include a standardised comprehensive clinical interview with a clinical psychologist using a standardised assessment form, followed

by a review by a psychiatrist and completion of the CAARMS instrument. However this was not a research interview where all items were rated and as such, we cannot be certain that data were not subject to bias due to some answers not being recorded systematically in the clinical files. Childhood adversity would routinely be enquired about during an initial assessment at the UHR clinic, however it could be that our methodology has underestimated the true rates of adversity when compared to those studies utilising self-rated scales. The cross-sectional nature of this data does not allow us to draw any inference about the direction of the associations or causation. It should be noted that the findings with regards to perceptual abnormalities and depression or borderline personality disorder are likely limited to those who are also UHR.

Clinical implications

Our findings indicate that in the UHR population certain types of perceptual abnormalities could be understood as markers of a co-morbid non-psychotic disorder. The use of detailed phenomenology of psychotic symptoms may help to shape our understanding of risk in UHR patients.

The finding that childhood trauma was associated with an increased prevalence of perceptual abnormalities at baseline supports the existing literature. However, the finding that a history of childhood bullying was associated with perceptual abnormalities at baseline has not been reported previously in a UHR population and warrants further investigation in a longitudinal study.

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