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# Hallucinations in the Child and Adolescent "Ultra-High Risk" population: A Systematic Review

# Michelangelo Di Luzio<sup>\*,1,0</sup>, Maria Pontillo<sup>1</sup>, Cristina Di Vincenzo<sup>1</sup>, Domenica Bellantoni<sup>1</sup>, Francesco Demaria<sup>1</sup>, and Stefano Vicari<sup>1,2</sup>

<sup>1</sup>Child and Adolescence Neuropsychiatry Unit, Department of Neuroscience, IRCCS "Bambino Gesù" Children's Hospital, Rome, Italy; <sup>2</sup>Department of Life Sciences and Public Health, Università Cattolica del Sacro Cuore, 00168 Rome, Italy

\*To whom correspondence should be addressed; Michelangelo Di Luzio, MD, Child and Adolescence Neuropsychiatry Unit, Department of Neuroscience, IRCCS "Bambino Gesù" Children's Hospital, Piazza Sant'Onofrio 4, 00165, Rome, Italy; tel.: +39-06-6859-2735, fax: +39-06-6859-2450, e-mail: michelangelo.diluzio@opbg.net

Background and Hypothesis. "Ultra-high risk" for psychosis young adults are assumed to be at higher risk of developing a psychotic spectrum disorder. Predominantly, the ultrahigh-risk population is aged 18-35 years, but it may also include younger children and adolescents. Individuals in this population experience psychosis prodromes in the form of attenuated or brief psychotic symptoms (particularly perceptual abnormalities). Albeit diagnosis is made via structured interviews, such measures fail to sufficiently assess the precise form and content of perceptual abnormalities, especially as they manifest in children and adolescents.Study Design. The present study involved a systematic review of the literature on perceptual abnormalities (particularly hallucinations) in ultrahigh-risk children and adolescents. Results. The analysis reviewed five studies and drew conclusions about the perceptual abnormalities (ie, hallucinations) experienced by the study samples, focusing on form, content, and associations with other symptoms. Of note, 2 of the investigated studies suggested a relationship between hallucinations and experiences of childhood trauma. Conclusions. The transition to psychosis and experiences of childhood trauma could correspond to different types of hallucinations in ultrahigh-risk children and adolescents. This knowledge could improve the identification of prodromal states in the young, ultrahigh-risk population.

*Key words:* transition/prodromes/perception/psychosis/UHR/trauma.

#### Introduction

Over the past 20 years, increasing attention has been placed on potential predictive factors of psychotic disorders (eg, schizophrenia). As part of this work, the "ultra-high risk" (UHR) state-also known as the "at-risk mental state" (ARMS) or "clinical high risk" (CHR) state—has been defined as a risk condition for developing full-blown psychosis in young adults.<sup>1-3</sup> UHR individuals manifest typical symptoms of schizophrenia spectrum disorders (eg, thought disorders, perceptual abnormalities) in attenuated or brief forms. In addition, some UHR individuals could have only a genetic risk (first-degree relatives with a psychotic disorder) associated with a decrease in global functioning. Some authors pointed out as even a genetic liability for psychosis can lead to typical gray matter alterations in the brain structure.<sup>4</sup> Accordingly, researchers have developed the Comprehensive Assessment of At-Risk Mental States (CAARMS)<sup>1</sup> and the Structured Interview for Prodromal Symptoms (SIPS)<sup>5</sup> to assess symptoms associated with the UHR state<sup>6,7</sup> and to identify individuals at higher risk of developing a schizophrenia spectrum disorder.

Importantly, both the CAARMS and the SIPS assess changes in perception, with respect to subthreshold hallucinations (in frequency and/or intensity). Hallucinations are "a perception-like experience with the clarity and impact of a true perception but without the external stimulation of the relevant sensory organ."<sup>8</sup> In a true psychotic disorder, hallucinations are not caused by

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psychoactive substances or organic pathologies.<sup>8</sup> In particular, schizophrenia is associated with verbal auditory hallucinations. However, perceptual abnormalities and hallucinations may also be nonspecific, especially when they appear isolated, and several studies have accounted for their presence in even healthy populations or among individuals who do not go on to develop psychotic disorders or require specialist medical assistance—in particular children and adolescents<sup>9–12</sup>

The CAARMS and SIPS items that assess hallucinations (eg, P4 in the SIPS) seem to be not enough specific related to the risk of conversion in psychosis.<sup>13–15</sup> For this reason, it is important to differentiate between perceptual abnormalities of varying forms and with varying contents, in order to improve our understanding of the relationship between specific forms of perceptual abnormalities and other psychotic symptoms and the conversion to psychosis, especially in children and adolescents.

Indeed, the UHR child and adolescent population represent an age group that shows a specific clinical pattern with respect to the adult population.<sup>16-18</sup> Several studies<sup>17,18</sup> have reported that, in addition to attenuated positive symptoms, UHR children and adolescents exhibit several negative symptoms (especially social anhedonia) and significant functional impairment. For these patients, worse global and academic functioning will likely present in the first year,<sup>17</sup> similar to the profile of First-Episode Psychosis (FEP) children and adolescents. Furthermore, UHR states at younger ages showed less specificity in predicting conversion to psychosis.<sup>19–21</sup> In light of the above observations, the aim of this review was to examine the perceptual abnormalities in UHR children and adolescents, with a focus on hallucinations, as these are considered a close approximation of psychotic disorder symptomatology. Such insight would allow us to refine the tools used to identify UHR children and adolescents, and thus improve the early detection of psychosis. Therefore it seems important to deepen this topic as there are few literatures about how prevention in younger people is an important issue in mental health services.

# Methods

#### Search Strategy

We searched PubMed, EMBASE, and PsycINFO for studies published between database inception and January 1, 2022, using the search terms: "High AND risk AND psychosis AND clinical AND child AND adolescent AND hallucination." All members of the research team agreed on the search strategy and contributed to the literature review. The selected articles met the following eligibility criteria: (1) they were original research studies, (2) they included children and young adults with a UHR diagnosis,<sup>3</sup> as assessed by the SIPS or the CAARMS, (3) they applied interviews or questionnaires to assess hallucinations and discriminated between various forms of hallucination (ie, auditory, visual, tactile, somatic, and olfactory), (4) they provided separate data for UHR individuals with at least 2 different types of hallucination, and (5) they assessed children, adolescent and young adults populations with a maximum age of 21 years and mean age of 18 years.

# Eligibility and Study Selection

The following studies were excluded: (1) reviews and metaanalyses (however, the reference lists of these studies were reviewed to identify possible eligible studies that eluded the initial database search) (ie, "Review"), (2) studies that did not assess individuals with a UHR diagnosis (eg, studies that only assessed patients with full-blown psychosis) (ie, "No UHR"), (3) studies that did not assess hallucinations or perceptual abnormalities and did not discriminate between different forms of hallucinations (ie, "No Ha"), (4) studies that assessed a UHR population with an age of 22 years and/or a mean age of 19 years or older (ie, "Adults"), (5) editorials, letters to the editor with no data, opinion articles not supported by data, and surveys of doctor opinions about hallucinations in UHR young adults (ie, "Opinions"), (6) studies with no relation to the subject matter (ie, "Unrelated"), (7) case reports or case series (ie, "Case"), (8) studies that did not provide separate data for UHR subjects versus healthy controls or individuals with other psychiatric diagnoses (ie, "Lumping), (9) protocols and ongoing studies, (10) qualitative studies with no data; (11) surveys or consensus meetings; (12) studies that employed a research design that was inadequate to assess change, and (13) corrections to a previous study (although such corrections were taken into account, where necessary, for the review of the original study).

All authors agreed on the study inclusion and exclusion criteria, which were established through two Delphi rounds. The research was conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines.<sup>22</sup> The online supplementary includes the PRISMA checklist and flowchart, as well as the detailed results and inclusion/ exclusion data (see online supplementary, supplementary figures 1 and 2).

# Data Extraction and Synthesis

Data from the selected articles were extracted and recorded on a standardized spreadsheet. Specifically, the following variables were captured: first author, year of publication, sample size, age of participants, sex ratio (male/female), study design (including the type of interview or questionnaire used to gather details about perceptual abnormalities), and findings regarding the association between perceptual symptomatology and the UHR profile in young adults.

#### Risk of Bias Assessment

To assess the degree of reliability and quality of the review and to critically examine the results of the selected studies, a risk of bias analysis was conducted using the indications and criteria proposed by the Agency for Health Care Research and Quality.<sup>23</sup> The online supplementary set out the criteria for risk of bias assessment. The assessment of biases according to the reported criteria (selection bias, performance bias, detection bias, attrition bias, and reporting bias) has been conducted on each study and a bias level has been identified for each study (low, medium, or high). M. Di Luzio, D. Bellantoni, and C. Di Vincenzo evaluated the studies included independently, the differences in the evaluation were resolved by discussion.

#### Results

#### Search Results

The abovementioned search retrieved an initial set of 35 articles, ranging in publication from May 2000 to November 2021. An additional 11 studies were identified from a review of reference lists, ranging in publication from December 2004 to August 2020. The exclusion criteria led to the rejection of 41 articles, resulting in a final set of 5 articles (table 1)(for each study reason of rejection see online supplementary, supplementary table 1), which ranged in publication from April 2013 to July 2019. All of the included articles were in English, although the non-English language was not established as an exclusionary criterion. The PRISMA flowchart (see Online supplementary, supplementary figure 1) displays the full search results, including the reasons for exclusion, where relevant.

# Overview of the Included Studies

Three of the included studies focused on the relationship between perceptual abnormalities and the risk of developing full-blown psychosis. The remaining 2 studies investigated the link between hallucinations and childhood trauma. The following 2 sub-sections discuss each of these sets of studies, respectively.

Hallucination and the Risk of Developing Full-Blown Psychosis. Niles et al.<sup>24</sup> focused on the role of perceptual abnormalities in the risk of transitioning to full-blown psychosis in 164 UHR individuals with a mean age of 16.7 years. The SIPS was used to assess both the UHR state and perceptual abnormalities, and the P4 score was taken as the original composite, split into 4 sub-scores: Auditory, visual, somatic/tactile, and gustatory/olfactory.

Furthermore, auditory hallucinations were characterized as either verbal auditory hallucinations (AVH) or nonverbal auditory hallucinations (NAVH). UHR outpatients were prospectively assessed at follow-ups (6–24 months) or until conversion to psychosis. The structured clinical interview for the DSM-IV (SCID-IV) was used to diagnose psychosis. The results showed that neither the P4 score nor any of the four sub-scores predicted conversion to psychosis or time to conversion. While the presence of AVH was significant in predicting the transition to psychosis, the presence of NAVH seemed to confer protection against this transition.<sup>24</sup> These data come from 105 APS patients with auditory hallucinations, of these 32 with AVH and 73 with NAVH. 15 of 32 subjects with AVH had a conversion with a conversion rate of 46.9%. Instead in NAVH individuals, only 13 of 73 showed psychosis with a conversion rate of 17.8%. The conversion rate of the total population was 27%.

In 2016, O'Connor et al.25 retrospectively analyzed data for 118 UHR out-patients with a mean age of 18.3 years, using the CAARMS, the Operational Criteria for Psychotic Illness (OPCRIT),<sup>26</sup> and an original audit tool (AT).<sup>25</sup> Both the CAARMS<sup>27,28</sup> and the OPCRIT were used to assess the transition to full-blown psychosis, while the CAARMS, alone, was used to diagnose the UHR state. The AT was used to gather detailed information on participants' hallucinations, with reference to all of the criteria assessed in the OPCRIT as well as additional symptoms related to hallucinatory content.<sup>25</sup> Hallucinations were divided into three subgroups (ie, "any," auditory, and visual) and associated with psychotic symptoms (ie, delusion, thought disorder, ego boundary disorder, negative symptoms, and dissociation) and substance abuse. The authors also evaluated the association between transition to psychosis and each hallucination sub-group, both independently and in conjunction with each psychotic symptom and substance use. For this purpose, the UHR sample was divided into those who ultimately transitioned to psychosis (cases) and those who did not (controls). The results showed that hallucinations, alone, did not significantly lower the risk of transition to psychosis. However, some associations between hallucination and other conditions could reduce the risk of conversion. This "protection" effect comes from the analysis of the hazard ratio for each symptomatology association. Those associations with a significant hazard ratio < 1 were considered as a protective factor to conversion. In this way hallucinations in the absence of thought disorders were significant in reducing this risk. The same was observed for hallucinations without dissociation symptoms or ego boundary disorders. Moreover, visual and auditory hallucinations, alone, seemed unrelated to the risk of psychosis. However visual hallucinations in the absence of drug misuse were associated with a reduced risk of conversion to psychosis.<sup>25</sup>

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et al., <sup>24</sup> [64 ids with UHR Propertive observational study. (Fig. 35) and and field to observational study. (Fig. 36) and an opposite offset for oversion to psychosis. The additory Ph were coded. The Ph modifive characterized or y visu. CHR followed for $6-24$ months or WHH and YS 148. Note of the PH modifive characterized or y visu. CHR followed for $6-24$ months or WHH ( $= 0.00$ ), and an opposite offset for WHH ( $= 0.00$ ), and an opposite offset for WHH ( $= 0.00$ ), and an opposite offset for WHH ( $= 0.00$ ), and an opposite offset for WHH ( $= 0.00$ ), and an opposite offset for WHH ( $= 0.00$ ), and an opposite offset for WHH ( $= 0.00$ ), and an opposite offset for WHH ( $= 0.00$ ), and an opposite offset for WHH ( $= 0.00$ ), and an opposite offset for WHH ( $= 0.00$ ), and an opposite offset for WHH ( $= 0.00$ ), and an opposite offset for WHH ( $= 0.00$ ), and an opposite offset for WHH ( $= 0.00$ ), and an opposite offset for WHH ( $= 0.00$ ), and an opposite offset for WHH ( $= 0.00$ ), and an opposite offset for WHH ( $= 0.00$ ), and an opposite offset for WHH ( $= 0.00$ ), and an opposite offset for WHH ( $= 0.00$ ), and an opposite offset for WHH ( $= 0.00$ ), and an opposite offset for WHH ( $= 0.00$ ). Such a set of the Ph ( $= 0.00$ ), and an opposite offset for WHH ( $= 0.00$ ), and an opposite offset for WHH ( $= 0.00$ ). The set of the Ph ( $= 0.00$ ) and an opposite offset for which were deteriled at the addition opposite offset for the Ph ( $= 0.00$ ). The set of the Ph ( $= 0.00$ ) and an opposite offset for the Ph ( $= 0.00$ ), and an opposite offset for the Ph ( $= 0.00$ ). The set of the Ph ( $= 0.00$ ) and an opposite offset for the Ph ( $= 0.00$ ) and an opposite offset for the Ph ( $= 0.00$ ). The set of the Ph ( $= 0.00$ ) in the monthly addition opposite offset for the Ph ( $= 0.00$ ). The set of the Ph ( $= 0.00$ ) in the monthly the ph ( $= 0.00$ ), and an opposite offset for the Ph ( $= 0.00$ ). The ph ( $= 0.00$ ), and an opposite offset for the Ph ( $= 0.00$ ), and an opposite offset for the Ph ( $= 0.00$ ). The ph ( $= 0.00$ for the Ph ( $= 0.00$	Study	Population	Design	Results	Conclusions/Observations
mpson et120 ids with UHRRetrospective case-control study. asses spycholic symptoms and specif asses spycholic symptom content i =18,3 ± 2.7).None of the PA assessed were significantly assessed symptom content i any symptom content assessed. Any Ha, auditory Ha, auditory Ha, $(P = .50)$ , aditory Ha $(P = .29)$ , hypnagogichypnopompic Ha, visual lilu- spratation precision i unor-affective auditory lilusions. Inp- anorddistortions is visual Ha, tracing and ther Ha (actile somatic, olfactory, gustatory, ormplex).None of the PA assessed were significantly associated with transition to psychosis at uni- any significantly pristal lilusion/distortions ( $P = .00$ ), with $(P = .29)$ , visual lilusion/distortions ( $P = .00$ ), other Ha ( $P = .29$ ), isinal lilusion/distortions ( $P = .00$ ), in co- morbidistortions ( $P = .00$ ), in co- morbidistor and specif.onnor et al. <sup>10</sup> 118 ids with UHR who had transitioned to psychosis and who did not.Pa significantly more in F ( $P = .00$ ), in co- morbidity with depression ( $P = .00$ ), in co- morbidity with depression ( $P = .00$ ), in co- morbidity with depression ( $P = .00$ ), in co- morbidity with depression ( $P = .00$ ), with VPA also common ( $6.6\%$ ).nomor et al. <sup>10</sup> 118 ids with UHR with diperson and specif cases: 59, age $\overline{x} = 18.3 \pm 2.7$ ).Pa significantly more in F ( $P = .00$ ), in co- morbidity with depression ( $P = .00$ ), in co- morbidity with depression ( $P = .00$ ), in co- phy and file. PA and also common ( $\overline{y} = .00$ ), with VPA also common via the rescined with all PA ( $P = .00$ ), in co- to an adviracible of a secociated with all PA ( $P = .00$ ). <td< td=""><td>Niles et al.,<sup>24</sup></td><td>164 ids with UHR (F 66; M 98; age ⊼ =16.7 ± 4.1).</td><td>Prospective observational study. SIPS Separate component ratings for audi- tory, visual, somatic/tactile, and gusta- tory/olfactory PA were coded. Auditory PA is further characterized in AVH and NAVH. CHR followed for 6–24 months or until conversion to psychosis.</td><td>105 ids had auditory Ha, of these 32 had AVH and 73 NVAH. None of the P4 modality component scores significantly predicted days to conversion in the multivariate Cox survival analyses (<math>P &gt; .05</math>). Cox proportional hazards regression demonstrated a significant effect for AVH (<math>P = .004</math>) and an opposite effect for AVH (<math>P = .004</math>) and an opposite effect for NVAH (<math>P = .008</math>). NVAH (<math>P = .008</math>). NOne of the P4 component subscales demonstrated a significant relationship to conversion status in a multivariate regression (<math>P &gt; .05</math>).</td><td>No significant evidence that the SIPS perceptual abnormality (P4) score, taken as the original composite or split into modality-specific sub-scores, predicts conversion to psychosis or time to conversion in a sample of 164 UHR. Significant interaction between audi- tory Ha severity and verbal content, with severity of AVH predicting con- version and the presence of NAVH conferring protection against conver- sion. While hearing voices may indicate increased risk, many types of per- ceptual (auditory or not) abnormal experiences often considered patho- logical may not be so</td></td<>	Niles et al., <sup>24</sup>	164 ids with UHR (F 66; M 98; age ⊼ =16.7 ± 4.1).	Prospective observational study. SIPS Separate component ratings for audi- tory, visual, somatic/tactile, and gusta- tory/olfactory PA were coded. Auditory PA is further characterized in AVH and NAVH. CHR followed for 6–24 months or until conversion to psychosis.	105 ids had auditory Ha, of these 32 had AVH and 73 NVAH. None of the P4 modality component scores significantly predicted days to conversion in the multivariate Cox survival analyses ( $P > .05$ ). Cox proportional hazards regression demonstrated a significant effect for AVH ( $P = .004$ ) and an opposite effect for AVH ( $P = .004$ ) and an opposite effect for NVAH ( $P = .008$ ). NVAH ( $P = .008$ ). NOne of the P4 component subscales demonstrated a significant relationship to conversion status in a multivariate regression ( $P > .05$ ).	No significant evidence that the SIPS perceptual abnormality (P4) score, taken as the original composite or split into modality-specific sub-scores, predicts conversion to psychosis or time to conversion in a sample of 164 UHR. Significant interaction between audi- tory Ha severity and verbal content, with severity of AVH predicting con- version and the presence of NAVH conferring protection against conver- sion. While hearing voices may indicate increased risk, many types of per- ceptual (auditory or not) abnormal experiences often considered patho- logical may not be so
118 ids with UHRNumber of the term of te	Thompson et al. <sup>29</sup>	120 ids with UHR (F 71; M 49; age $\bar{x}$ =18.3 ± 2.7). Cases 60, Controls 60.	Retrospective case-control study. An auditing tool was developed to assess psychotic symptoms and specif- ically symptom content. Separate perceptual abnormalities assessed: Any Ha, auditory Ha, non-affective auditory illusions, hyp- nagogic/hypnopompic Ha, visual illu- sion/distortions, visual Ha, other Ha (tactile, somatic, olfactory, gustatory, complex). Retrospective study differentiating ids who had transitioned to psychosis and who did rot	None of the PA assessed were significantly associated with transition to psychosis at uni- variate analysis. Any Ha ( $P = .56$ ), auditory Ha ( $P = .52$ ), non-affective auditory illusions ( $P = .17$ ), hypnagogic/hypnopompic Ha ( $P = .29$ ), visual illusion/distortions ( $P = .15$ ), visual Ha ( $P = 1.0$ ), other Ha ( $P = .63$ ).	None of the PA assessed were signif- icantly associated with transition to psychosis.
	O' Connor et al. <sup>30</sup>	118 ids with UHR (F 69; M 49; age x̄ =18.3 ± 2.7). Cases:59, Controls:59.	who during tool was developed to An auditing tool was developed to assess psychotic symptoms and specif- ically symptom content. PA were divided into: all PA, APA, VPA, and "other" PA (tactile, olfac- tory, somatic, gustatory). In addition, verbal APA were divided into: abu- sive, second-person, third person and command. Logistic regression analysis was used to assess association between comorbid diagnosis or an adverse event and PA variables.	PA significantly more in F ( $P = .001$ ), in comorbidity with depression ( $P .004$ ) and in employment ( $P = .001$ ). APA most common type ( $50.8\%$ ) with VPA also common ( $46.6\%$ ). PA iso common ( $46.6\%$ ). PA iso common ( $46.6\%$ ). DD is associated with higher GAF scores ( $P = .001$ ). DD is associated with APA ( $P = .004$ ) and in particular with VPA ( $P = .02$ ). BPD associated with APA ( $P = .02$ ). Childhood trauma associated with all PA ( $P = .02$ ). Childhood bullying is associated with all PA ( $P = .02$ ). Childhood bullying is associated with all PA ( $P = .01$ ).	UHR with PA are mostly F, in em- ployment and with higher GAF. UHR with PA have more DD and have a history of trauma or a history of bullying. No association was found between trauma and specific hallucinatory content.

Table 1. Summary of Included Studies

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Study	Population	Design	Results	Conclusions/Observations
O'Connor et al. <sup>25</sup>	118 ids with UHR (F 69; M 49; age x̄ =18.3 ± 2.7). Cases:59, Controls:59	Retrospective case-control study. An auditing tool was developed to assess psychotic symptoms and specif- ically symptom content. Ha is divided into any Ha, audi- tory Ha, visual Ha, and associated or not with different psychotic symptoms (delusion, thought dis- order, ego boundary disorder, negative symptoms, dissociation) or substance use.	BPD associated with second-person APA ( $P = .04$ ). No association between a childhood history of trauma or bullying and hallucinatory content (all $P > .1$ ). At univariate analysis, Ha alone at baseline are not associated with a reduced risk of transition to psychosis ( $P = .67$ ). Any Ha and no dissociation ( $P = .03$ ), visual Ha with no ego boundary disorder ( $P = .044$ ), and visual Ha with no substance use ( $P = .045$ ) were associated with a reduced risk of transition to psychosis (hazard ratio < 1). At multivariate analysis, Ha without any thought disorder ( $P = .045$ ) were associated with a reduced risk of transition to psychosis ( $P = .045$ ) were associated with a reduced risk of transition to psychosis. The multivariate analysis, ha without any thought disorder ( $P = .045$ ) were associated with a reduced risk of transition to psychosis.	UHR ids who present with Ha alone were not found to be at significantly lower risk of transition to psychosis. Ha in the absence of thought disorder reduces the risk of transition to psy- chosis by around 40%. Individual forms of Ha (eg, auditory and visual) in isolation may not be associated with increased or reduced risk of transition to psychosis. Visual Ha in the absence of sub- stance use were associated with a 55%
Velthorst et al. <sup>31</sup>	127 ids with UHR (F 74;M 53; age x̄ =18.2 ± 2.7).	Retrospective case-control study. An auditing tool was developed to assess psychotic symptoms and specif- ically symptom content. Relationship between Ha form and content and trauma [physical abuse, sexual abuse, emotional abuse and neglect and other (ie, verbal abuse, domestic violence, witnessing of shooting, watching someone suicide, death of a close relative/friend, car ac- cident, severe physical injury)]	Higher PA intensity in history of phys- ical abuse ( $P = .023$ ) and of "others" abuse ( $P = .007$ ) but physical abuse was no longer significant when other types of trauma were adjusted for, instead "others" abuse remains significant ( $P = .039$ ). No significant difference with respect to audi- tory Ha. Instead, visual Ha linked with physical abuse ( $P = .02$ ) but this association was no longer significant after adjusting for other types of trauma ( $P = .07$ ). Sexual trauma associated with PA with abusive content ( $P = .008$ ). This as- sociation remains significant after adjustment for other types of trauma ( $P = .02$ ).	psychosis. Small but significant associations were found between a history of partic- ular types of trauma and intensity of attenuated psychotic symptoms. Spe- cifically, having experienced physical abuse or an "other type" of trauma during childhood was associated with a higher intensity of PA although the physical abuse association must be considered cautiously. Stronger association between physical abuse and visual as opposed to audi- tory Ha.

At-Risk Mental States; DD, depressive disorder; F, females; GAF, global assessment of functioning; Ha, hallucination/s; ids, individuals; M, males; NAVH, non-verbal auditory hallucinations; OPCRIT, Operational Criteria for Psychotic Illness; PA, perceptual abnormalities; P4, fourth positive symptoms item of the SOPS; SIPS, Structured Interview for Psychosis-risk Syndromes;  $\bar{x}$ , mean age; UHR, ultrahigh risk for psychosis; VPA, visual perceptual abnormalities.

In 2013, Thompson et al.<sup>29</sup> addressed psychosis conversion risk in young UHR outpatients, using the CAARMS to assess UHR state. They divided the sample into those who ultimately developed a frank psychotic illness and those who did not (ie, controls). Both the CAARMS and the OPCRIT were used to diagnose psychosis. The AT developed by O'Connor et al. in 2016<sup>25</sup> was used to assess hallucinations. The authors retrospectively assessed 120 UHR subjects (mean age 18.3 years) presenting with a range of perceptual abnormalities, including: Any hallucinations, auditory hallucinations, non-affective auditory illusions, hypnagogic/hypnopompic hallucinations, visual illusion/distortions, visual hallucinations, and "other" hallucinations (ie, tactile, somatic, olfactory, gustatory, and complex). The statistical analyses showed that none of the perceptual abnormalities were significantly associated with transition to psychosis.<sup>29</sup>

Hallucinations and Trauma. In 2017, O'Connor et al.<sup>30</sup> retrospectively observed the correlations between a history of childhood trauma, perceptual abnormality variables, and comorbid conditions in a sample of 118 UHR outpatients with a mean age of 18.3 years. The CAARMS was used to diagnose the UHR state. The authors divided the UHR sample into a case group of participants who ultimately transitioned to psychosis and a control group who did not (according to the CAARMS). An AT was applied to measure perceptual abnormalities<sup>25</sup> in the following categories: "any," auditory, visual, and "other" (ie, tactile, olfactory, somatic, and gustatory). In addition, the authors differentiated between abusive, second-person, third-person, and command verbal auditory hallucinations. The logistic regression analysis showed that visual perceptual abnormalities were associated with depressive disorder, while auditory hallucinations were mainly linked to borderline personality disorder. Childhood trauma was significantly associated with perceptual abnormalities, in general, and visual and auditory hallucinations, specifically; however, childhood bullying was only associated with perceptual abnormalities, in general. No association was found between specific verbal hallucinatory contents and trauma, and only borderline personality disorder emerged as correlated with second-person verbal auditory hallucinations.<sup>30</sup>

Finally, Velthorst et al.<sup>31</sup> retrospectively assessed 127 UHR outpatients with a mean age of 18.2 years. Participants were divided into control and case groups, depending on whether or not they ultimately transitioned to psychosis. The CAARMS was used to assess both the UHR state and the transition to full-blown psychosis. An AT<sup>25</sup> was applied to investigate the relationship between hallucination form and content and different types of trauma (ie, physical abuse, sexual abuse, emotional abuse and neglect, "other" [ie, verbal abuse, domestic violence, witnessing a shooting, witnessing a suicide, death of a close relative/friend, car accident, and severe physical injury]). The AT assessed childhood trauma using multiple items related to the abovementioned subcategories. The results showed a small but significant association between childhood physical abuse or "other" trauma and higher-intensity perceptual abnormalities; however, the association with physical abuse should be considered with caution. Furthermore, relative to auditory hallucinations, visual hallucinations were found to be more strongly correlated with physical abuse. Finally, perceptual abnormalities with abusive content emerged as associated with sexual trauma.<sup>31</sup>

# Reliability and Quality of Included Studies

Four studies were classified as having medium levels of risk of bias while only one was considered with a low presence of bias. A table with a summary of the risk of bias assessment for each study is reported in the Online supplementary materials (Online supplementary table 2). The main possible biases reported were about the selection and the detection bias. In particular, most of the studies have a medium risk of bias level because of the retrospective study design. Albeit these retrospective studies<sup>25,29-31</sup> satisfied majority of the criteria for risk of bias assessment. Main concerns about their methodology were about the not complete blindness of research assistants with respect to conversion status and the retrospective extraction of data from the initial clinical assessment. Moreover, in these studies, the auditing tool developed by the authors was considered as a possible source of bias because it is not a tool validated by scientific literature. However, this tool was developed by a research group of authors expert in UHR subjects evaluation, and that significantly contributed to the definition of UHR criteria.<sup>1,32</sup> The only one study classified with a low risk of bias<sup>24</sup> shows a good satisfaction of risk of bias criteria. Nevertheless, we point out a possible bias in selecting only UHR subjects with attenuated psychotic syndrome (APS) and the retrospective collection of severity scores for perceptual modalities. In general, the review shows a medium quality of evidence. However main limitations to quality evidence come from the small number of included studies and the overlap between the assessed populations, rather than the risk of bias of examined studies.

# Discussion

# Hallucinatory Symptoms

The present research found that the relationship between hallucinations and the risk of conversion to psychosis in UHR children and adolescents is not unique. In general, hallucinations do not appear to be significantly correlated with the risk of developing psychosis, even when hallucinatory subgroups are considered (ie, auditory, visual, tactile, olfactory, gustative, and somatic).<sup>24,25,29</sup> Rather, significant

correlations with the risk of transitioning to psychosis only emerge with more complex characterizations of symptomology. Specifically, it appears that hallucinations without an associated thought disorder or the presence of nonverbal auditory hallucinations are less suggestive of the transition to psychosis.<sup>24,25</sup> Furthermore, only auditory hallucinations with verbal content appear to be associated with a higher risk of psychosis development.<sup>24</sup> In examining these studies it must be said that the samples have a medium size and the time of follow-up may be a limitation. However, these issues are common problems in studies about the risk of conversion. For example, the time of follow-up is aligned with similar studies on this topic.<sup>3</sup> The studies with a retrospective design have many limitations, as pointed out in the risk of bias assessment, but show a longer observational time of follow-up. The "others" perceptual abnormalities as the tactile/somatic or the olfactory appear to be less reported. In particular when there is no association with auditory or visual abnormalities. However, these kinds of hallucinations have to be deepened in the UHR young population as they seem to be relevant in psychotic disorders. The somatic/tactile ones especially.<sup>32,33</sup> Nevertheless the findings are partly aligned with the results of studies involving older samples (mean age 19-21 years), which have found auditory-rather than visual-hallucinations to be more predictive of conversion to psychosis.<sup>14,34</sup> Additionally in two included studies<sup>24,25</sup> emerges an interesting data: Some types of hallucinations could be protective against conversion to psychosis. This result is understandable if we reflect on what will be said later about hallucinations as alterations of thought. In fact, hallucinations could be significant for a risk of psychosis only if present as an alteration of thought (eg. auditory with a verbal content) and therefore associated with other thought-disorder symptoms. The literature on psychotic disorders (especially schizophrenia) shows that the most characteristic hallucinations are auditory verbal (eg, voices dialoguing, commenting, or presenting imperatives), which are more associated with thought disorders (eg, disorganization or delusions), rather than visual. Consequently, changes in perception in the absence of thought disturbances—or with visual or auditory but non-verbal hallucinationsdo not appear to be typical manifestations of a schizophrenia spectrum disorder.<sup>35</sup> Therefore, the classification of hallucinations could be improved by differentiating perceptual abnormalities according to form and content, and thereby identifying some as more significant (eg, verbal auditory hallucinations)-even if attenuated or brief—in predicting conversion to psychosis. In addition, as the (non-)association between hallucinations and other psychotic-like symptoms seems important,<sup>25</sup> diagnostic weight should be given to not only specific hallucinatory symptoms, but also the cooccurrence of symptoms. In fact, the delineation of detailed "constellations" of symptoms may increase our ability to recognize at-risk

children and adolescents and provide more targeted psychiatric care.  $^{13,36}$ 

The investigated studies also examined the correlation between positive psychotic symptoms (ie, hallucinations) and childhood trauma. While the findings were heterogeneous, 2 studies suggest an association between perceptual abnormalities and trauma.<sup>30,31</sup> However these results are gathered on a small population and need to be confirmed on larger samples. Indeed no one of the trauma sub-groups overcome the number of 52 subjects. In particular, in Velthorst<sup>31</sup> the group with sexual trauma was composed of 26 individuals, and the one with physical abuse of 35. While in O'Connor<sup>30</sup> the group with a history of trauma was composed of 52 individuals but there was no further sub-group classification of trauma and the characterization of perceptual abnormalities is not deepened.

Although our results about trauma are poor, there is extensive literature associating childhood trauma with the development of psychotic disorders,<sup>37–39</sup> as well as with APS and the UHR state,<sup>40-42</sup> for a meta-analysis see: Kraan, T. et al..43 Specifically some studies confirmed the association between a history of childhood trauma and higher perceptual abnormalities on psychotic patients, 44,45 while others do not clearly delineate this relationship in UHR young adults.41,42 Moreover results remain nonunique also focusing on form and content of perceptual abnormalities in presence of history of trauma. In some studies noted as the history of trauma, in early psychotic patients, could promote the onset of visual hallucinations<sup>46</sup>rather than verbal auditory hallucinations<sup>47</sup> or specific contents in auditory hallucinations.<sup>30</sup> However a study by Begemann and colleagues<sup>48</sup> shows a great presence of malignant/omnipotence AVH in psychotic patients with multiple traumas. This latter interesting data, beyond their heterogeneity, could suggest the cooccurence of PTSD and psychotic symptoms in patients with childhood trauma. The comorbidity could lead to an increase in "visual symptoms" as a flashback or in abusive egodystonic thoughts that can be confused with hallucinations or could manifest as mixed symptomatology. Only one study has explored comorbidities with hallucinations in a UHR population, finding that visual hallucinations are associated with depressive disorder, while auditory (and specifically verbal) hallucinations in the second person are associated with borderline personality disorder.<sup>30</sup>

A deeper understanding of the relationship between childhood trauma and hallucinations of varying types (with respect to form and content) could improve our characterization and differentiation of UHR individuals. The present results suggest that with further studies it may be possible to discriminate between hallucinations that emerge from a history of childhood trauma versus those that arise from the progressive evolution of a psychotic disorder, according to their form and content. Specifically, we hypothesize that auditory verbal hallucinations in conjunction with thought disorders may suggest progression toward a psychotic disorder, while isolated visual hallucinations could suggest other conditions. Further studies need to define if visual hallucinations could be related to a history of childhood trauma and if specific contents are linked with a specific type of trauma. However, this framework should be applied with caution, as a history of trauma and the transition to psychosis appear to be correlated, as previously described.

# Auditory hallucinations

In recent years, much work has been done to define the at-risk condition for psychosis among children and adolescents.<sup>1-3</sup> However, some of the inclusion criteria that have been developed seem insufficiently specific (eg, perceptual abnormalities, in general). For this reason, it is critical to improving our understanding of the specific forms and contents of hallucinations that are most indicative of a risk of developing psychosis. Phenomenologically, hallucinations may differ significantly, and their forms and contents may shed important light on patients' altered states of consciousness, thought processes, and perceptions of self versus others. Hallucinations-and especially verbal auditory hallucinations-suggest an altered experience as a firstperson subject and disturbed thought agency and ownership, leading to the objectification and externalization of thoughts in the form of "audible" voices. 49,50 For this reason, verbal auditory hallucinations may be more significantly associated with schizophrenia and qualitatively different from other types of perceptual abnormalities. To confirm these hypotheses, further research is needed to investigate whether UHR individuals who develop psychosis have more visual, auditory, or other hallucinations. With respect to auditory hallucinations, specifically, research should explore whether these hallucinations tend to include verbal commenting or dialoguing content; whether the voices address the subject in the first, second, or third person; whether they have abusive or grandiose content; and whether these characteristics are associated with other factors that predict psychosis (eg. an altered state of consciousness, an altered sense of self and agency, disorganized thought, bizarre thought, ideas of reference or influence, blocked thought, etc.). Finally, research should attempt to uncover how such prodrome symptoms interact with comorbid conditions, as well as with trauma. In particular, such research should be directed at the younger population, which experiences a higher frequency of perceptual abnormalities than the adult population, though not always with pathological significance.<sup>12,51</sup> In fact, the population of children and adolescents with UHR status shows particular characteristics compared to adults. There are few studies on this issue but some have pointed out that in general, psychotic symptomatology in juvenile age shows a low specificity in predicting conversion into full-blown psychosis.<sup>19,20</sup>

# Limitations and Strengths

To the best of our knowledge, the present study was the first to review the literature on hallucinations among UHR children and adolescents and summarize the results in a systematic way. However, there are several limitations of the research. First, only a small number of studies meet the inclusion criteria of our review and none of the studies included focused on only the child population. Indeed, the age of individuals was heterogeneous including young adults. Second, the included studies did not assess the presence of neurodevelopment disorders that could represent a trait of vulnerability, especially in the child UHR population. Third, the assessment of hallucinations was quite homogeneous across the investigated studies: almost all of the studies utilized the CAARMS as a diagnostic tool, while only one assessed subjects using the SIPS. Of note, almost all of the investigated studies classified perceptual disturbances using the same assessment tool, which characterized the form and content of participants' hallucinations. However, all of the studies utilized the same theoretical basis and approach to the subject, which generated coherence in the results even if there is an overlapping in assessed populations. In fact, the investigated studies focused on only two variables linked to hallucinations in young UHR: the presence of childhood trauma and the risk of transition to psychosis.

# Conclusions

The present review contributes to clarifying and discriminating between the multiform manifestations of hallucinations in children and adolescents at ultrahigh risk of developing a psychotic spectrum disorder. While the number of relevant studies was limited and none was found specifically focused on the child population, the results suggest a preliminary framework for further research, with the aim of defining a more precise UHR profile and thereby improving diagnostic tools-particularly for the younger population. Briefly, we have a main message emerging from wanting to emphasize this paper. The actual assessment of hallucinations in juvenile UHR state is not enough reliable, a more accurate clinical differentiation of perceptual abnormalities is necessary. Such research is critically needed to help clinicians develop effective treatment plans for UHR children and adolescents, tailored to their specific symptomatology.

# **Supplementary Material**

Supplementary data are available at *Schizophrenia Bulletin Open* online.

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