

Course of auditory vocal hallucinations in childhood: 11-year follow-up study

Bartels-Velthuis AA, Wigman JTW, Jenner JA, Bruggeman R, van Os J. Course of auditory vocal hallucinations in childhood: 11-year follow-up study.

Objective: Childhood auditory vocal hallucinations (AVH) are mostly transient but may predict clinical outcomes. Little is known about their course over time and associations with risk factors, and how this may inform early intervention. Our objective was to assess the 11-year course of AVH, associated psychopathology and risk factors.

Method: A 5-year (T1) and 11-year (T2) follow-up of a baseline case–control sample ($n = 694$, of whom 347 with AVH). At T2, online assessment of AVH, other psychotic experiences, psychopathology, trauma and cannabis use was completed by 293 adolescents aged 18–19 years.

Results: The AVH 6-year (T1–T2) persistence rate was 18.2%, and the AVH 11-year (T0–T2) persistence rate was 6.2%. AVH at T2 were associated with higher levels of T2 other psychotic experiences, T2 psychopathology and T2 traumatic events, but not with T2 stress or T2 cannabis use. Persistence of AVH (i.e. AVH reported two or three times from T0) was associated with T2 traumatic events and higher risk for post-traumatic stress disorder.

Conclusion: Auditory vocal hallucinations in early childhood are mostly transitory. AVH in adolescence, especially when persistent, are associated with affective symptoms and environmental risk, particularly traumatic events.

**A. A. Bartels-Velthuis¹,
J. T. W. Wigman¹, J. A. Jenner²,
R. Bruggeman¹, J. van Os^{3,4}**

¹University of Groningen, University Medical Center Groningen, University Center for Psychiatry, Groningen, ²Jenner Consult, Haren, ³Maastricht University Medical Centre, Department of Psychiatry and Psychology, Maastricht, the Netherlands and ⁴King's College London, King's Health Partners, Department of Psychosis Studies, Institute of Psychiatry, London, UK

Key words: trauma; psychoses; affective disorders; early intervention

Agna A. Bartels-Velthuis, University Center for Psychiatry, University Medical Center Groningen, University of Groningen, PO Box 30001 (CC72), 9700 RB Groningen, the Netherlands. E-mail: a.a.bartels@umcg.nl

Accepted for publication February 22, 2016

Significant outcomes

- Childhood auditory hallucinations are transient in most cases.
- Persistence of auditory hallucinations is associated with affective symptoms and higher risk for post-traumatic stress disorder.
- Large-scale programmes for early auditory vocal hallucinations detection are not recommended.

Limitations

- Not all children of the baseline case–control sample could be included in the follow-up studies (47.3% at 11-year follow-up).
- At baseline, only behaviour (as measured with the Child Behaviour Checklist) was included as possible predictor variable.
- The participants were not assessed on healthcare consumption.

Introduction

Subclinical psychotic experiences such as auditory vocal hallucinations (AVH) are prevalent in children, adolescents and adults in the general popula-

tion outside the context of a clinical disorder (1, 2). These experiences may predict a range of mental health problems in addition to later psychotic conditions. In a representative general population survey of 11- and 12-year-olds in Denmark (3), the

majority of children with psychotic experiences either had a diagnosable DSM-IV mental disorder (31.4%) or self-reported mental health difficulties in the absence of a diagnosis (31.4%). These data suggest AVH may represent a transdiagnostic dimension (4) and that psychotic symptoms are important risk markers for a wide range of later non-psychotic disorders (5). Another study (6) found that those with psychotic experiences at age 11 had an increased risk of developing schizophrenia or other psychiatric disorders by 38 years of age. A systematic review (7) showed that poorer outcome of hallucinatory experiences is associated with severity of the experiences, presence of comorbid psychopathology and poorer level of functioning.

Although the majority of developmental psychotic experiences is transient in nature, meta-analyses (2, 8) suggest that their persistence is a risk factor for developing psychotic and non-psychotic disorders. Besides, it was demonstrated that those with persisting psychotic experiences from the age of 12 years were 12.6 times more likely to have a psychotic disorder at age 18 (9). Greater persistence of psychotic experiences in adolescents from the general population was shown to predict risk for transition to a clinical psychosis state 8.4 years later in a dose–response fashion (10). Similarly, persistence of AVH was related to 2-year follow-up delusional ideation, depressed mood and general psychopathology (11, 12), whereas a cohort study in children showed an association between persistent psychotic experiences and later internalizing and externalizing psychopathology (12).

Onset and persistence of psychotic experiences is associated with exposure to environmental risk factors (2) including early childhood adversity (13, 14), bullying (15) and cannabis use (2).

Therefore, it is important to determine the impact of childhood AVH on the development of later mental disorder and to map possible triggering conditions, such as persistence of experiences and exposure to trauma and cannabis use, as this may inform early intervention strategies.

Aims of the study

The aim of this study was to assess incidence and persistence of auditory vocal hallucinations (AVH) in a Dutch case–control sample of 7- and 8-year-old children after a follow-up period of 11 years and to examine associations of AVH with non-psychotic psychopathology including depression, anxiety and stress, and with well-known risk factors such as traumatic events and cannabis use.

Material and methods

Participants and procedure

Adolescents pertaining to the original case–control sample with and without AVH of the baseline (T0) assessment ($N = 694$) (16) were invited to participate in the second follow-up (T2), 11 years later. To obtain their collaboration, a newsletter with the results of the baseline and first (5-year) follow-up (T1) assessment was sent to all baseline participants and (separately) to their parents, together with a reply card to obtain their email addresses, facilitating correspondence about participation. Non-responders were sent a second request by letter. In case of persisting non-response, trained research assistants tried to get in touch with participants or their relatives by telephone in order to explain the study and, if people consented to this, to obtain email addresses.

In total, 362 adolescents agreed to participate in the study and disclosed their email addresses, after which they were sent an information letter and consent form, together with a stamped envelope. The 293 participants who provided informed consent were sent an email with a link to the questionnaires. After completion of the online assessment, a gift voucher was sent by mail. Figure 1 depicts the flow chart of the inclusion process. The study was approved by the Medical Ethical Committee of the University Medical Center Groningen, the Netherlands (ABR number NL42619.042.12).

Design

At the University Center for Psychiatry (UCP, Groningen, the Netherlands), an application for online data collection was developed, denoted as RoQua (www.roqua.nl). Data are stored in the UCP Data Warehouse according to strict database management regulations of the University Medical Center Groningen, and researchers have access only to anonymous data.

Measures

At the web-based assessment, participants were first screened on the experience of hearing voices in the past six years, using the following question ‘In the past six years, did you hear one or more voices that only you could hear?’. Participants with AVH were asked to complete the AVHRS-Q (17), the self-report version of the 16-item Auditory Vocal Hallucination Rating Scale interview (AVHRS) (18). The AVHRS-Q measures characteristics of AVH [i.e. voices speaking separately or simultaneously,

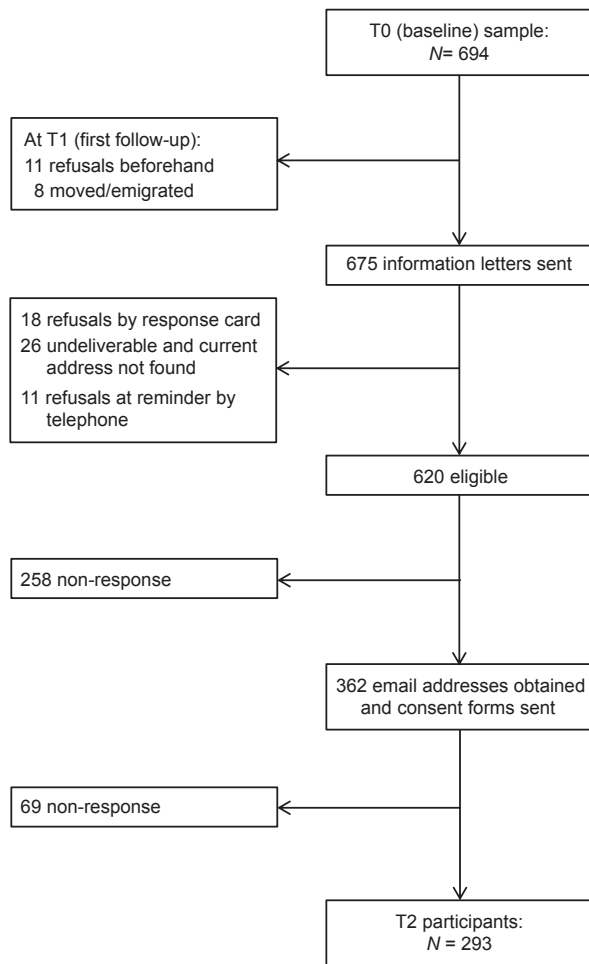


Fig. 1. Flow chart of the inclusion.

frequency, duration, location, form of address, loudness, (severity of) negative content, anxiety, interference with daily life and with thinking, control, attribution, frequency and intensity of distress or suffering]. Psychometric properties of the AVHRS are good (19). Psychometric properties of the AVHRS-Q have not been established yet, but preliminary examination of the concurrent validity of the AVHRS-Q in 27 adult patients of the Psychosis Department of the University Medical Center Groningen revealed a correlation of 0.88 between the severity indices computed from both measures. Cronbach's alpha of the AVHRS-Q in this study was good ($\alpha = 0.89$).

All participants completed several other questionnaires. A separate sociodemographic questionnaire contained items about present educational level, study, employment, having a partner and living situation.

Subclinical psychotic experiences were assessed with the 42-item Community Assessment of Psychotic Experience (CAPE) (20), covering three dimensions (positive, negative and depressive). The

CAPE measures both frequency and distress of the experiences. Frequency and distress scores range from 1 ('absent', respectively, 'no distress') to 4 ('almost always', respectively, 'much distress') (20). The distress dimension is only reported when participants endorse the frequency dimension of the item. To assess associations with delusional ideation, frequencies of the delusion-items from the positive subscale were dichotomized (0 'no delusions reported' and 1 'at least one delusion reported'). The internal consistency of the CAPE frequency items in this study was good ($\alpha = 0.90$).

Symptoms of anxiety, depression and stress were examined with the 21-item Depression, Anxiety and Stress Scale [DASS-21 (21); Dutch translation: De Beurs et al. (22)]. Each subscale contains seven items. For comparability with the 42-item DASS, scores were multiplied by 2 in accordance with Lovibond and Lovibond (21). Reliability of the DASS-21 in this study was good ($\alpha = 0.90$).

Traumatic and stressful events were assessed with the Trauma Screening Questionnaire (TSQ) (23). Eight predefined events were presented (i.e. performing sexual acts against one's will, bodily harm, mental/emotional cruelty, long-term neglect, having experienced a psychotic episode, having witnessed a disaster, war or accident, death of parents, being bullied); respondent could also rate the item 'other event', with scoring options 0 = 'not experienced', 1 = 'once' and 2 = 'more than once'. Ten items from the TSQ rated the person's subjective reactions to traumatic events in the past week, that is five re-experiencing symptoms and five hyperarousal symptoms (e.g. upsetting dreams about the event, bodily reactions, sleep problems, outbursts of anger), with scores 0 = 'no or <twice in the past week' and 1 = 'yes, at least twice in the past week'. A total score of five or more on the subjective reactions scale is considered a risk factor for developing post-traumatic stress disorder (PTSD) (24). In this study, the scale's reliability was adequate ($\alpha = 0.76$).

Substance use was examined with a 22-item self-report questionnaire about use of tobacco, alcohol, cannabis and other substances (based on the Composite International Diagnostic Interview; CIDI) (25). In the analyses, a subset of items from the CIDI was used, namely four items about cannabis use ('no/yes' ever, past year and age at first use).

At T0, parents had completed the Child Behaviour Checklist (CBCL) (26) for children aged 4–18 years. This self-report questionnaire has 113 questions, grouped into nine syndrome scales of behavioural, social and physical functioning: social withdrawal, somatic complaints, anxious/depressed, social problems, thought problems,

attention problems, rule-breaking behaviour, aggressive behaviour and sexuality. Items are rated on a 3-point scale (0, not true; 1, somewhat or sometimes true; 2, very or often true). The reliability of the CBCL in our baseline study was good ($\alpha = 0.94$).

Statistical analysis

Analyses were carried out using the software package IBM SPSS Statistics version 23 (IBM Corp., Armonk, NY, USA). Consistent with baseline analysis (16), an AVH severity index was computed by recoding item scores to 0 = 'none or mild consequences' vs. 1 = 'considerable to severe consequences'. Consistent with previous analyses (16, 27), the item on hypnagogic and hypnopompic hallucinations was not included in the calculation of AVH severity. Based on the validation study of the AVHRS, the item on 'localization of the voices' was not included in the severity index (19). Based on this index, two groups were defined: a 'severe AVH' group (those scoring ≥ 5) and a 'mild AVH' group (scores < 5). The scores on the variables 'educational level' and 'living situation' were dichotomized into 'high/low' and 'alone/with others' respectively. A variable 'number of times reporting AVH' was created to examine differences between the groups. Logistic and multinomial regression analyses were performed to calculate odds ratios with 95% confidence intervals. The CBCL was completed by 423 parents. To facilitate the use of these data in the complete T2 sample, a multiple imputation procedure was carried out on the T0 dataset, assuming the missing cases ($N = 271$) were missing at random. Missing values for the CBCL were imputed 10 times.

Results

Sample characteristics

In total, 293 participants (57.7% female) completed the online assessment at T2. Mean age of the participants was 18.9 years ($SD = 0.40$, range 18.0–20.1). Mean interval between T0 and T2 was 10.9 years ($SD = 0.23$, range 10.4–11.6). The participation of baseline cases and controls was evenly distributed (145 cases vs. 148 controls; $\chi^2_1 = 0.05$; $P = 0.82$). The participation rate (compared with T0) of females, compared with males, was higher (57.3% vs. 42.7%; $\chi^2_1 = 12.2$; $P = 0.000$). Non-participants had significantly higher T0 CBCL total scores than those participating at T2 (24.9 vs. 21.8; $t = 2.59$, $P = 0.01$). The sample included 88 participants who were not interviewed at T1, evenly dis-

tributed over baseline cases ($N = 43$) and controls ($N = 45$). Of the 205 children who participated at all three assessments, 102 reported AVH at T0 and 103 were control children at T0. There was one participant whose AVH had remitted by T1, but who experienced an AVH relapse from T1 to T2. A flow chart of follow-up participation ($N = 293$) with respect to cases and controls is presented in Fig. 2.

In Table 1, demographic data and outcome of the participants are presented by AVH follow-up status.

AVH persistence and incidence rates (T0–T2 and T1–T2)

In the T2 sample, the AVH 6-year (T1–T2) persistence rate was 18.2% $[(3 + 3)/(21 + 6 + 3 + 3)]$ and the AVH 11-year (T0–T2) persistence rate (including those who did not participate in T1) was 6.2% $[(5 + 3 + 1)/(38 + 77 + 21 + 5 + 1 + 3)]$. The AVH incidence rate for T1–T2 was 2.1% $[2/(92 + 2)]$, and for T0–T2 (excluding those who had remitted at T1), this was 2.2% $[(2 + 1)/(92 + 44 + 2 + 1)]$ (see Fig. 2).

AVH and sociodemographic characteristics at T2

T2 participants with and without AVH did not differ in sociodemographic characteristics (see Table 1).

AVH and psychopathology at T2

T2 participants with AVH had higher CAPE scores for all three dimensions (positive, negative and depressive) on both frequency and distress than participants without AVH. This was not the case for the positive subscale delusional ideation. AVH were associated with higher levels of depression and anxiety, but not stress, indexed by the DASS-21.

AVH and risk factors at T2

Auditory vocal hallucinations were associated with both the reported frequency of T2 traumatic events and the concomitant distress. The proportion of participants at risk for PTSD was significantly higher in those with AVH compared with those without AVH. Cannabis use in the past year was not significantly associated with AVH (OR = 2.02, 95% CI: 0.69–5.88).

AVH severity at T2

Of the 15 participants with AVH at T2, nine scored 'mild' on the severity index, vs. six 'severe'. Participants with severe AVH at T0 were not more likely

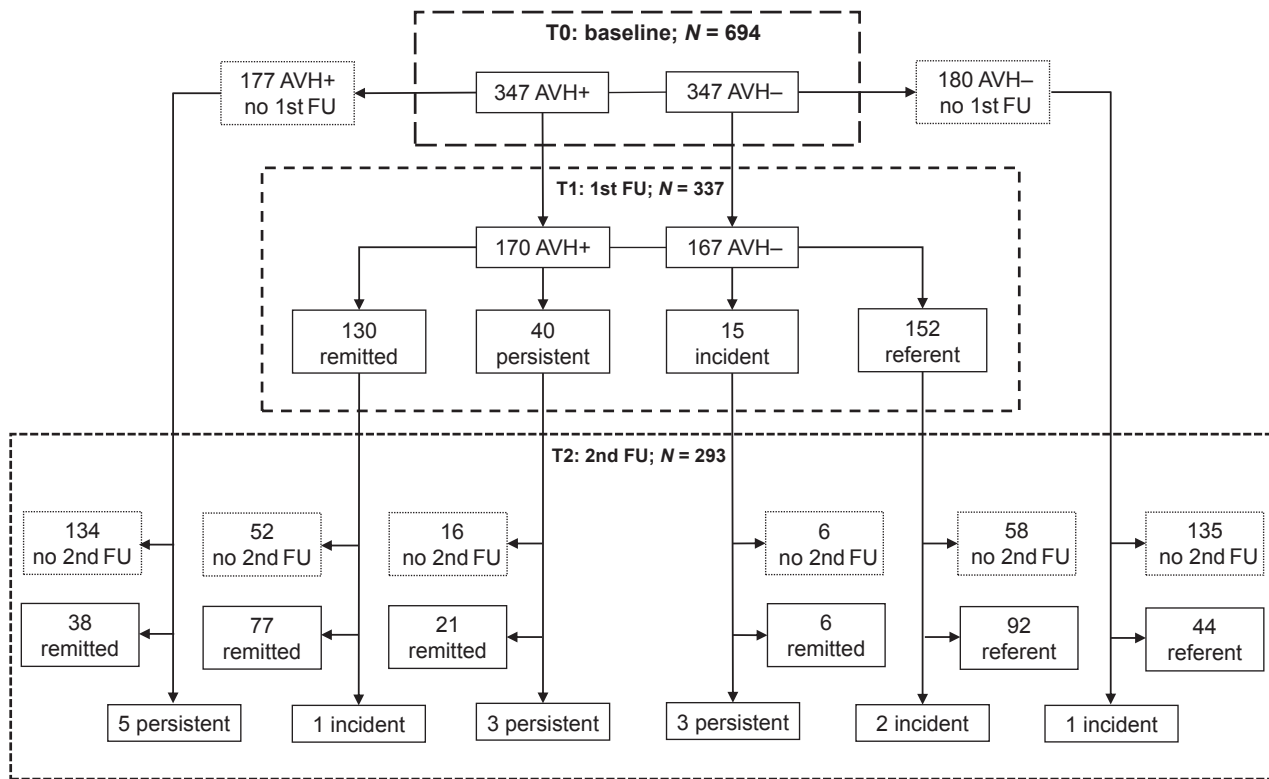


Fig. 2. Flow chart of auditory vocal hallucinations in baseline and follow-up participants.

to report AVH at T2 (OR = 0.86, 95% CI: 0.17–4.33). Given the small number of participants with severe AVH at T2, no further analyses were performed with respect to AVH severity.

Persistence of AVH

As only three participants reported AVH thrice, the differences with regard to number of times reporting AVH were studied between three groups that had (i) never reported AVH, (ii) reported AVH once and (iii) reported AVH twice or thrice.

The ‘AVH twice/thrice’ group (but not the ‘AVH once’ group) reported more psychotic experiences (CAPE) and related distress, more traumatic events and were more at risk for PTSD, compared with the ‘AVH never’ group (see Table 2). No significant differences between these two groups compared with the ‘AVH never’ group were observed with regard to other CAPE subscales, DASS subscales and cannabis use.

Discussion

To our knowledge, this study is the first that followed a case-control sample of young children with and without AVH into young adulthood over a period of 11 years.

The 11-year (T0–T2) and 6-year (T1–T2) AVH persistence rates were 6.2% and 18.2% respectively, and the 11-year and 6-year AVH incidence rates were 2.2% and 2.1% respectively. The 5-year persistence rate of 23.5% at first follow-up (27) was higher than the 6-year persistence rate of 18.2% at second follow-up, indicating decreasing levels of persistence with increasing age, making AVH a more transitory phenomenon in adolescents compared with young children. The persistence rate in the current study is lower than the 40% found by Escher et al. (28), but their sample consisted of both children (mean age 12.9 years) with and without a need for mental health care and, moreover, the follow-up period was only 3 years. De Loore et al. (11) found a 2-year AVH persistence rate of 27% in young adolescents (13/14 years). Other researchers report persistence rates of 21.3% [6-year; (9)], 39% [2-year; (12)], 26% and 31% [3-year; (29)], but the latter four studies were not solely restricted to AVH.

The exact reason for the lower T1–T2 AVH persistence rate compared with the T0–T1 persistence is unclear. Some youngsters may have been treated for their experiences, but this was not assessed. Another explanation is that AVH in early adolescence can present as a benign developmental sensation, especially in the absence of trauma. Another

Table 1. Demographic characteristics and outcome of participants by AVH status (*N* = 293)

	AVH+ (<i>N</i> = 15)		AVH- (<i>N</i> = 278)		OR (95% CI)
	Mean, %	SD (range)	Mean, %	SD (range)	
Age (years)	19.0	0.5 (18–20)	18.9	0.4 (18–20)	2.03 (0.57–7.31)
Gender (% female)	66.7		57.2		1.50 (0.50–4.50)
Level of education (% high)	30.8		47.3		0.50 (0.15–1.65)
Studying (% yes)	86.7		87.2		0.95 (0.21–4.40)
Having a paid job (% yes)	53.3		56.9		0.86 (0.31–2.45)
Having a partner (% yes)	46.7		42.3		1.19 (0.42–3.38)
Living situation (% with others)	93.3		85.8		0.43 (0.06–3.37)
CAPE (frequency; <i>N</i> = 284)					
Positive	11.1	8.1 (4–29)	4.0	3.8 (0–26)	1.21 (1.11–1.32)
Negative	14.0	5.2 (5–21)	8.0	5.5 (0–30)	1.15 (1.07–1.24)
Depressive	7.1	3.3 (1–12)	4.6	3.4 (0–22)	1.18 (1.04–1.33)
Delusional ideation (<i>N</i> = 284)	64		44		1.20 (0.13–11.05)
CAPE (distress)					
Positive (<i>N</i> = 252)	6.4	5.3 (0–20)	2.6	3.1 (0–19)	1.16 (1.08–1.24)
Negative (<i>N</i> = 274)	12.6	6.2 (5–22)	7.2	5.6 (0–27)	1.11 (1.04–1.17)
Depressive (<i>N</i> = 271)	7.7	4.2 (1–15)	5.1	4.2 (0–21)	1.10 (1.02–1.19)
DASS (<i>N</i> = 283)					
Depression	10.4	7.4 (2–24)	6.2	6.7 (0–36)	1.15 (1.01–1.30)
Anxiety	8.7	4.3 (4–18)	5.4	5.7 (0–30)	1.17 (1.01–1.36)
Stress	13.1	7.8 (0–30)	9.3	7.8 (0–38)	1.11 (0.99–1.25)
TSQ (<i>N</i> = 14/ <i>N</i> = 267)					
Traumatic events	7.9	6.3 (0–20)	1.6	2.8 (0–15)	1.35 (1.20–1.52)
≥1 traumatic event	78.6		40.8		5.32 (1.45–19.50)
Reactions*	4.3	2.1 (0–6)	1.7	2.0 (0–8)	1.64 (1.22–2.19)
≥5 reactions (PTSD risk)	54.5		11.0		9.70 (2.57–36.67)
Cannabis use (<i>N</i> = 14/ <i>N</i> = 265)					
Ever used (% yes)	42.9		44.2		0.95 (0.32–2.81)
Used in the past year (% yes)	100		59.0		2.02 (0.69–5.88)
Age at first use (years)	16.2	1.3 (14–17)	16.1	1.4 (13–19)	1.03 (0.56–1.89)
TO CBCL total score	28.2	14.18 (0–93)	21.4	14.16 (0–93)	1.03 (0.99–1.06)

AVH, auditory vocal hallucinations; AVH+, AVH in the past six years; AVH-, no AVH in the past six years; *N*, number; SD, standard deviation; OR, odds ratio; CI, confidence interval; CAPE, Community Assessment of Psychic Experience; DASS, Depression, Anxiety and Stress Scale; TSQ, Trauma Screening Questionnaire; PTSD, post-traumatic stress disorder; CBCL, Child Behaviour Checklist.

Significant differences are shown in bold.

*Reactions consist of five re-experiencing items and five arousal items.

plausible explanation is the relatively high rate of AVH in the non-participants. A replication study is therefore warranted.

One baseline difference was observed between T2 participants and non-participants: the non-participants had significant higher CBCL total scores at baseline. Reported effects may therefore represent an underestimate, as those with more behaviour problems were slightly underrepresented.

Youngsters reporting AVH at T2 scored significantly higher on depression, anxiety and stress (although the latter not significantly so). Our results confirm the idea that psychotic experiences are associated with a broader range of common mental disorders (3, 5, 6, 11). This is also endorsed by findings in older individuals (4, 30, 31). Contrary to the results of our first follow-up study (32) and those of Nuevo et al. (33), we did not observe any associations with delusional ideation.

The current study showed a positive association between AVH and environmental risk factors.

Those with AVH had experienced significantly more traumatic events. Moreover, the percentage of those at risk for PTSD was five times higher in AVH-reporting youngsters than in those without AVH at that time point. Other population-based studies have shown similar results (14). Likewise, it was found that the perception of being bullied at secondary school was associated with the predisposition to psychotic experiences (34), and also a five times greater likelihood of verbal hallucinations in those who had experienced trauma was observed (35).

For the definition of PTSD risk, the stress reactions to traumatic events were set at five in our study, in accordance with Kenardy et al. (24) who used this cut-off for children aged 7–16 years. A cut-off at six reliably predicted a diagnosis of PTSD in two adult samples (mean ages 38 and 35 years) (23). As our participants were only just adult at the time of the second follow-up assessment, we chose a cut-off of five in marking

Course of childhood auditory hallucinations

Table 2. Differences between groups who never, once and twice/thrice reported AVH

	AVH never* (<i>N</i> = 136) Mean (SD)	AVH once (<i>N</i> = 124) Mean (SD)	OR (95% CI)	AVH twice/thrice (<i>N</i> = 33) Mean (SD)	OR (95% CI)
CAPE (frequency) (<i>N</i> = 284)					
Positive	3.7 (3.2)	4.5 (4.5)	1.05 (0.99–1.13)	6.4 (6.8)	1.13 (1.04–1.22)†
Negative	7.8 (5.6)	8.5 (5.7)	1.02 (0.98–1.07)	9.6 (5.5)	1.06 (0.99–1.13)
Depressive	4.2 (3.0)	5.1 (3.7)	1.09 (1.01–1.18)	5.7 (3.7)	1.13 (1.02–1.26)
CAPE (distress)					
Positive (<i>N</i> = 252)	2.6 (2.9)	2.6 (2.9)	1.00 (0.92–1.10)	4.6 (5.5)	1.15 (1.03–1.27)†
Negative (<i>N</i> = 274)	7.3 (5.9)	7.4 (5.5)	1.00 (0.96–1.05)	9.0 (6.0)	1.05 (0.99–1.12)
Depressive (<i>N</i> = 271)	4.5 (3.6)	5.7 (4.8)	1.07 (1.01–1.14)	6.3 (4.2)	1.10 (1.01–1.21)
DASS (<i>N</i> = 283)					
Depression	5.7 (6.5)	6.9 (7.4)	1.03 (0.99–1.07)	7.4 (5.6)	1.04 (0.98–1.09)
Anxiety	4.1 (4.4)	6.7 (5.9)	1.10 (1.04–1.15)	7.6 (7.5)	1.12 (1.05–1.20)
Stress	8.5 (7.4)	10.4 (8.4)	1.03 (0.99–1.07)	9.9 (7.3)	1.02 (0.97–1.08)
TSQ (<i>N</i> = 281)					
Traumatic events	1.3 (2.3)	2.0 (3.4)	1.08 (0.99–1.18)	4.2 (5.2)	1.23 (1.11–1.36)†
≥1 traumatic event	40.3	40.8	1.02 (0.62–1.70)	59.4	2.16 (0.98–4.76)
Reactions‡	1.3 (1.7)	2.4 (2.2)	1.32 (1.07–1.63)	2.8 (2.6)	1.44 (1.11–1.86)
≥5 reactions (PTSD risk)	7.7	18.4	2.70 (0.77–9.43)	26.3	4.29 (1.01–18.1)†
Cannabis use (<i>N</i> = 279)					
Ever used (% yes)	39.1	47.9	1.43 (0.87–2.38)	50.0	1.56 (0.72–3.40)
Used in the past year (%) (<i>N</i> = 123)	64.0	57.9	1.18 (0.67–2.07)	62.5	1.41 (0.61–3.28)

AVH, auditory vocal hallucinations; *N*, number; SD, standard deviation; OR, odds ratio; CI, confidence interval; CAPE, Community Assessment of Psychic Experience; DASS, Depression, Anxiety and Stress Scale; TSQ, Trauma Screening Questionnaire; PTSD, post-traumatic stress disorder; CBCL, Child Behaviour Checklist.

*Reference group. Significant differences as compared to the reference group are shown in bold.

†Significant differences between 'AVH once' group and 'AVH twice/thrice' group.

‡Reactions consist of five re-experiencing items and five arousal items.

prone to developing PTSD, given that participants could not undergo a formal diagnostic procedure. However, the findings underline the importance of assessing trauma in young individuals reporting psychotic experiences.

The mean age at first cannabis use in our sample was 16 years for participants both with and without AVH. The OR for past year use was suggestive as all participants reporting AVH at T2 had used cannabis in the past year. Hence, our results concur with those reported in a review (36) evidencing an increased risk of psychotic outcomes in cannabis users. More recently, it was reported that cannabis use at age 16 years was associated with psychotic experiences at age 18 years (37). Currently, it is not yet evident whether those who reported AVH and cannabis use at T2 will make a transition to clinical disorder; however, adolescent cannabis use is considered a risk factor for later mental disorders (38).

A recent study on clinical high-risk adolescents revealed that two CBCL subscales (Withdrawn/Depressed and Thought Problems) had clinical and diagnostic utility as a screening measure for the early detection of at-risk youth for developing psychosis (39). We therefore performed post hoc logistic regression analyses with CBCL subscale scores at baseline (T0) and AVH (yes/no) at second follow-up (T2), using the pooled dataset after multiple imputation of the T0 CBCL subscales data.

At baseline, an earlier version of the CBCL was used (16) than the version in the aforementioned study (39). The analyses revealed that in our sample, the T0 CBCL subscales Anxious/Depressed and Thought Problems were significantly associated with AVH at T2 (OR = 1.18, 95% CI: 1.03–1.36 and OR = 1.57, 95% CI: 1.16–2.14, respectively), with T0 AVH in the model, indicating that participants with AVH at T2 had higher scores on these subscales (i.e. showing more problematic behaviour) at T0. Closer inspection revealed that T2 participants with AVH also scored higher on all other T0 CBCL subscales (except for Sexuality where they scored lower), but these differences did not reach statistical significance. We thus may conclude that our results correspond with those of Simeonova et al. (39).

Important strengths of this study are the long follow-up period and the fact that there was no selective attrition regarding the case-control status at the second follow-up: both were equally represented in the T2 sample.

Follow-up of participants with AVH at multiple assessments until the age of 24/25 years is worthwhile and intended. More prospective studies are needed to replicate our findings. Practical recommendations for future research are proposed in Jardri et al. (40). In addition, future epidemiological research may include measures for coping styles and/or resilience to uncover

possible characteristics underlying remittance or persistence of AVH.

Limitations

This study has several limitations. First, not all children of the baseline case–control sample could be included. Some families had indicated that they did not want to be approached for follow-ups and others had moved and could not be traced despite much effort. The T2 participation rate (of T0 participants) of 47.3% (293/620 eligible) and the T2 participation rate (of eligible T1 participants) of 60.8% (205/337) are far from complete but not disappointing considering the long follow-up periods. Contrary to expectation, 88 youngsters, who did not participate in the first follow-up, did participate in the second follow-up. On closer inspection, these participants were shown to be evenly distributed regarding baseline case–control status (cases $N = 43$; controls $N = 45$), supporting representativeness of our sample. A second limitation is that at baseline, no other possible predictor variables were included but the CBCL. Third, although urbanicity is considered a risk factor for developing psychotic experiences in adolescence (41), we did not study this at the current assessment because at age 18/19 years, it is difficult to disentangle the influence of urbanicity, as the majority of the youngsters were still living with their parents, either in the city or in rural areas, whilst they may work and/or study in more urban areas. A fourth limitation is that we did not question the participants on healthcare consumption, which may have resulted in the relatively favourable outcome as some of the participants may have been treated for unpleasant experiences in between assessments. Finally, only a small number of participants reported AVH at T2, resulting in low power.

Nevertheless, the findings without exception point in the same direction suggesting that AVH are associated with psychopathology and with environmental risk factors, even if the majority of AVH remain transitory.

Clinical implications

Our results show that most AVH will disappear over time, which is also underpinned by a decreasing persistence rate with age. Yet, a subsample of those reporting AVH may be at risk for developing more severe or persistent psychopathology. Based on the current results, large-scale programmes for early AVH detection may not be practical as a method for prevention of transitions to more

severe clinical states. However, if youngsters do report AVH, talking about their experiences, reassuring and monitoring them is essential, emphasizing the need for destigmatization of AVH (42, 43). Examining the presence and development of comorbid psychopathology is advisable, given associations with more severe outcomes. Also, given the evident association between traumatic events and AVH, it is necessary to sensitively inquire about childhood adversity in help-seeking youngsters presenting with AVH and, if necessary, address these traumas (44, 45).

Acknowledgements

The authors are most grateful to all youngsters who took part in the second follow-up study. This study received funding from the Stichting tot Steun VCVGZ (Foundation for Support, Christian Union for Care of Mentally Ill), the Bendorp Fund, Maastricht University Medical Centre and the Rob Giel Research Center. Johanna T.W. Wigman is supported by a Netherlands Organization for Scientific Research (NWO) Veni Grant (number 016.156.019). This study was supported by the European Community's Seventh Framework Program under Grant Agreement No. HEALTH-F2-2009-241909 (Project EU-GEI).

Declarations of interest

The authors report no conflict of interests in relationship with this study.

References

1. 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* 2012;**42**:1857–1863.
2. LINSKOTT RJ, Van Os J. An updated and conservative systematic review and meta-analysis of epidemiological evidence on psychotic experiences in children and adults: on the pathway from proneness to persistence to dimensional expression across mental disorders. *Psychol Med* 2013;**43**:1133–1149.
3. JEPPESEN P, CLEMMENSEN L, MUNKHOLM A et al. Psychotic experiences co-occur with sleep problems, negative affect and mental disorders in preadolescence. *J Child Psychol Psychiatry* 2015;**56**:558–565.
4. PRETI A, SISTI D, ROCCHI MB et al. Prevalence and dimensionality of hallucination-like experiences in young adults. *Compr Psychiatry* 2014;**55**:826–836.
5. KELLEHER I, KEELEY H, CORCORAN P et al. Clinicopathological significance of psychotic experiences in non-psychotic young people: evidence from four population-based studies. *Br J Psychiatry* 2012;**201**:26–32.
6. FISHER HL, SCHREIER A, ZAMMIT S et al. Pathways between childhood victimization and psychosis-like symptoms in the ALSPAC birth cohort. *Schizophr Bull* 2013;**39**:1045–1055.
7. RUBIO JM, SANJUAN J, FLOREZ-SALAMANCA L, CUESTA MJ. Examining the course of hallucinatory experiences in children and adolescents: a systematic review. *Schizophr Res* 2012;**138**:248–254.

8. KAYMAZ N, DRUKKER M, LIEB R et al. Do subthreshold psychotic experiences predict clinical outcomes in unselected non-help-seeking population-based samples? A systematic review and meta-analysis, enriched with new results. *Psychol Med* 2012;**42**:2239–2253.
9. ZAMMIT S, KOUNALI D, CANNON M et al. Psychotic experiences and psychotic disorders at age 18 in relation to psychotic experiences at age 12 in a longitudinal population-based cohort study. *Am J Psychiatry* 2013;**170**:742–750.
10. DOMINGUEZ MD, WICHERS M, LIEB R, WITTCHEN HU, Van Os J. Evidence that onset of clinical psychosis is an outcome of progressively more persistent subclinical psychotic experiences: an 8-year cohort study. *Schizophr Bull* 2011;**37**:84–93.
11. De LOORE E, GUNTHER N, DRUKKER M et al. Persistence and outcome of auditory hallucinations in adolescence: a longitudinal general population study of 1800 individuals. *Schizophr Res* 2011;**127**:252–256.
12. DOWNS JM, CULLEN AE, BARRAGAN M, LAURENS KR. Persisting psychotic-like experiences are associated with both externalising and internalising psychopathology in a longitudinal general population child cohort. *Schizophr Res* 2013;**144**:99–104.
13. TROTTA A, MURRAY RM, FISHER HL. The impact of childhood adversity on the persistence of psychotic symptoms: a systematic review and meta-analysis. *Psychol Med* 2015;**45**:1–18.
14. VARESE F, SMEETS F, DRUKKER M et al. Childhood adversities increase the risk of psychosis: a meta-analysis of patient-control, prospective- and cross-sectional cohort studies. *Schizophr Bull* 2012;**38**:661–671.
15. Van DAM DS, Van der VEN E, VELTHORST E, SELTEN JP, MORGAN C, de HAAN L. Childhood bullying and the association with psychosis in non-clinical and clinical samples: a review and meta-analysis. *Psychol Med* 2012;**42**:2463–2474.
16. BARTELS-VELTHUIS AA, JENNER JA, Van de WILLIGE G, Van Os J, WIERSMA D. Prevalence and correlates of auditory vocal hallucinations in middle childhood. *Br J Psychiatry* 2010;**196**:41–46.
17. VAN DE WILLIGE G, JENNER JA, BARTELS-VELTHUIS AA. The self-report version of the Auditory Vocal Hallucination Rating Scale (AVHRS-Q). Groningen, the Netherlands: University of Groningen, University Medical Center Groningen, University Center for Psychiatry, 2010.
18. JENNER JA, VAN DE WILLIGE G. The auditory vocal hallucination rating scale (AVHRS). Groningen, the Netherlands: University of Groningen, University Medical Center Groningen, University Center for Psychiatry, 2002.
19. BARTELS-VELTHUIS AA, Van de WILLIGE G, JENNER JA, WIERSMA D. Consistency and reliability of the auditory vocal hallucination rating scale (AVHRS). *Epidemiol Psychiatr Sci* 2012;**21**:305–310.
20. KONINGS M, BAK M, HANSEN M, Van Os J, KRABBENDAM L. Validity and reliability of the CAPE: a self-report instrument for the measurement of psychotic experiences in the general population. *Acta Psychiatr Scand* 2006;**114**:55–61.
21. LOVIBOND PF, LOVIBOND SH. The structure of negative emotional states: comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. *Behav Res Ther* 1995;**33**:335–343.
22. De BEURS E, Van DYCK R, MARQUENIE LA, LANGE A, BLONK RWB. De DASS: een vragenlijst voor het meten van depressie, angst en stress. *Gedragstherapie* 2001;**34**:35–53.
23. BREWIN CR, ROSE S, ANDREWS B et al. Brief screening instrument for post-traumatic stress disorder. *Br J Psychiatry* 2002;**181**:158–162.
24. KENARDY JA, SPENCE SH, MACLEOD AC. Screening for post-traumatic stress disorder in children after accidental injury. *Pediatrics* 2006;**118**:1002–1009.
25. ANDREWS G, PETERS L. The psychometric properties of the Composite International Diagnostic Interview. *Soc Psychiatry Psychiatr Epidemiol* 1998;**33**:80–88.
26. ACHENBACH TM. Manual for the Child Behaviour Checklist/4-18 [Dutch translation: Verhulst et al., 1996]. Burlington, USA: University of Vermont, Department of Psychiatry, 1991.
27. 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**:296–302.
28. 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–s18.
29. COUGNARD A, MARCELIS M, MYIN-GERMEYS I et al. Does normal developmental expression of psychosis combine with environmental risk to cause persistence of psychosis? A psychosis proneness-persistence model. *Psychol Med* 2007;**37**:513–527.
30. VARGHESE D, SCOTT J, WELHAM J et al. Psychotic-like experiences in major depression and anxiety disorders: a population-based survey in young adults. *Schizophr Bull* 2011;**37**:389–393.
31. 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**:327–346.
32. BARTELS-VELTHUIS AA, Van de WILLIGE G, JENNER JA, WIERSMA D, Van Os J. Auditory hallucinations in childhood: associations with adversity and delusional ideation. *Psychol Med* 2012;**42**:583–593.
33. NUEVO R, Van Os J, ARANGO C, CHATTERJI S, AYUSO-MATEOS JL. Evidence for the early clinical relevance of hallucinatory-delusional states in the general population. *Acta Psychiatr Scand* 2013;**127**:482–493.
34. CAMPBELL ML, MORRISON AP. The relationship between bullying, psychotic-like experiences and appraisals in 14–16-year olds. *Behav Res Ther* 2007;**45**:1579–1591.
35. FREEMAN D, FOWLER D. Routes to psychotic symptoms: trauma, anxiety and psychosis-like experiences. *Psychiatry Res* 2009;**169**:107–112.
36. MOORE TH, ZAMMIT S, LINGFORD-HUGHES A et al. Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. *Lancet* 2007;**370**:319–328.
37. GAGE SH, HICKMAN M, HERON J et al. Associations of cannabis and cigarette use with psychotic experiences at age 18: findings from the Avon Longitudinal Study of Parents and Children. *Psychol Med* 2014;**44**:3435–3444.
38. RUBINO T, ZAMBERLETTI E, PAROLARO D. Adolescent exposure to cannabis as a risk factor for psychiatric disorders. *J Psychopharmacol* 2012;**26**:177–188.
39. SIMEONOVA DI, NGUYEN T, WALKER EF. Psychosis risk screening in clinical high-risk adolescents: a longitudinal investigation using the Child Behavior Checklist. *Schizophr Res* 2014;**159**:7–13.
40. JARDRI R, BARTELS-VELTHUIS AA, DEBBANÉ M et al. From phenomenology to neurophysiological understanding of hallucinations in children and adolescents. *Schizophr Bull* 2014;**40**:S221–S232.
41. SPAUWEN J, KRABBENDAM L, LIEB R, WITTCHEN HU, Van Os J. Evidence that the outcome of developmental expression of psychosis is worse for adolescents growing up in an urban environment. *Psychol Med* 2006;**36**:407–415.

Bartels-Velthuis et al.

42. MCGORRY PD, KILLACKEY E, YUNG A. Early intervention in psychosis: concepts, evidence and future directions. *World Psychiatry* 2008;**7**:148–156.
43. RUESCH N, CORRIGAN PW, HEEKEREN K et al. Well-being among persons at risk of psychosis: the role of self-labeling, shame, and stigma stress. *Psychiatr Serv* 2014;**65**:483–489.
44. 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**:330–350.
45. MORRISON APSC, READ J, TURKINGTON D. Trauma and psychosis: theoretical and clinical implications. *Acta Psychiatr Scand* 2005;**112**:327–329.