Chapter 1

General introduction
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AT THE EXTREME END OF THE SPECTRUM...

She was about 14 years of age, referred to our first psychosis ward as she suffered from hallucinations. More specifically, she saw and heard a man that commanded her to commit suicide by throwing herself in front of a train. Although she knew the man was not real, it was almost impossible for her to ignore his comments and assignments, so she often ended up alongside the tracks. The referring psychiatrist and her family asked for our expertise to distinguish whether she suffered from a psychotic disorder or not. Although we had not seen any more signs indicative of psychosis, we were struck by her distress and wanted to understand what was happening to her. However, she claimed to be suffering even more due to intense homesickness and wanted to return home. Although her family and we preferred to continue her admittance, during her stay there were not enough legal grounds to keep her against her will. It was only a few weeks later her psychiatrist informed us that she had committed suicide.

This was my first encounter with an adolescent that primarily suffered from hallucinations. Of course, I understood that this was even a tragic as exceptional case, but it did make me curious to learn more about voice hearing in youth. For example, how often do auditory hallucinations occur in youth, do all children and adolescents suffer from their hallucinations and could we offer not more than merely determining whether they were part of a psychotic disorder or not?

Integrating clinical work with research and vice versa

Auditory hallucinations (AH) are known to occur all over the world and to be experienced from childhood to old age, both males and females. Many researchers are intrigued by this phenomenon and studies regarding auditory hallucinations have been accumulating rapidly. This is in line with the increasing awareness that a symptom-based approach may offer new insights in unraveling psychopathology. Despite all these studies on auditory hallucinations in both adult and young populations, the results have had little impact on the improvement of care, especially for youth. Only few articles provided directions on how to assess children with stressful AH. During my residency, it appeared to me that clinicians do not have the tendency to actively ask about hallucinations. Or, when AH are put forward by a patient, clinicians merely screen for the presence of any more symptoms to understand whether they might be part of a psychotic disorder or not. I came to think that this might be due to a lack of knowledge and/or confidence to further address hallucinations. Nevertheless, children and adolescents with distressing hallucinations do engage mental health care facilities and we are obliged to provide them with the best care possible.
Therefore, in March 2013, we started an outpatient clinic at the UMC Utrecht Brain Center for youth with auditory hallucinations, specifically hearing voices. We used several forms of media to create awareness of voice hearing in youth and the opportunity to visit the outpatient clinic. Also, we implemented a longitudinal study so that we could follow up on the families that entered the outpatient clinic. We included entire families to learn which factors (e.g. perinatal problems, parenting styles, personality traits, drug abuse or trauma) might have contributed to the development, persistence and/or remission of AH on the one hand and to unravel resilience factors from siblings that would not develop AH on the other. Although the outpatient clinic was well visited and appreciated, only a minority of the families opted to participate in research and to enter the longitudinal study. Unfortunately, after three years, we had to abort the study for lack of power.

In the past years we undertook collaborations with clinicians and researchers in the Netherlands and abroad. With these colleagues we developed assessment and treatment strategies and completed several research projects. The work presented in this thesis aims to contribute to scientific insights on AH in youth and also (and perhaps more importantly) to clinical care for this vulnerable group.

**Auditory hallucinations in youth**

**Definitions**

Auditory hallucinations can be defined as auditory perceptions in the absence of identifiable stimuli. Often, an exception is made for perceptions during drowsiness or sleep. While AH includes all kind of auditory perceptions, auditory verbal hallucinations (AVH) specifically refer to hearing one or more voices.

Next to delusions, hallucinations were traditionally considered psychotic symptoms, indicative of psychotic spectrum disorders. However, as in adults, we have come to understand that (auditory) hallucinations and delusions in youth are not restricted to psychotic spectrum disorders, but can also occur in the presence of anxiety, mood and behavioral disorders. Hence the term psychotic(-like) experiences (PE). PE are also found to occur in otherwise healthy individuals. Nevertheless, non-psychotic and psychotic individuals with more frequent AH do share risk factors such as childhood trauma as well as characteristics such as disorganized speech, indicative of a shared vulnerability. Moreover, hallucinations and delusions are found not to be restricted to psychotic spectrum disorders, but to be associated with a broad range of psychiatric (and somatic) disorders. Therefore, auditory hallucinations and other PE are increasingly conceptualized to occur on a continuum; from healthy individuals at one end to patients with a broad variety of psychopathology at the other end.
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**Epidemiology**

Children and adolescents are known to experience auditory hallucinations from young ages\(^4\) and are included in studies from the age of 5\(^{15,16}\). Most epidemiological studies point to a frequent occurrence of AH in youth. However, as in adult studies, prevalence estimates vary widely (2-37.5\% \(^{15,17}\)).

Auditory hallucinations are presumed to be mostly sporadic and to generally disappear over time spontaneously. AH persistence rates vary from 27\% for a 2-year follow-up (from age 13/14 to age 15/16)\(^{18}\), 24\% for a 5-year follow-up (age 7/8 to 12/13 years)\(^{19}\), 18.9\% for a 6-years follow-up (age 12/12 to 18/19 years)\(^{20}\) and 6.2\% for an 11-year follow-up (age 7/8 to 18/19 years)\(^{20}\). Overall, auditory hallucinations in youth are transient in up to 95\% of cases\(^{20,21}\).

**Clinical relevance of auditory hallucinations**

Although the transient character of auditory hallucinations might point to a possibly typical developmental nature, AH should not be regarded as merely a benign phenomenon.

The presence of hallucinations is associated with greater impairment across a range of functional domains. Young people with hallucinations have been found to demonstrate poorer global functioning than their peers, even when compared with other young people with a mental disorder (but without hallucinations)\(^{22,23}\). Children and adolescents who report persistent hallucinations demonstrate poorer functioning in terms of cognitive performance as they have significantly worse primary school test scores and are at lower secondary school levels compared to peers with remitted AH\(^{19}\).

Moreover, even in a young (7/8 year olds) and non-clinical setting, 15\% of children were found to suffer from their AH and experienced comorbid problem behavior\(^{24}\). Also, the presence of AH in childhood increases the risk of developing psychopathology later in life. For example, they have a threefold increased risk to develop a depressive disorder\(^{25}\) and a 5 to 16 times increased risk to develop a schizophrenia-spectrum disorder, depending on number and severity of psychotic symptoms\(^{26}\). Furthermore, persistence of AH is associated with the development of delusional ideation and with the risk of developing more general psychopathology\(^{28}\), particularly post-traumatic stress disorder (PTSD)\(^{20}\). Although rare at young age, AH can be a symptom of childhood onset schizophrenia (first psychotic episode before the age of 12 years), often accompanied by a high rate of hallucinations in all domains\(^{27}\). With increasing age, AH are more indicative of present psychopathology\(^{28}\). Nevertheless, even at young age, a wide range of other psychiatric disorders such as mood disorder, attention deficit hyperactivity disorder (ADHD) and PTSD are found to accompany AH in both epidemiologic and clinical samples\(^{14,20,28,29}\).
Also, the presence of AH proved to be a strong marker for the presence of multiple co-occurring Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) diagnoses.

Like in adults, AH in youth can also occur in the context of a somatic disorder, ranging from neurological (e.g. migraine, aura's or seizures) to genetic, autoimmune and metabolic disorders.

**Diagnostic and treatment strategies**

Although the few studies providing guidelines for clinicians seem to lack data derived pointers, the overall message with regard to the assessment and treatment of AH seems to be one of ‘good clinical practice’. This means that a clinician should thoroughly assess the context in which AH exist, in order to unravel possible underlying causative factors and/or co-occurring health problems. In case of present causative factors and/or other health problems, treatment should target these first. In the absence of pathological signs, caregivers are advised to normalize and destigmatize these phenomena. However, guidance how to specifically assess AH and, subsequently, what educational information should be shared, is lacking and thus depends on the caregivers’ experience and knowledge.

Moreover, the 2014 International Consortium on Hallucination Research (ICHR) working group emphasizes the urgent need for psychotherapeutic interventions specifically developed for children. In accordance with the proven effectiveness of tailored Cognitive Behavior Therapy (CBT) for voice hearing adults, a similar approach has been suggested to be an effective strategy for the treatment of psychotic symptoms in children and adolescents. However, a targeted treatment protocol had not yet been developed.

When AH are present in the context of a confirmed psychotic disorder, treatment with antipsychotic medication is recommended. Antipsychotics have proven to be highly effective in reducing severity of (positive) psychotic symptoms in youth with schizophrenia-spectrum disorders. Nevertheless, youngsters are also more vulnerable than adults to the adverse effects, such as extrapyramidal signs (specifically Parkinsonism and dystonia), hormonal dysregulation (hyperprolactinemia), somnolence (interfering (social) functioning and cognitive performances at school), and weight gain and consequent metabolic effects. These side effects may also lead to premature (and sometimes undisclosed) discontinuation of medication. Therefore, young patients and their parents should always be actively included in a risk-benefit analysis when choosing an antipsychotic.
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Outline

For both research purposes and for clinical and societal educational aims, it is indispensable to have more exact insight in the prevalence of AH. In chapter 2, we reviewed youth and adult general population studies on the prevalence of auditory hallucinations. We combined all findings in a meta-analysis to calculate the mean lifetime prevalence and grouped mean prevalence across the lifespan; children, adolescents, adults and the elderly.

Epidemiological and clinical studies on AH in youth so far used active screening methods to identify children and adolescents with AH. These studies do not inform clinicians very well about the features of the children and adolescents needing and/or seeking help for AH. In chapter 3 we describe the characteristics of children and adolescents seeking help for AH at our outpatient clinic. This was a naturalistic study. We provide both insight in the morbidity of these youngsters and pointers for diagnostic and treatment strategies.

Despite the transient character of AH, a subgroup of children and adolescents with AH do warrant clinical care. To identify these children and adolescents at the earliest stage possible and offer interventions timely, it is important to understand the extent of children and adolescents with AH in the general population that might actually be in need of clinical care. In chapter 4 we estimate which proportion of young adolescents (12/13 year olds) with AH in the general population might be in need for clinical care. To identify this subgroup, we compared characteristics of our help seeking sample (see chapter 3) with the characteristics of a previously described general population sample. Next, we explored whether this ‘need for care’ subgroup could have been identified at earlier age (at age 7/8 years), and how they functioned retrospectively (again at age 7/8 years) and prospectively (at age 18/19 years).

In 2014, Jardri and colleagues published a review, synthesizing research results on childhood and adolescent hallucinations, as part of the ICHR working group. In 2017, a renewed ICHR working group was brought together, resulting in an updated review in chapter 5. In this updated review, the need for consensus definitions regarding the onset and persistence of hallucinations, new insights regarding etiology and clinical relevance, methods to assess hallucinations in children and adolescents and therapeutic strategies are discussed. For clinicians, a more tailored care model, based on the current knowledge, is outlined.

In chapter 6 we present the feasibility study of the Stronger Than Your Voices (STYV) treatment protocol. STYV is a symptom-based psychotherapy for children and
adolescents suffering from AVH. The intervention was developed at our outpatient clinic in close collaboration with the Dutch ‘Gedachten Uitpluizen Foundation’ (www.gedachtnieuwpluizen.nl). In a second stage, we trained caregivers from different mental health care facilities across the Netherlands to work with this protocol. In return, we received anonymized pre- and post-measures from patients and feedback from both patients and caregivers regarding their experience with the protocol.