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Review article

Understanding auditory verbal hallucinations in healthy individuals and individuals with psychiatric disorders

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ABSTRACT

Auditory verbal hallucinations(AVHs) are psychiatric manifestations that are common in patients with psychiatric disorders and can occur in healthy individuals. This review summarizes the existing literature on the phenomenological features of auditory verbal hallucinations, imaging findings, and interventions, focusing on patients with schizophrenia who experience auditory verbal hallucinations, in addition to patients with borderline personality disorder, bipolar disorder, major depressive disorder, and posttraumatic stress disorder, as well as healthy individuals. The phenomenological features of AVHs vary in different psychiatric disorders, and the symptoms are associated with changes in specific brain structures and disturbances in brain function, blood flow, and metabolism. Interventions for auditory verbal hallucinations include antipsychotic drugs, neurostimulation, and cognitive behavioral therapy.

1. Introduction

An auditory verbal hallucination (AVH) is the perceived experience of hearing others speaking while in an awake state and in the absence of externally appropriate stimuli (Northoff and Qin 2011). AVHs are experienced by patients with psychiatric disorders as well as healthy people (Mccarthy-Jones 2013). Sixty to eighty-three percent of patients with schizophrenia, 46% of patients with borderline personality disorder (BPD) (Kingdon et al., 2010), 23% of patients with bipolar disorder (BD) (Upthegrove et al., 2015), and up to 40.6% of patients with major depressive disorder (MDD) report experiencing AVHs (Baethge et al., 2015). Patients with posttraumatic stress disorder (PTSD) also report AVHs (Anketell et al., 2010). Fifty to sixty-seven percent of British military veterans, a highly studied population in which PTSD is prevalent, are affected by AVHs (Brewin and Patel 2010). In addition, 10–15% of healthy individuals may experience AVHs (Sommer et al., 2010). In healthy populations, AVHs are isolated experiences associated with psychotic conditions such as difficulty concentrating, depressed mood, anxiety, suspiciousness, or withdrawal from family and friends.

AVHs are common psychiatric symptoms that can cause mental distress to patients and even affect their behavior (Saskia and Emma 2013). Particularly, patients with schizophrenia can lose control of their actions while experiencing auditory hallucinations, and they may harm themselves and others as a result. The aim of this review is to describe the clinical features and imaging characteristics of AVHs and AVH interventions in patients with psychiatric disorders, including those with schizophrenia, BPD, BD, MDD, and PTSD, as well as in healthy subjects to provide a better understanding of the development of AVHs among those individuals.

2. Review of the current literature

We conducted a targeted review of the literature using PubMed and the following keywords: auditory verbal hallucination* OR (hear* voice*) OR verbal hallucination* AND phenomenon* OR imaging* OR intervention * AND schizophrenia* OR borderline personality disorder * OR bipolar disorder* OR major depressive disorder* OR posttraumatic stress disorder* OR healthy individuals*.

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3. Clinical features of AVHs in psychiatric patients and healthy individuals

The clinical features of AVHs include perceiving the spatial location of a sound and sensing the loudness and clarity of the sound. In patients with schizophrenia, auditory hallucinations are perceived as having an intracranial or extracranial origin, with some patients reporting sounds from both places, and some patients indicating that the location is difficult to define (Hoffman et al., 2008). Studies including patients with schizophrenia, obsessive compulsive disorder, and first-order psychosis as well as nonclinical controls revealed that most hallucinated sounds are heard clearly at a normal conversational volume, although some may be hushed voices or loud screams (Moritz and Larøi 2008) and difficult to discern (Rachel et al., 2016).

Other important features of AVHs are their frequency, auditory identity, content, and the emotional reactions they trigger. With respect to frequency, it was found that 12% of psychiatric patients with AVHs experience auditory hallucinations 1–2 times a day, 36% experience auditory hallucinations during a limited part of the day, 37% experience auditory hallucinations most of the day, and 15% experience auditory hallucinations throughout the day (Nayani and David 1996). With respect to duration, 33% of patients experiencing AVHs report that each AVH lasts a few seconds or minutes, 25% experience AVHs that last less than an hour, and 42% experience AVHs that last more than an hour. Patients who experience more frequent AVHs tend to experience a longer-duration of AVHs (Nayani and David 1996). With respect to the development of AVHs, some subjects never experience AVHs, some experience them only during the acute phase, and some have long-term AVHs, which may become refractory (Larøi et al., 2012).

In a study of patients with schizophrenia, obsessive compulsive disorder, and nonclinical controls, auditory hallucinations mainly comprised someone else's voice and multiple sounds (Moritz and Larøi 2008). Patients with acute schizophrenia reported being able to distinguish most voices by gender, with male voices being more common than female voices (Garrett and Silva 2003). In a large study of patients with psychiatric disorders, researchers found that most AVHs were adult voices (71%), few were children's voices (2%), and some patients heard both adult and children's voices (26%) (Nayani and David 1996). Some patients recognized the voices they heard and could even tell the voice-bearer's name (Nayani and David 1996). Most patients (79%) heard voices with accents that differed from their own (Nayani and David 1996). A study in patients with schizophrenia confirmed that local accents are rare (Hoffman et al., 2008). A systematic review of studies that included patients with psychosis and healthy controls revealed that auditory sounds may be familiar voices, unfamiliar voices, or both (all, 33%) (Upthegrove et al., 2016).

AVH content can be positive, neutral, or negative. First-rank AVHs are characterized by a running commentary or a conversing voice (Rosen et al., 2011). Abusive, accusatory, and persecutory voices are common (Daalman et al., 2011a). A study in patients with psychiatric disorders and healthy controls showed that individuals attribute AVHs to self (my own voice) (41%) or others (other people talking to me) (42%), and a small number (17%) are unsure whether the sounds are real or imaginary (Daalman et al., 2011b). The clinical features of AVHs in patients with schizophrenia, patients with other psychiatric disorders, and healthy individuals are summarized in Fig. 1.

3.1. AVHs in schizophrenia

Auditory hallucinations in patients with schizophrenia are often verbal, described as ‘like listening to other people's voices’. Very few patients perceive a “silent voice” (no sound) with semantics that provide information (Jones 2010). The frequency of AVHs in patients with schizophrenia is quite variable and can range from once or twice a week to being persistent.

The content of AVHs in patients with schizophrenia is typically exaggerated and bizarre, often involving unfamiliar topics (Leudar et al., 1997), and the content is often repeated (Hoffman et al., 2008). AVHs in patients with schizophrenia have a negative emotional tone, manifesting as criticism, ridicule, threats, abuse, and orders that can cause emotional reactions such as anger, depression, anxiety, panic, and an urge to escape. Furthermore, AVHs can impair mental and social functions, and imperative AVHs may lead to automatization, suicidal behavior, or even harming others and society (Hugdahl 2015). Nayani and David found that patients with schizophrenia were particularly likely to attribute hallucinated sounds to external factors (72%) (Nayani and David 1996). Patients with schizophrenia have little control over the occurrence and cessation of AVHs, which can lead to mental distress (Larøi et al., 2012).

3.2. AVHs in MDD and BD

Patients with MDD also experience AVHs (Larøi et al., 2012). The AVHs they experience are usually brief and simple (e.g., a single word or phrase) and consistent with the patient's emotions. The gender distribution of the voices heard by patients with MDD is similar to that in patients with schizophrenia.

Generally, patients with BD hear argumentative speech, persistent comments, and accusatory voices. The frequency of AVHs in patients with BD varies with the stage of the disorder. Episodes are usually brief and intermittent. In general, AVHs in patients with BD are associated with delusions and high levels of anxiety (Toh et al., 2015). The hallucinations are commonly reported in an acute mood state and may be more frequent in mania than in depression phases (Smith et al., 2017).

3.3. AVHs in PTSD

The phenomenological characteristics of AVHs in patients with PTSD are similar to those in patients with psychiatric disorders (Anketell et al., 2010). In a study of 45 patients with PTSD, 50% of the patients experienced AVHs, and 50% of these patients experienced imperative, loud, and clear hallucinations that were directly related to the traumatic incident from which the PTSD developed. Although the hallucinations associated with PTSD are manifestations of a person's own thoughts, patients indicate that the loudness and clarity of the auditory hallucinations are similar to external sounds (Strom et al., 2012).

3.4. AVHs in BPD

AVHs in patients with BPD are regarded as malevolent, omnipotent, and consisting of content that is mostly negative and critical (Kingdon et al., 2010). The mean frequency of AVHs in patients with BPD is at least once per day, occurring for a few minutes per episode. The distress associated with them is as bad or worse than in patients with schizophrenia. There is an increase in suicide attempts and hospitalization frequency in BPD patients experiencing AVHs. The auditory hallucinations in patients with BPD are associated with PTSD and emotional abuse (Slotema et al., 2017).

3.5. AVHs in healthy individuals

Healthy individuals can experience intracranial and extracranial auditory hallucinations (Nemeroff et al., 2013) that are triggered by major life stressors or sleep deprivation and can be followed by delusions (Sommer et al., 2010).

One study comparing AVHs in patients with schizophrenia and healthy controls found no significant differences between groups in most of the phenomenological features of AVHs, including spatial localization, loudness, and quantity of sounds (Daalman et al., 2011b). In healthy individuals, hallucinated sounds are usually the voice of a

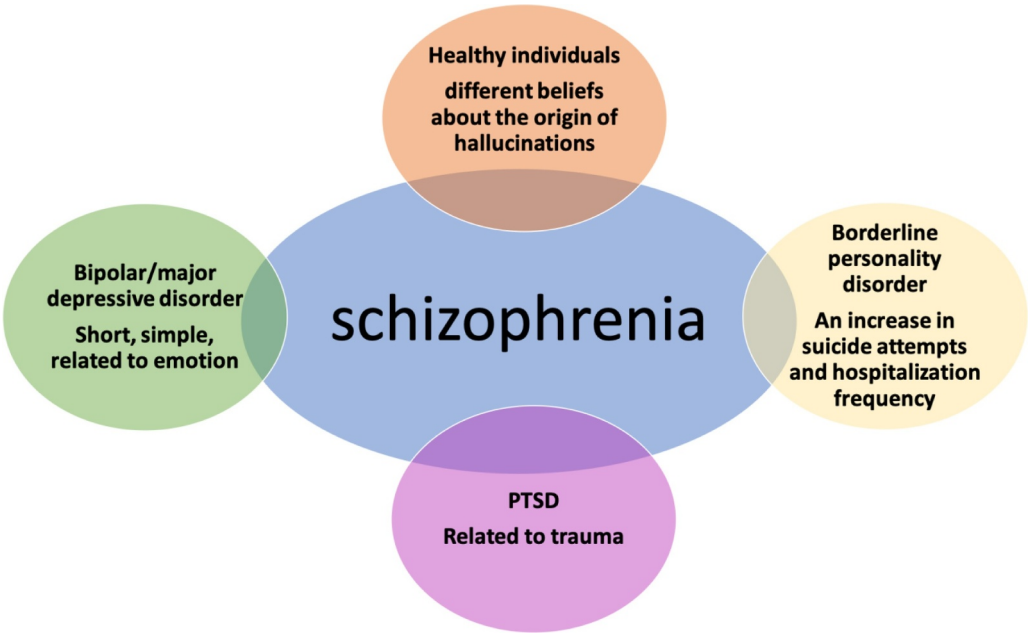

Fig. 1. Summary of the clinical features of AVHs in schizophrenic patients, patients with other psychiatric disorders, and healthy individuals.

familiar (nonself) person (Faccio et al., 2013) and are believed to originate from souls of the deceased, guardian angels, and ghosts. Conversely, patients with schizophrenia often attribute auditory hallucinations to a real-world external source, such as the secret police, psychically connected people, drug dealers, or vicious neighbors. Interestingly, in a study (including 103 healthy individuals who experienced AVHs) that evaluated whether AVHs occur as an isolated phenomenon or as part of a subtle schizotypal tendency, all subclusters of the Schizotypal Personality Questionnaire (SPQ) and the Peters et al. Delusion Inventory significantly increased, indicating that healthy individuals with AVHs have a schizotypal and delusional tendency (Sommer et al., 2010).

4. The relationship between childhood abuse or trauma and AVHs

Childhood sexual abuse has been directly and indirectly associated with AVHs. Hammersley et al. found that 39.6% of patients with BD and AVHs suffered from trauma, and 15.8% were sexually abused in childhood (Hammersley et al., 2003). These rates are similar to findings in patients with schizophrenia who experience AVHs (Offen et al., 2003). Post-traumatic symptomatology (e.g., re-experiencing, avoidance, and hyperarousal) is a mediator in the relationship between childhood sexual abuse and AVHs (Mccarthyjones 2017).

5. Imaging of psychiatric patients and healthy subjects who experience AVHs

5.1. Structural alterations

Substantial progress has been made in identifying structural alterations in the brains of patients with AVHs (Allen et al., 2012). In patients with schizophrenia who experienced AVHs, numerous studies have identified structural changes in the brain, such as decreased gray matter in the medial and inferior regions of the frontal lobe, the insular cortex, and the temporal lobe. Specifically, reduced gray matter volumes in the left and right superior temporal gyri and the primary auditory cortex have been consistently associated with AVHs in patients with schizophrenia (Modinos et al., 2013). Weijer et al. found that the integrity of white matter fiber bundles was altered in projections linking the temporal/front and the parietal lobe brain regions in patients with schizophrenia and AVHs (de Weijer et al., 2011, 2013). In a structural magnetic resonance imaging (MRI) study, Cierpka et al. utilized cerebellum-optimized voxel-based morphometry and found reduced gray matter volumes in the right cerebellar hemisphere in patients with schizophrenia and persistent AVHs compared to healthy individuals (Cierpka et al., 2017). In a diffusion tensor imaging study comparing white matter alterations in 21 first-episode (first-AVH) patients with schizophrenia and AVH, 12 chronic (chronic-AVH) patients with schizophrenia and AVHs, and 26 healthy controls with tract-based spatial statistics, the fractional anisotropy in white matter tracts was decreased and the radial diffusivity was increased in patients with AVHs (Zhang et al., 2018). There were more abnormalities in the chronic-AVH group than in the first-AVH group; specifically, there were more widespread white matter alterations in the chronic-AVH group than in the first-AVH group, as well as increased axial diffusivity in some discrete regions.

5.2. Functional disturbances

The structural alterations in the brains of patients with schizophrenia who experience AVHs appear to be associated with alterations in at least three networks, including a language network, attention center/perceptual network, and emotional network (Curčić-Blake et al., 2015), which may manifest as disturbances in language production, auditory processing, and language perception (Kubera et al., 2014; Wolf et al., 2012). In patients with BD and a history of AVHs, one report showed increased connectivity between the right dorsolateral prefrontal cortex and Broca's area, and the left superior-middle temporal gyrus and the bilateral anterior cingulate cortex, and decreased connectivity between the superior-middle temporal gyrus and the bilateral supplementary motor area (Sprooten et al., 2009).

5.3. Functional MRI

Recent functional MRI (fMRI) studies in patients with schizophrenia experiencing AVHs have looked beyond activation in specific regions of the brain into alterations in cortical networks. The findings confirmed that AVHs in patients with schizophrenia are associated with dysfunctions affecting the linguistic information processing network, cognitive control/execution function network, and attention network

(Hugdahl 2017). A meta-analysis found significantly increased activation likelihoods in bilateral neural networks, including Broca's area and the anterior insula, precentral gyrus, frontal operculum, middle and superior temporal gyri, inferior parietal lobule, and hippocampus/parahippocampal region, in patients with schizophrenia who experienced AVHs (Jardri et al., 2011). Other studies showed that patients with schizophrenia who experienced "intrusive, self-uncontrollable" AVHs had abnormalities in task-related activation. In patients performing a task requiring inner speech processing during functional brain scanning, there was a reduced connectivity between Broca's and Wernicke's areas, as well as reduced input from the temporal lobe to the frontal lobe, suggesting a compromised language information network, at least in the task performing state (Ćurčićblake et al., 2013). In patients performing a metrical stress evaluation task, there were activation-level abnormalities in the insula cortex, anterior cingulate cortex, angular gyrus, inferior frontal gyrus, and parahippocampal gyrus, which are important components of networks associated with cognitive control and execution, attention assignment, memory, and emotion (Vercammen et al., 2011) (Raij and Mholi 2009).

5.4. Electroencephalography

Electroencephalography is a common method used in the clinic to record spontaneous electrical activity in the brain and is valuable for the diagnosis of brain disorders (Jellinger 2011). Findings from studies using electroencephalography indicate that an excitatory-to-inhibitory (E/I) imbalance related to disturbed N-methyl-D-aspartate receptor (NMDAR) functioning and may be associated with an underlying altered connectivity and AVHs in schizophrenia. NMDAR antagonists, such as ketamine, induce an E/I imbalance and are known to elicit schizophrenia-like symptoms (including AVHs) in healthy volunteers, depending on the ketamine dose. In a single-blind, randomized, placebo-controlled crossover study, healthy participants were administered ketamine to elicit hallucinations. Psychiatric symptoms were evaluated by the Positive and Negative Syndrome Scale (PANSS) and the Altered State of Consciousness (5D-ASC) questionnaire. At the same time, 64-channel electroencephalography was used to detect the functional connectivity between auditory cortices. The findings showed that the occurrence of AVHs under ketamine administration was associated with altered interhemispheric gamma-band connectivity during the perception of left ear syllables(Stephanie et al., 2018).

5.5. Arterial spin labeling imaging

Arterial spin-labeling (ASL) technology, including both continuous and pseudocontinuous ASL, has become a major approach in studying the characteristics of cerebral blood flow in psychiatric patients, although limited research using ASL has been applied to AVHs. Homan et al. reported that schizophrenic patients who experienced AVHs had increased blood perfusion of the superior temporal gyrus. Although repetitive transcranial magnetic stimulation (TMS) relieved the patients' hallucinations, increased blood flow to the superior temporal gyrus persisted (Homan et al., 2012; Philipp et al., 2013), consistent with previous single-photon emission computerized tomography findings (Suzuki et al., 1993).

6. Interventions for AVHs

6.1. Antipsychotics

Commonly, patients with hallucinations have elevated levels of dopamine synthesis and release (Brisch et al., 2014). Antipsychotics, the first-line treatment for hallucinations, can block dopamine receptors, thereby attenuating the abnormalities of dopamine metabolism (Howes et al., 2012). A systematic review (n = 36 studies and 1263 patients) showed positive effects of both typical and atypical antipsychotics on AVHs in patients with BPD (Slotema et al., 2018), although some patients had refractory hallucinations that were resistant to the antipsychotics.

6.2. Transcranial magnetic stimulation

TMS is a noninvasive neurostimulation procedure in which a changing magnetic field is used to trigger the flow of an electric current in a target brain region. In fMRI, auditory hallucinations in patients with schizophrenia were associated with activation in the inferior frontal/insular, anterior cingulate, and temporal cortex bilaterally (with greater responses on the right), the right thalamus and inferior colliculus, and the left hippocampus and parahippocampal cortex (Shergill et al., 2000). Accordingly, TMS can reduce the excitability of the temporoparietal cortex (Lefaucheur et al., 2014). In a randomized controlled study in patients with schizophrenia, AVH symptoms, evaluated with the Psychotic Symptom Rating Scales and the Auditory Hallucination Rating Scale, were improved following continuous theta burst stimulation with 1 Hz of repetitive TMS for 10 days. On the PANSS, both positive and general subscores were decreased following treatment, while negative subscores were not (Koops et al., 2015). Nathou et al. found that TMS efficacy in patients with schizophrenia was dependent on the distance from the scalp to the cortex and the gray matter density in the temporal and frontal areas (Nathou et al., 2015).

6.3. Transcranial direct current stimulation

Transcranial direct current stimulation is a noninvasive, neuromodulatory intervention that is safe and well tolerated by human subjects. In transcranial direct current stimulation, a low-intensity direct current (2 mA) is applied via scalp electrodes to create polarity-specific neuromodulation in focal brain regions (Nitsche et al., 2008). In a randomized, double-blind, controlled clinical trial, 5 days of twice-daily sessions (but not sham stimulation) significantly reduced AVH scores in patients with schizophrenia (Bose et al., 2017).

6.4. Cognitive behavioral therapy (CBT)

CBT is effective for decreasing AVHs in patients with schizophrenia (Turner et al., 2014). In a large single-blind, randomized controlled trial, patients with schizophrenia, schizoaffective disorder, or mood disorders who had experienced harmful command hallucinations for at least 6 months received either a CBT intervention plus treatment or treatment alone. At 18 months after randomization, 46% of the patients in the treatment only group were fully complying with hallucinated voices, whereas only 28% of those in the CBT plus treatment group did so. These findings suggest that CBT could lead to a meaningful decrease in risky behaviors related to commanding hallucinations (Birchwood et al., 2014). Another study reported CBT-mediated improvements in patients with BPD regarding the power attributed to hallucinated voices, the perceived need to comply, and levels of concomitant distress and depression (Trower et al., 2012).

6.5. Virtual reality therapy

Because many patients with schizophrenia who experience AVHs do not respond to face-to-face therapy and antipsychotic drugs (Harrow et al., 2014), there is an increasing demand for novel treatment approaches. Virtual reality technology can be used to place people in a three-dimensional space in which they can move and interact with targets. Users can interact with, and even alter, the virtual environment through a sensor device. Immersive perception and experiences are created in which the user's feelings and actions mimic those experienced in the real world (Diemer et al., 2015).

Virtual reality treatment is a CBT-based intervention (Fernándezcaballero et al., 2017) conducted in a computer-generated

Table 1
Summary of AVH interventions in patients with psychiatric disorders and healthy individuals.

Pharmacological treatment	Conventional treatment	Unconventional treatment
Antipsychotics	Cognitive behavioral therapy Virtual reality treatment	Transcranial magnetic stimulation Transcranial direct current stimulation

virtual environment such that patient responses are under control. The patient is encouraged to manage his/her symptoms through a human-computer interaction.

In a pilot clinical trial of virtual reality therapy, patients with schizophrenia and refractory AVHs were randomly assigned to a virtual reality-assisted therapy (VRT) group or a treatment-as-usual (TAU) group. Patients in the VRT group underwent one avatar creation session and six 45-min therapy sessions. First, the patient was asked to create an avatar associated with a dominant AVH voice. In sessions 1–3, patients were encouraged to enter a dialogue with the avatar. In session 4, patients were encouraged to express themselves and consider the personal characteristics of the avatar. In the last sessions, patients were encouraged to apply what they had learned in the earlier sessions. The VRT group showed a decrease in distressing hallucination symptoms, generally diminished schizophrenia and depressive symptoms, and an improved quality of life (Du et al., 2018).

7. Discussion

This review aimed to describe the clinical features and imaging characteristics of AVHs and AVH interventions in patients with psychiatric disorders and in healthy individuals. The findings showed an overlap in the phonemic features of AVHs among patients with various psychiatric disorders and healthy individuals. In fact, there appears to be a continuum in the phonemic features of AVHs from healthy individuals to patients with psychiatric disorders. A recent systematic review revealed that the subjective experiences associated with AVHs (e.g., loudness and spatial orientation of sounds) were similar in nonclinical individuals who experienced auditory hallucinations and patients with AVHs requiring intervention (Baumeister et al., 2017). However, the patients with psychiatric disorders experienced a higher frequency of AVHs, more negative content, and less control of the auditory hallucinations. There were differences in the suffering and emotional response to hallucinations between the healthy individuals and patients with psychiatric disorders. Despite this, the risk factors (e.g., family history and trauma in childhood) for AVHs were similar between the groups (Baumeister et al., 2017). Some researchers have compared the phenomenological characteristics of AVHs across different patient populations, making several notable similarities. Patients with schizophrenia and BPD generally hear sounds of the same gender that consist of argumentative speech, persistent comments, and accusatory voices (Larøi et al., 2012). In addition, the phenomenological characteristics of AVHs in patients with PTSD are similar to those in patients with schizophrenia (Table 1).

There is also a continuum in the imaging features of AVHs from healthy individuals to patients with psychiatric disorders. In a study by Lutterveld et al. comparing brain structure imaging results across nonclinical individuals who experienced auditory hallucinations, patients with AVHs requiring intervention, and healthy controls without hallucinations, they observed that the thicknesses of the left adjacent central lobule, left iliac crest, right fusiform gyrus, and right axillary cortex were significantly reduced in the clinical group relative to the nonhallucinating controls. Meanwhile, the cortical thickness in nonclinical individuals was intermediate between the healthy controls and patients (Lutterveld et al., 2014). Diederen et al. conducted a functional magnetic resonance study of “symptom capture” in demographically matched groups of healthy individuals with AVHs and psychiatric patients. The results showed that the two groups had similar patterns of brain activity during the occurrence of AVHs (Diederen et al., 2012).

8. Conclusion

AVHs in clinical and nonclinical populations have some similar phenomenological features. AVH symptoms have been related to alterations in particular brain structures and disturbances in brain function, blood flow, and metabolism. Antipsychotic medications can reduce hallucinations in patients with psychiatric disorders. Brain stimulation and CBT can also help to alleviate AVHs and its associated symptoms. Virtual reality therapy represents a new and promising approach for the treatment of hallucinations. The severity of AVHs varies from person to person, but there appears to be a continuum in the phenomenological features and imaging characteristics of AVHs from healthy individuals to patients with psychiatric disorders. Further studies are required to understand the development and core characteristics of AVHs within the context of our knowledge of their phenomenological and imaging features.

Conflicts of interest

None.

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Supplementary materials

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