



Comparison of auditory hallucinations across different disorders and syndromes

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Practice points

- Auditory hallucinations in psychiatric disorders
 - The co-occurrence of psychotic symptoms such as delusions and formal thought disorder points towards the existence of a psychiatric disease.
 - Comorbid negative symptoms suggest a schizophrenia spectrum disorder.
 - Age of onset can be a coarse but valuable indicator for distinguishing between hallucinations occurring in the context of neurological and psychiatric disorders. The former are assumed to start at an advanced age, whereas the latter typically begin in late adolescence or early adulthood.
- Auditory hallucinations in healthy individuals
 - If social/occupational functioning is undiminished, hallucinations may not be part of any disorder or syndrome.
- Auditory hallucinations in neurological disorders
 - Experiencing mostly visual hallucinations suggests a neurological disorder, with the exception of temporal epilepsy.
 - Comorbid neurological symptoms (e.g., Parkinsonism or seizures) are key features in the differential diagnosis.
- Release hallucinations in sensory deprivation
 - In cases of hearing loss, auditory hallucinations may be release phenomena.
 - Hallucinations that are unilateral in nature suggest possible release hallucinations.
- Conclusion
 - Major clues in the differential diagnosis are the presence or absence of visual hallucinations and comorbid symptoms, such as delusions, hallucinations, formal thought disorder, Parkinsonism or seizures.
 - In older patients, (comorbid) delirium should always be considered.

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SUMMARY Auditory hallucinations can be experienced in the context of many different disorders and syndromes. The differential diagnosis basically rests on the presence or absence of accompanying symptoms. In terms of clinical relevance, the most important distinction to be made is between auditory hallucinations occurring in the context of psychotic disorders and those that are due to a somatic disorder. Auditory hallucinations are also quite common in otherwise healthy individuals and are therefore not necessarily disease-related. As auditory hallucinations are often accompanied by hallucinations in other modalities, pinpointing the modality in which hallucinations are experienced most frequently may provide a first – albeit coarse – indication of whether the auditory hallucinations are part of a neurological disorder (mainly visual), a psychiatric disorder (mainly auditory), an ear disorder (mainly auditory) or whether they occur in the absence of any disorder (mainly auditory). Epilepsy is the most important exception to this coarse differentiation. Another traditional distinction between hallucinations occurring in the context of neurological and psychiatric disorders is that the former are assumed to start at an advanced age, whereas hallucinations in the context of psychiatric disorders typically begin in late adolescence or early adulthood. Although there are many exceptions to this rule of thumb – as in psychotic depression, late-onset schizophrenia and epilepsy – age of onset can still be a valuable clinical indicator. The content of auditory hallucinations is notoriously unreliable for differential diagnosis and the safest way to an accurate diagnosis rests with the detection of psychiatric and somatic comorbid symptoms.

Auditory hallucinations (AHs) can be experienced in the context of many different disorders and syndromes. The differential diagnosis basically rests on the presence or absence of accompanying symptoms. In terms of clinical relevance, the most important distinction to be made is that between AHs occurring in the context of psychotic disorders (designated in the DSM-IV-TR as schizophrenia, schizoaffective disorder, schizophreniform disorder and brief psychotic disorder) and those that are due to a somatic disorder (i.e., neurological disorder, general medical disorder or even a hearing disorder, as discussed later). It should be noted, however, that AHs are also quite common in otherwise healthy individuals, and that they are therefore not necessarily disease-related. The present paper will focus on the differential diagnosis of AHs and compare their phenomenological characteristics in the context of psychosis, Parkinson's disease (PD), delirium, dementia, epilepsy, hearing disorders and psychoactive substance abuse, as well as in the absence of any pathology.

AHs in psychiatric disorders

In clinical practice, AHs are associated foremost with schizophrenia spectrum disorders, in which they occur in at least 70% of cases [1]. Many clinicians have the impression that hallucinations are ubiquitous in schizophrenia, but as a certain percentage of patients deny these experiences, the reported prevalence is usually approximately 70%.

Patients thus diagnosed also tend to experience hallucinations in other sensory modalities, such as the visual, tactile, olfactory and gustatory ones, but within this diagnostic group, AHs are far more common than any other type of hallucination [2]. Traditionally, this is considered an important indicator for diagnosis: while visual hallucinations tend to be more prevalent in neurological disorders, AHs tend to prevail in psychiatric disorders. However, since between 38 and 57% of all voice-hearers diagnosed with a schizophrenia spectrum disorder also experience visual hallucinations at some point in their lives [3], this indicator should not be given too much weight. Moreover, it should be noted that hospitalized patients in Africa and Asia who are diagnosed with schizophrenia tend to experience more visual hallucinations [4].

Whenever a patient presents with AHs, the first step in the diagnostic process should be to assess their phenomenological characteristics, and to determine whether they fulfill the criteria of hallucinations proper (rather than those of obsessive thoughts, ruminations or thought insertions, for example). Second, one should question the patient for hallucinations in any of the other sensory modalities. Pinpointing the modality in which they are experienced most frequently, and in which they are indicated as the most severe, may well provide a first – albeit coarse – indication of whether we are dealing with a neurological disorder (mainly visual hallucinations), a psychiatric disorder (mainly AHs)

or an ear disorder (mainly AHs), or whether they occur in the absence of any disorder (mainly AHs). Another traditional distinction between hallucinations occurring in the context of neurological and psychiatric disorders is that the former are assumed to start at an advanced age, whereas hallucinations in the context of psychiatric disorders typically begin in late adolescence or early adulthood. Of course, there are many exceptions to this rule of thumb – such as in psychotic depression and so-called ‘late-onset schizophrenia’ – but nevertheless, age of onset can sometimes be a valuable clinical indicator.

When occurring in the context of psychiatric disorders, the presence and severity of AHs strongly correlates with the presence of delusions, as these two symptoms have a tendency to co-occur. This co-occurrence has been demonstrated in multiple factor analyses on symptoms in schizophrenia [5–7]. The combination of hallucinations and delusions has been referred to as the reality distortion syndrome. The reality distortion syndrome is one of the independent dimensions in the three-syndrome classification of schizophrenia symptoms. The other two are disorganization and negative symptoms, which are discussed later.

If AHs constitute the sole or dominant type of hallucination, the next step should be to search for delusions, as they are part of the same symptom dimension. Severe delusions can usually be established quite easily, especially when the patient is preoccupied by them and brings them up on numerous occasions. However, some patients – especially those suffering from paranoia – may try to conceal their idiosyncratic beliefs or bluntly deny their existence. Mild, subclinical delusions are often more difficult to establish, especially when they present in the form of mild paranoia or an inclination towards magical beliefs. An instrument that may be helpful in detecting such subclinical delusional tendencies is the Peters Delusion Inventory [8], which taps into mild ideas of reference, magical beliefs and paranoid ideations. Another dimension of the three-syndrome classification is formal thought disorder [5–7]. Severe formal thought disorder, similar to severe delusion, can hardly be missed in clinical practice. In its most extreme form – called incoherence or Wortsalat – sentences lack a proper grammatical structure and are therefore unintelligible. Milder cases may be less obvious, however, and may only manifest when the patient is confronted with rather complex

questions or interviewed at considerable length. A striking feature of such milder cases is that the interviewer may find himself repeating the same question, meanwhile failing to understand the answer or being puzzled by the direction in which the conversation continues. In such cases, the interviewer may blame themselves for not paying enough attention, but usually situations such as these hint in the direction of a subtle formal thought disorder. An important note is that formal thought disorder can be subdivided into positive formal thought disorder (alogia) and negative formal thought disorder (disorganized speech). It was found by Sommer *et al.* that positive formal thought disorder is not specifically associated with AHs, as it was only found in schizophrenia patients with AHs, and not in nonpsychotic subjects with AHs [9]. However, negative formal thought disorder was found in both populations and has therefore been associated with AHs [9]. The distinction between positive and negative formal thought disorder may be an important clue in the diagnostic process. If delusions or negative formal thought disorders are present, a primary psychotic disorder is the most likely clinical diagnosis. Yet on the basis of these symptoms alone one cannot rule out the presence of a delirium or intoxication. In order to do so, auxiliary investigations would obviously be necessary.

When delusions and other psychotic symptoms are rather mild, and the AHs cause no significant impairment of functioning, there may be insufficient criteria to establish any diagnosis at all. If the level of daily functioning is impaired, however, another important step is to determine the presence or absence of negative symptoms, which is the third dimension in the three-syndrome classification of schizophrenia symptoms (i.e., avolition, loss of motivation and initiative, low level of energy and lack of social engagement). If negative symptoms are present in addition to AHs, delusions and formal thought disorder, the most likely diagnosis is a schizophrenia spectrum disorder (i.e., schizophrenia, schizophreniform disorder or schizoaffective disorder).

■ AHs in organic psychosis

Psychotic symptoms, including AHs, can also be caused by organic disorders. If so, the syndrome at hand is referred to as ‘organic’ or ‘secondary’ psychosis [10]. Organic psychosis is diagnosed in 3% of all patients presenting with psychotic symptoms [10]. Most psychiatric

hospitals employ routine screening methods to check for the causes of such psychoses, including virology tests for lues maligna and HIV infection and tests of calcium and hormone levels (to exclude thyrotoxicity and Cushing's disease). Other causes of organic psychosis include brain tumors, prion disease, hyperhomocysteinuria, 22q11 deletion syndrome, sarcoidosis and intracerebral arteriovenous malformations [11–14]. It is important to detect these organic cases of psychosis as their response to antipsychotic medication may be low and, more importantly, the underlying disorder may require urgent treatment.

■ AHs in affective psychosis

When AHs and delusions are present but negative symptoms are lacking, other diagnostic possibilities may be affective psychoses or borderline personality disorder (BPD). In mania or severe depression, formal thought disorder may also be present [15,16]. In affective psychosis, the psychotic symptoms are permanently accompanied by severe affective (i.e., depressive or manic) symptoms. In clinical practice, it may be hard to distinguish affective psychosis from schizophrenia spectrum disorders because many patients diagnosed with schizophrenia also display affective symptoms. Approximately 80% of the patients diagnosed with schizophrenia are familiar with depressive episodes, which – with hindsight – often preceded their first psychotic episode. But these affective symptoms can also co-occur with psychotic episodes or follow after the psychosis has subsided [17]. The mere co-occurrence of affective and psychotic symptoms is therefore insufficient to justify the diagnosis of affective psychosis. To fulfill the diagnostic criteria, it is crucial that the affective symptoms are severe and that they accompany the psychotic symptoms at all times. The mood-congruent nature of the content of AHs (e.g., “They tell me to jump off a bridge, and they are probably right because I am a bad person”) is an unreliable criterion, as this is also a common feature in schizophrenia spectrum disorders. Epidemiological data can sometimes provide an extra clue, as (unipolar) psychotic depression is more common in older patients (>50 years of age) who have experienced one or more prior depressive episodes [18], whereas a first psychotic episode in the context of a primary psychotic disorder is usually experienced in one's early 20s. To differentiate between bipolar disorder and

schizophrenia, epidemiological data are seldom helpful, and in some patients, the course of the illness must provide additional clues in order to arrive at a conclusive diagnosis. The more episodic occurrence of affective psychosis with relatively symptom-free periods can be a helpful distinction, as schizophrenia is usually accompanied by more chronic symptoms. According to the DSM-IV-TR, negative symptoms typically persist between episodes of positive symptoms. For example, disorganized speech tends to persist in schizophrenia, but not in mania [19]. Thus, the degree of persistence of negative symptoms can be useful in differentiating between affective psychosis and schizophrenia. However, co-occurrence of schizophrenia and depressive disorder not otherwise specified or bipolar disorder not otherwise specified is possible, which further complicates the diagnostic process.

■ AHs in BPD

BPD may not seem to be a likely diagnosis when a patient complains of AHs and delusions, yet a substantial percentage of BPD patients suffer from these two psychotic symptoms [20]. Although many textbooks suggest that psychotic symptoms occurring in the context of BPD tend to be mild and short-lasting, two recent studies indicate that this is not the case [20,21]. To differentiate between schizophrenia spectrum disorders, affective psychosis and BPD, the content and phenomenological characteristics of AHs are not very helpful. In all three disorders, AHs tend to present in the form of voices. These voices may have a derogatory content, issue commands or prohibitions and comment on the patient's actions and thoughts. In the majority of patients, the voices have a negative emotional content and tend to be experienced as distressing and frightening. A recent study found no differences in the content and phenomenological characteristics of AHs experienced by patients diagnosed with a schizophrenia spectrum disorder or with BPD [21]. However, as the main purpose of differential diagnosis is to serve as a signpost for adequate treatment, the failure to differentiate between these two disorders and affective psychosis is quite venial, as AHs in all three disorders tend to respond well to antipsychotic medication [22]; although, of course, patients diagnosed with affective psychosis need additional pharmacological treatment for their mood symptoms, as may BPD patients. In addition, patients with psychotic depression may

be candidates for electroconvulsive treatment, while schizophrenia patients are not.

AHs in healthy individuals

AHs are also experienced by a significant minority of otherwise healthy individuals. Some 15% of the healthy population report being familiar with the hearing of voices [23]. Most of them hear these voices only rarely (e.g., after periods of sleep deprivation or during times of severe distress). In others, AHs may occur weekly or even daily, and be accompanied by subclinical delusions [24] and formal thought disorder [9]. The latter group cannot be sharply distinguished from the schizophrenia spectrum group described above, and this group is better conceptualized as lying at the other end of the spectrum. The spectrum as a whole starts with the group of healthy subjects who hear voices on relatively rare occasions and includes the group of healthy subjects with frequent AHs and subclinical levels of paranoid ideation, paranormal beliefs or formal thought disorder, the group of individuals diagnosed with schizotypal personality disorder and finally the group of individuals diagnosed with full-blown schizophrenia or schizoaffective disorder.

While healthy hallucinating individuals can also experience additional psychotic symptoms, including hallucinations in any of the other sensory modalities, negative symptoms are absent [24], in contrast to patients diagnosed with schizotypal personality disorder or schizophrenia/schizoaffective disorder. Similar to all individuals who experience AHs, they seek to explain those puzzling symptoms in accordance with their personal and sociocultural beliefs. As a consequence, they may end up engaging in paranormal or spiritual activities and hold jobs, for example, as a magnetizer, paranormal healer, reiki master or medium. People with a religious background may well seek – and obtain – special posts within their religious communities. In the Muslim world, the hearing of voices is frequently attributed to djinns, which are described in the Quran as powerful spirits created by Allah out of smokeless fire [25]. Medical practitioners, and especially western medical practitioners, tend to hear precious little from their Islamic patients about those djinns. What we know is that many of those patients, who – by western biomedical standards – may fulfill the criteria of a schizophrenia spectrum disorder go on to consult religious healers for years on end before ever seeking help from a physician. When they finally

do seek a physician's help, they tend to remain reticent about their culturoreligious explanations. Another group of Islamic voice-hearers who are completely hidden from the view of mental health practitioners are those who experience predominantly benevolent AHs. Based on the distribution of AHs in the general population and on the conviction of some Muslims that djinns are not only capable of haunting or possessing people, but also of helping them to obtain certain goals that they pursue, as well as accompanying them and guiding them through the hardships of life, it is safe to assume that there is a group of substantial yet unknown size that has no reason whatsoever to seek help for the voices that they hear, and thus remains off the radar of mental health practitioners [26].

AHs in healthy individuals are usually not distressing, and in the majority of cases they have a positive emotional content, typically providing useful warnings or words of comfort [27]. Most of those healthy individuals do not require any form of treatment for the voices they hear, but when they do, it may suffice to provide them with an explanation, and give them the reassurance that the hearing of voices is not necessarily a sign of mental illness or possession.

Differentiating the AHs experienced by healthy individuals from those experienced by individuals diagnosed with a schizophrenia spectrum disorder is not always possible, as they constitute a continuum, rather than two separate entities, but in accordance with the DSM criteria, the presence or absence of social and occupational dysfunction should be given the most weight in such cases. The differential diagnosis with sensory deprivation is also important (see below), because that type of AH also occurs in otherwise healthy subjects, but fails to respond well to antipsychotic medication.

AHs in neurological disorders

■ AHs in PD & dementia with Lewy bodies

Psychotic symptoms are quite common in patients with PD and Parkinson-plus disorders such as progressive supranuclear palsy, with reported lifetime prevalence rates of up to 80% [28]. The psychotic symptoms at hand are usually hallucinations, and these are typically visual in nature, less commonly auditory, and rarely involving any of the other sensory modalities. Cross-sectional studies show that visual hallucinations occur in approximately a third of PD patients, whereas up to three-quarters of all PD patients develop

them over a 20-year period [29]. AHs are present in up to 20% of these cases [30]. These symptoms are often due to dopaminergic intoxication as a result of PD medication; however, as discussed below, there are also disease-related factors that influence the occurrence of hallucinations in PD. Prospective longitudinal cohort studies show that hallucinations tend to persist and worsen in individual patients, and that their prevalence increases over time [29]. Hallucinations and other psychotic symptoms can have substantial psychosocial effects and constitute the main reason to place PD patients in nursing homes [30].

In dementia with Lewy bodies (DLB), a condition closely associated with PD, the prevalence of hallucinations and other psychotic symptoms is even higher, although mainly for visual hallucinations. Such patients almost without exception present with visual hallucinations, while pure AHs are extremely rare. If present, AHs tend to be encountered in the context of complex hallucinations (i.e., hallucinated persons speaking to the patient) [31]. Hallucinations experienced in the context of PD and DLB tend to be less distressing and frightening than those in psychiatric disorders. A frequent type of hallucination in PD and DLB is the hallucinated presence of a familiar visitor (i.e., an old friend, a spouse or even a dog). When the hallucinations are complex, patients may engage in conversations with these 'visitors'. Delusions occur in approximately 5–10% of drug-treated PD patients, and are considerably more disruptive than hallucinations, although they are usually less severe than in psychiatric disorders. Typical forms of delusion in PD and DLB include the delusional misidentification of a person and the reduplication of persons [32]. Capgras syndrome is also prevalent in those disorders, as well as delusions of theft, spousal infidelity and abandonment by the family [33]. There is no solid literature tapping into the presence of formal thought disorder in PD and DLB, but our clinical experience suggests that this may be present as well.

Our understanding of the pathophysiology of psychosis in PD has expanded dramatically over the past 15 years, from an initial interpretation of symptoms as pure dopaminergic drug adverse effects to the current view of a complex interplay of extrinsic and disease-related factors. These include central dopaminergic overactivity and an imbalance of dopaminergic and cholinergic neurotransmission, dysfunction of the visual pathways, including specific

PD-associated retinopathy and functional alterations of the extrastriate visual pathways, alterations of brainstem sleep–wake and dream regulation and impaired attentional focus [30]. The most important extrinsic factor, however, is medication. While hallucinations can be triggered by amantadine and anticholinergics, they are more commonly experienced after changes in dopaminergic medication. In the latter category, dopamine agonists have a greater potential to induce hallucinations than L-dopa [34].

In contrast to AHs in psychiatric disorders, the treatment of hallucinations in PD and DLB involves patient-initiated coping strategies, a reduction of anti-Parkinson medication and cholinesterase inhibitors. Augmentation with low doses of atypical antipsychotic medications can be tried, but is likely to increase the motor symptoms [35].

Differentiating between schizophrenia spectrum disorders and PD should not be difficult, as the onset of AHs in PD and DLB is much later in life, and mostly secondary to the visual hallucinations. Unipolar psychotic depression can also occur at advanced age, and may present with visual hallucinations and AHs, as well as motor retardation [36], thus mimicking PD with hallucinations. In such cases, the differential diagnosis can be difficult, as PD patients frequently suffer from comorbid depression, while patients with psychotic depression can suffer from quite severe motor retardation. If hallucinations accompany PD, they usually occur after the onset of motor symptoms, which facilitates the diagnostic process. However, in DLB, this may not always be the case, with hallucinations constituting the first sign of disease [37]. In some cases, the correct diagnosis cannot be made until the moment that the illness has fully developed.

Another challenge for differential diagnosis concerns the differences between AHs occurring in the context of PD or DLB and AHs in the context of delirium (see below), because the somatic disease causing the delirium may not always be clear. Hallucinations and delusions in the context of delirium typically wax and wane over the course of 24 h, with more severe symptoms occurring in the evening and night. However, in PD and DLB, hallucinations may also occur predominantly in the afternoon and evening, when daylight is fading (crepuscular hallucinations [38]). Disturbances of consciousness and orientation are characteristic of delirium, but may be missed when occurring only at

night. If typical Parkinsonian motor, gait and balance symptoms can be detected, this provides a significant clue, but even then, delirium cannot be ruled out completely. To make things even more complex, PD and DLB can co-occur with delirium, as PD and DLB patients are more vulnerable to developing a delirium. There are no significant differences in the severity of hallucinations, delusions, psychomotor behavior or sleep–wake cycle disturbances among patients with both dementia and delirium and patients with only delirium. However, disturbances in consciousness (arousal and awareness), as well as impairments in multiple cognitive domains, tend to be significantly more severe in patients with delirium superimposed on DLB [39]. In cases of doubt, establishing a somatic cause of the hallucinations should be the first priority, with the aid of urine and blood tests to detect common infections, dehydration and electrolyte disturbances. In such cases, misdiagnosis is inexcusable, as antipsychotic medication may improve AHs occurring in the context of delirium, but could aggravate PD and DLB motor symptoms. Cholinesterase inhibitors, on the other hand, can improve AHs in PD and DLB patients, whereas they tend to aggravate the symptoms of delirium [40]. More importantly, when the underlying cause of delirium is not discovered and treated, severe illness and even death may follow.

■ AHs in Alzheimer’s dementia

In Alzheimer’s disease (AD), the occurrence of psychosis in 30–50% of cases has serious consequences for both patients and caregivers [41]. In contrast to DLB, hallucinations usually occur later in the course of AD [42]. Visual hallucinations tend to prevail, but AHs are not uncommon [43,44]. Both hallucinations and delusions in AD predict a faster rate of cognitive decline, functional impairment and institutionalization [45]. The optimal type of treatment for hallucinations in AD is still elusive. Interventions that optimize environmental and interpersonal factors can be helpful [46] and should be attempted in all cases, although their overall effectiveness and applicability are not entirely clear. Cholinesterase inhibitors such as donepezil may have a beneficial effect on the hallucinations, with a relatively mild side-effect profile [47]. In a similar vein, memantine has been shown to be more effective than placebo treatment without causing any disturbing side effects [48]. Although antipsychotic medication can have a positive

effect on hallucinations in dementia, several reports issue warnings against the excess risk of morbidity and even death associated with its use in older patients [49].

The differential diagnosis of AHs in the context of AD on the one hand, and AHs in the context of delirium on the other, may well be the most challenging. A rapid onset of psychotic symptoms may hint in the direction of delirium, because the development of psychosis in AD tends to be more gradual. However, confusion may also occur in the context of DLB, concurrent with AHs, which demonstrates once more that not all dementias can be diagnosed as strictly AD or DLB [42].

■ AHs in Huntington’s disease

Another type of dementia that frequently features AHs is Huntington’s disease [50], an inherited form of dementia that tends to manifest at approximately 50 years of age in the form of involuntary movements of the face, head and limbs. In contrast to AD, hallucinations may occur early in the course of Huntington’s disease, and may, in some cases, constitute the sole presenting symptom [51]. Other psychotic symptoms, especially delusions, generally coexist.

■ AHs in delirium

Delirium is an acute neuropsychiatric syndrome, by definition resulting from an organic disease, which is characterized by psychotic symptoms such as hallucinations and delusions in the presence of decreased attention, fluctuating consciousness and other cognitive dysfunctions. It is very common in patients admitted to intensive care units, with a reported cross-sectional frequency of 32% [52], and a marked association with poor prognosis and increased mortality [53].

Hallucinations occurring in the context of delirium are typically visual in nature, but they can also be complex and thus include the auditory modality [54]. Patients with delirium typically experience zoopsia (i.e., visual hallucinations consisting of animals such as insects or spiders) and visual hallucinations in which blood or knives play an important role [55]. Patients are usually upset by these hallucinations, and tend to react upon them by pulling apart intravenous lines and oxygen meters, or tearing off their pajamas and bed clothes. Suspicious and paranoid delusions frequently co-occur.

The only causal treatment of delirium is the improvement of somatic health. Sometimes this

can be accomplished by relatively simple means (e.g., by restoring the volume of the blood plasma in dehydration or by treating a urinary tract infection). However, delirium frequently affects severely ill patients suffering from multiple somatic conditions such as cardiac failure complicated by cardiac asthma and diabetes, as well as other combinations that can be very hard to treat.

In such cases, the symptomatic treatment of hallucinations and other symptoms of delirium should commence with measures aimed at improving the patient's circadian rhythm and orientation. Symptomatic pharmacological treatment should preferably consist of haloperidol or olanzapine, as recommended by the latest guidelines from NICE [56].

The differential diagnosis with hallucinations occurring in AD, PD and DLB may primarily rely on the presence of fluctuating consciousness and the rapid onset of symptoms, which are characteristic of delirium. Yet in severe cases of dementia, the circadian rhythm may be disturbed, which may thus mimic the fluctuation of consciousness. Hallucinations occurring in the context of delirium are usually experienced as frightening, which is generally not the case in PD and in dementias, but this is an unreliable criterion. As delirium can co-occur with PD, AD and DLB, possible somatic causes of delirium should be investigated in all cases of doubt.

■ AHs in epilepsy & migraine

The reported cross-sectional incidence of hallucinations and other psychotic symptoms in epilepsy is 3.3%, and in temporal lobe epilepsy is as high as 14% [57]. These symptoms can occur shortly before a seizure (i.e., as an epileptic aura), during (ictal hallucination) or after an epileptic seizure (postictal hallucination) and even independently of any motor seizures. Ictal hallucinosis is considered relatively rare, although patients may well experience these hallucinations but not remember them. Postictal hallucinosis comprises some 25% of the hallucinatory episodes in epileptic patients. As post- and inter-ictal psychotic episodes resemble those in patients diagnosed with schizophrenia, they are also designated as 'schizophrenia-like psychoses of epilepsy'. In contrast to hallucinations in other neurological disorders, hallucinations occurring in the context of epilepsy are frequently in the auditory modality (although they can also occur in any of the other sensory modalities). They may co-occur with

delusions, and possibly also with positive formal thought disorder, in which case the similarity with primary psychotic disorders is high.

The treatment of ictal as well as post- and inter-ictal hallucinations should start with minimizing any medication capable of inducing these symptoms. Various antiepileptic drugs, such as phenobarbital, zonisamide, levetiracetam and gabapentin, are known for their potential to induce hallucinations [58]. In such cases, dose reduction or a switch to another antiepileptic drug may lead to a relatively quick cessation of the hallucinations. When antiepileptic drugs cannot be reduced or traded, or when such an intervention is unsuccessful, antipsychotic medication is the next therapeutic step. Clozapine, olanzapine and chlorpromazine should be avoided because of their epileptogenic properties. Fluphenazine, haloperidol, pimozide and risperidone are antipsychotics with relatively low epileptogenicity, making them very useful in treating epileptic patients [59].

The differential diagnosis is notoriously difficult when the symptoms at hand mimic a primary psychotic disorder, or when there is no temporal correlation between epileptic seizures and psychotic symptoms, which is frequently the case. In such cases, diagnosis depends heavily on the presence of epileptic seizures, which can either be grand mals, partial attacks or absences. EEG recordings may help to verify the presence of seizures, but cannot rule out epilepsy when epileptic activity cannot be captured during the recorded period. A sleep deprivation EEG may help in some cases, but even then certainty may be unobtainable. While epilepsy and psychosis frequently co-occur, a causal relationship between the two can only rarely be detected. When such a relationship is absent, seizure control may not help to diminish the psychotic symptoms, which will then need to be treated independently.

Similar to epilepsy, migraine also tends to be accompanied by auras. Most auras occurring in the context of migraine are visual in nature, but tactile and auditory ones also occur [60]. If an aura is auditory in nature, it tends to consist of nonverbal sounds such as single tones or a whistling sound, as in tinnitus, and less frequently of more complex sounds such as music or speech. However, it should be kept in mind that the AHs occurring in the context of migraine are rare, that they tend to be stereotypic and repetitive in nature and that they are typically – although not invariably – followed by a headache.

Release hallucinations in sensory deprivation

Visually impaired patients may experience complex visual hallucinations, a condition known as ‘Charles Bonnet syndrome’. Similarly, individuals with hearing loss may develop AHs consisting of music, voices or other sounds. Although the auditory variant of Charles Bonnet syndrome is less well known, it is just as frequent. It is believed that hallucinations occurring in the context of hearing loss are actually release phenomena due to a deafferentation of the auditory association areas of the cerebral cortex, a process capable of yielding so-called ‘phantom percepts’ [61]. Cognitive defects and social isolation may act as additional risk factors. Release hallucinations generally affect the elderly, as well as women more frequently than men [62]. Occasionally, this type of AH can also be diagnosed in younger persons who have suffered an acoustic trauma (i.e., disk jockeys, musicians or pavers). Auditory release hallucinations lie on a continuum with tinnitus, and can consist of pure sounds, but also of strings of words or sentences. However, this type of hallucination generally takes the form of music, usually familiar songs such as ‘Happy Birthday’, nursery rhymes or well-known church songs [63]. A classical case is the elderly lady who asks her neighbors when they will cease singing. Yet one cannot rely on the musical character of AHs alone for diagnostic purposes, as musical hallucinations can also occur in the context of psychiatric disorders. Hallucinations in the context of hearing loss may also be nonmusical and verbal. In these cases, patients may hear murmurs or speaking, frequently without understanding the meaning. The typical malevolent emotional content of hallucinations in psychotic disorders is not observed in these patients.

Patients who comprehend the unrealistic nature of their release hallucinations tend to be less severely affected by them, although they may still be distressed by the fear of imminent insanity. Reassurance and an explanation that the auditory percepts do not imply any kind of mental illness may have a powerful therapeutic effect [61]. Further therapeutic steps are not always necessary, because release hallucinations may cease either spontaneously or upon the termination of social isolation. If warranted and possible, the treatment of first choice is the restoration of hearing function (e.g., by cleaning the meatus externus or applying hearing

aids) [64]. In addition, one may consider the optimization of auditory stimuli. When interventions such as these are unsuccessful, pharmacological treatment may be considered, although the advantages do usually not outweigh the disadvantages, as side effects may be severe in the elderly. Both antipsychotic [65] and antiepileptic drugs have been reported to be effective in case reports and open-label case series [65,66], but unsuccessful attempts are probably under-reported.

The differential diagnosis may be facilitated by the fact that this type of hallucination does not tend to be accompanied by any other type of psychotic symptom, such as delusions or formal thought disorder. Patients frequently, but not always, have insight into the hallucinatory nature of their experiences. Diagnosis can be facilitated further by audiological testing. Release hallucinations may be more severe at the side where the hearing loss is most pronounced, but bilateral AHs also occur. If the hallucinations are unilateral and restricted to the side of hearing loss, a diagnosis of release hallucinations is most likely. However, differentiating between release hallucinations and a psychiatric disorder remains important, as antipsychotic medications are seldom effective. Moreover, misdiagnosis of this type of AH may forestall a valuable chance to restore the patient’s hearing. It should be noted, however, that it is also possible for sensory deprivation due to hearing loss to co-occur with other diseases associated with AHs. For example, patients with schizotypal personality may be more prone to develop this type of hallucinations upon hearing loss.

AHs in psychoactive substance addiction

Psychotic symptoms such as AHs may be a direct effect of abuse of psychoactive substances [67]. These symptoms highly overlap with the symptoms observed in schizophrenia. Differentiating between the two is important, as AHs and other psychotic symptoms will subside after detoxification [68]. The absence of bizarre delusions and formal thought disorder may be a clue to this differentiation, as these two symptoms predict a diagnosis of schizophrenia over a diagnosis of psychoactive substance abuse [67]. Onset and course of symptoms may be helpful as well; for example, an onset of psychotic symptoms after 35 years of age may be indicative of substance-induced psychotic disorder and, as stated in the DSM-IV-TR, if psychotic symptoms persist

after approximately 1 month of cessation of the substance use, other causes of the symptoms should be considered. However, comorbid abuse of psychoactive substances in psychiatric disorders such as schizophrenia is very common, and the cause of hallucinations may be twofold. The lifetime prevalence of substance-induced disorders in schizophrenia is close to 50% [69], complicating diagnosis.

Conclusion

In some cases, the differential diagnosis of AHs is of utmost importance, as it may be crucial for pointing us in the direction of the correct type of treatment (e.g., differentiating between dementia and delirium). We saw that there are some major clues in the differential diagnosis of AHs when considering the absence or presence of other symptoms accompanying the AHs. The most important questions to be answered during the diagnostic process are:

- Are visual hallucinations prevailing (in which case, neurological disease is more likely)?
- Was the onset of AH at an advanced age (in which case, neurological disease and release hallucinations are more likely)?
- Is the person with AHs in bad somatic health (rule out delirium first)?
- Are there any comorbid Parkinsonian symptoms (may hint in the direction of PD or DLB, but does not rule out delirium)?
- Are there any comorbid epileptic seizures (in which case, epilepsy is more likely, although a combination of epilepsy and a primary psychotic disorder remains possible)?
- Is there any hearing loss (in which case, suspect release hallucinations)?
- Are the AHs unilateral in nature (in which case, consider release hallucinations)?

- Is social and occupational functioning diminished (if not, consider 'no disorder')?
- Is there use of psychoactive substances (in which case, consider psychoactive substance addiction)?
- Are there any pronounced comorbid psychotic symptoms such as delusions and formal thought disorder (in which case, psychiatric disease is more likely)?
- Are there any comorbid negative symptoms (in which case, a schizophrenia spectrum disorder is more likely)?

Comorbidity of diseases and disorders may complicate the process of diagnosis. Careful consideration that the presented symptoms match the criteria for two separate disorders must be ensured before a dual diagnosis is made.

Future perspective

Research on the accuracy and reliability of establishing the presence of AHs and subsequent diagnoses would help guide the diagnostic process towards more accurate differential diagnoses. Such data do not currently exist, but would be of great value.

Furthermore, there are potential positive consequences of the upcoming publication of the DSM-V for the differential diagnosis of AHs across different disorders and syndromes.

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