Hallucinations in Neuropsychiatry and Drug Abuse: From Phenomenology to Pathophysiology

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Glossary

Delusions – A false belief based on incorrect inference about external reality that is firmly sustained despite what almost everyone else believes and despite what constitutes incontrovertible and obvious proof of evidence to the contrary.

Hallucinations – Perceptions that occur without external stimulation of the relevant sensory organ.

Hallucinosis – This poorly defined term has been applied to a variety of clinical situations, including hallucinatory syndromes without associated delusions, or hallucinations in the setting of neurological conditions or sensory impairment, usually with preserved insight.

Illusions – A misperception or a misinterpretation of a real external stimulus.

Insight – In neuropsychiatry, insight refers to people's understanding of their illness, and to understanding how the illness affects individuals' interactions with the world. Applied to hallucinations, insight refers to the awareness of the hallucinatory nature of the experience.

Introduction: General Aspects

Definitions

The term hallucination in its modern sense was first introduced by Jean Etienne Esquirol in his textbook *Des maladies mentales* (1837). Hallucinations are generally defined as perceptions that occur without external stimulation of the relevant sensory organ. Hallucinations are therefore linked to a sensory modality and may be auditory, visual, somatosensory (tactile or somatic), olfactory, gustatory, or multimodal, occurring in more than one modality. Visual hallucinations may be elementary or simple (lines, dots, geometrical patterns) or complex (objects, animals, people, landscapes, etc.). Auditory hallucinations may also be simple (knocks and rings) or complex (music and voices). The person may or may not have insight into the fact he or she is having a hallucination.

Hallucinations should be distinguished from illusions, which are misperceptions or misinterpretations of a real external stimulus. The term 'pseudohallucinations' has received various definitions (e.g., hallucinations with preserved insight or vivid internal images), none of which is universally accepted. The same holds true for the term 'hallucinosis' which has been applied to a variety of clinical situations. Both terms are confusing and unnecessary. Finally, hallucinations are also distinct from vivid mental imagery and from dreams, although, in the latter case, transitional forms exist.

Frequency

The prevalence of hallucinations in the general population is not negligible. In one prevalence study, hallucinations were occasionally present during the daytime in the quarter of a large, noninstitutionalized sample aged 15 years or over. In another study, the general incidence was 10–30 cases per 1000 persons per year, with variations related to age and gender. Although hallucinations occur in a range of organic and psychiatric conditions, and under the influence of drugs or alcohol, they also occur in normal individuals. The rest of this article focuses on hallucinations occurring in the course of neurological or sensory diseases, in psychiatric conditions, or under the influence of hallucinogenic substances.

Evaluation

To identify and rate hallucinations, the examiner relies on the patient's and/or the caregiver's accounts. Many patients do not spontaneously report their hallucinations, so that the information has to be sought by using specific questions or scales. To identify hallucinations, single items from scales have been used, as well as self-developed questionnaires or inventories. The latter are useful to record the variety of psychotic symptoms, but they do not allow examiners to rate the symptoms. Scales for rating hallucinations and other psychotic symptoms have been developed mainly in the field of psychiatry (e.g., the Positive and Negative Syndrome Scale, the Scale for Assessment of Positive Symptoms, or the Brief Psychiatric Rating Scale) and in the field of dementia (e.g., the Neuropsychiatric Inventory).

Hallucinations Associated with Neurological or Sensory Disease

Cortical Activation as a Common End Pathway for Hallucinations

Pioneering works following World War I established that occipital stimulation generated visual hallucinations, and that hallucinations became more complex when stimulation shifted from primary visual cortex to association visual cortices. It was also shown that seizures secondary to occipital lesions were often preceded by a visual aura. The role of the cortex in generating hallucinations was confirmed by Penfield and colleagues who obtained auditory and visual hallucinations in patients undergoing surgery for epilepsy by stimulating the auditory and visual cortices. The role of specific areas of cortex has been further demonstrated by using functional imagery. Using functional magnetic resonance imaging (fMRI) in patients with Charles Bonnet syndrome (see below), it was shown that various types of visual hallucinations correlate with cerebral activity in ventral extrastriate visual cortex, that the content of the hallucinations reflects the functional specializations of the region, and that the patients who hallucinate have increased ventral extrastriate activity, which persist between hallucinations. To summarize, hallucinations in a sensory modality result from the activation of cortical areas normally associated with the processing of sensory stimuli in the same modality. Simple (elementary) hallucinations result from primary sensory cortex activation, and complex hallucinations result from the activation of association sensory areas. In the context of neurological or sensory diseases, visual hallucinations are the more prevalent type, and cortical activation underlying hallucinations may result from various mechanisms which are now reviewed.

Cortical Irritation

In this model, hallucinations result from intrinsic overactivity in the corresponding sensory cortical area. This mechanism is generally considered to occur in migraine and in epilepsy auras. In migraine, visual symptoms precede the headache in 20% of the cases. Typically, the aura is a flickering uncolored unilateral zigzag line in the center of the visual field, which progresses toward the periphery, leaving a scotoma. The phenomenon is reversible in less than 30 min. Clinical and imaging studies indirectly suggest a relationship between migraine aura and cortical spreading depression, a wave of neuronal and glial depolarization, followed by long-lasting suppression of neural activity. In partial epilepsy, hallucinations were part of the aura in 13% of the cases in one large series. They are more often simple than complex, and involve the following sensory modalities in decreasing frequency order: visual, somato-sensory, auditory, olfactory, and gustatory. The simple hallucinations probably reflect epileptic discharges in a primary sensory cortex. However, other mechanisms have been advocated for epileptic complex hallucinations, relying on the Jacksonian concept of dissolution, or on the concept of activation of specific circuits by a focal discharge.

Deafferentation and Release Phenomena

General disinhibition theories for hallucinations were first forwarded by Jackson. In the perceptual release theory of West, hallucinations arise when the constant flow of sensory inputs is impaired, allowing the emergence of earlier perceptions or traces into consciousness. More specifically, the release or deafferentation theory has been applied to visual hallucinations associated with impairment of visual input. The core hypothesis is that stimulus-driven, bottom-up visual processing inhibits the spontaneous activity of the visual cortical areas and facilitates the release of stored images. More recent conceptualizations suggest that the lack of input leads to chronic hyperexcitability. Visual hallucinations associated with eye disease in nondemented persons have received the name of Charles Bonnet syndrome. The prevalence rate of visual hallucinations in visually impaired populations is around 10%, and their main risk factors are a lower visual acuity, a lower contrast sensibility, and an older age. Hallucinations may be simple or, more often, complex. Insight is preserved. The neurophysiological link from deafferentation to hallucinations remains unclear. Using induced hallucinations in normal-sighted individuals, ffytche has proposed that hallucinations in eye disease result from the shift from tonic to burst firing in thalamocortical circuitry. Lesions of the retrochiasmal visual pathways, typically ischemic, are associated in up to 40% of the cases with hallucinations in the hemianopic field. Hallucinations, simple or complex, are usually transient. Hallucinations are associated with circumscribed, occipital ischemic lesions, while larger lesions, affecting the temporal–visual associative areas, preclude the development of hallucinations. This finding supports the hypothesis that hallucinations result from release from inhibitory input of visual areas bordering the damaged occipital lesion.

The concept of cortical release has been applied to hallucinations in nonvisual sensory modalities associated with the impairment of the corresponding sensory pathways. For instance, hearing loss may be associated with auditory hallucinations, typically of a musical nature. In a series of 125 elderly subjects with hearing impairment, one-third had hallucinations, mostly elementary (including tinnitus), and 5% heard voices or music. In patients with musical hallucinations and deafness, a positron emission tomography (PET) study showed that brain activity

increased as a function of the severity of the hallucination in a distributed network distinct from the primary auditory cortex, which included the posterior temporal lobes, the right basal ganglia, the cerebellum, and the inferior frontal cortices. Phantom sensations, that is, the vivid impression that an amputated limb is still present, and, in some cases, is painful, are present in almost all patients with limb amputation. In this case, the hallucinatory phenomenon seems secondary to the reorganization of the somato-sensory cortical maps following the deafferentation.

Dream Intrusions and Status Dissociatus

Relations between dreams and hallucinations have been debated for a long time. It has been postulated that hallucinations may result from a dissociation between dream and sleep mechanisms. Jean Lhermitte, in the 1920s, first suggested this dissociation could occur in patients with peduncular hallucinosis (hallucinations secondary to a lesion of the upper brainstem). Hypnagogic and hypnopompic hallucinations (perceptions that occur while going to sleep and on waking) represent transitional forms of misperceptions, between dream and hallucination. They are not considered as hallucinations proper in some classifications. Hypnagogic and hypnopompic hallucinations occur in normal persons, but they are more frequent and severe in patients with narcolepsy, a chronic sleep disorder characterized by excessive daytime sleeping and cataplexy. In this condition, hypnagogic hallucinations occur when patients fall asleep directly into rapid eye movement (REM) sleep, suggesting that the hallucinations share mechanisms with dreams. Polysomnographic studies have suggested that narcoleptic-like mechanisms could explain some hallucinations in other conditions, such as Parkinson's disease. Prolonged dream-like vivid hallucinations are also present in status dissociatus, a parasomnia due to extreme dissociation between wakefulness, REM sleep, and nonrapid eyemovement (NREM) sleep. Status dissociatus is observed in various medical diseases, such as treated narcolepsy–cataplexy, dementia, multiple system atrophy, status-post-cardiac surgery, Morvan's chorea, protracted alcohol withdrawal, fatal familial insomnia, and the Guillain–Barré syndrome.

Multifactorial Models

Hallucinations may occur in the course of neurodegenerative diseases. Their lifetime prevalence is approximately 50% in patients with Parkinson's disease, and the prevalence is even higher in patients with dementia with Lewy bodies. In most cases, hallucinations occur with a clear sensorium and a chronic course. Complex visual hallucinations are the most common type, but other sensory modalities may be involved. Hallucinatory images are superimposed on the normal background scene, they may be relatively stereotyped in a given patient and, in most instances, the patient is an observer rather than an actor in the hallucinated scene. Insight may be preserved, fluctuating, or lost. In the two latter cases, cognitive impairment is usually present. Hallucinations often combine with other minor phenomena such as visual illusions and sense of presence, and, mostly in demented patients, with delusions. Although a number of clinical and biological risk factors have been identified, the pathophysiology of Parkinson's disease-associated psychosis remains unclear. Hallucinations could result from various and probably concomitant mechanisms, including: (1) dopaminergic overactivity and/or imbalance in monoaminergic (relatively preserved) and cholinergic (altered) neurotransmission; (2) alteration of brainstem sleep/wake and dream regulation; (3) dysfunction of the visual pathways, nonspecific (coincidental ocular disease) and/or specific, such as PD-associated retinal dysfunction and functional alterations in the ventral stream of visual cortical pathways; (4) dysfunction of top-down mechanisms of vision, such as impaired attentional focus; and finally, (5) antiparkinsonian drugs and other pharmacological agents may interfere with the preceding mechanisms at many levels. No simple model can account for the full diversity and heterogeneity of factors associated with hallucinations in PD. Diederich *et al.* forwarded an integrative model based on Hobson's work on factors regulating consciousness. This model emphasizes dysregulation of the gating and filtering of external perception and internal image production. A more general model for recurrent complex visual hallucinations occurring in the course of a variety of conditions has been proposed by Collerton *et al.,* based on cognitive models of scene perception. In this Perception and Attention Deficit model, a combination of impaired attentional binding and poor sensory activation of a correct proto-object (or template), in conjunction with a relatively intact scene representation, bias perception to allow the intrusion of a hallucinatory proto-object into a scene perception.

Hallucinations in Psychiatry

Hallucinations and Schizophrenia

Prevalence and phenomenology

Hallucinations are a core clinical feature of major psychiatric disorders. Besides disorganization and negative symptoms, hallucinations constitute a core dimension of schizophrenia with delusions (Schneider's first rank symptom), and are associated with poor social functioning. Hallucinations in schizophrenia may occur in any sensory modality, but auditory verbal hallucinations are the most common and characteristic. Voices are perceived

as distinct from the person's own thought and as coming from the extrapersonal space. The content is often pejorative or intrusive. The classical view is that schizophrenic patients lack insight into their illness and psychotic symptoms. However, poor awareness of psychotic experience seems to be a trait of the acute rather than the chronic psychopathology of schizophrenia. Lifetime prevalence rates of auditory vocal hallucinations in schizophrenia range from 50% to 70%. The phenomenology and the prevalence of hallucinations in schizophrenic patients vary according to the marital status, the educational level, and the cultural background, suggesting that environmental factors influence the expression of the hallucinations. The phenomenology may vary according to the age of onset. The French concept of 'chronic hallucinatory psychosis' refers to a chronic hallucinatory and delusional disorder affecting mainly women and that differs from paranoid schizophrenia by a late onset, the absence of formal thought disorder and intellectual impairment, a better response to treatment, and a better outcome. Accusatory or abusive auditory verbal hallucinations are more frequent in these late-onset cases. This entity is included into late-onset schizophrenia in current classifications such as the *Diagnostic and Statistical Manual of Mental Disorders* (DSM).

Brain structure and functional neuroimaging studies

Recent works using sophisticated analysis techniques such as voxel-based morphometry found that verbal hallucinations are associated with reduced gray matter volumes in the temporal lobe, more specifically in the left superior temporal gyrus, including the primary auditory gyrus, and in nonsensory regions such as the right dorsolateral frontal cortex. Studies aiming at capturing the cerebral activity associated with verbal hallucinations have shown temporal lobe activation, on the left side in most studies. This activation may include, or not, the primary auditory cortex (Heschl's gyrus). Nonsensory cortical and subcortical areas are also involved in some studies, including language production area (Brodman's area), anterior cingulate area, and cerebellar regions, suggesting that disturbances in a distributed network may be associated with verbal hallucinations. Finally, some studies have addressed the question of cerebral asymmetry and connectivity in patients with verbal hallucinations. Evidence for altered asymmetry is inconclusive, but there is evidence, from works using diffusion tensor imaging or fMRI, for disrupted connectivity between the temporal, prefrontal, and anterior cingulate cortex.

Cognitive models

The prevailing cognitive model was proposed by Frith in the 1990s and postulates that verbal hallucinations derive from inner speech that has been misidentified as coming outside the self, because of defective self-monitoring. In this model, frontal regions involved in verbal generation fail to modulate activation in areas involved in speech perception. This view has been later criticized or refined. Although most authors postulate an impaired processing of inner speech, the way to integrate the somewhat heterogeneous functional neuroimaging data may vary. Some models insist on the interactions between top-down and bottom-up processes. Furthermore, the role of emotion and attention is also supported by some activation studies.

Neurotransmitters

At a molecular level, studies in schizophrenic patients have reported dopaminergic abnormalities in a number of cortical and subcortical regions that have been related to positive symptoms such as hallucinations. Direct or indirect (preclinical or pharmacological) evidence suggest that schizophrenia is associated with excessive stimulation of striatal dopamine D2 receptors, which has been positively correlated with positive symptoms and more specifically hallucinations, and deficient stimulation of prefrontal dopamine D1 receptors, which could be a factor in the cognitive impairments of schizophrenia. However, other neurotransmitters, including serotonin, glutamate, γ-amino butyric acid (GABA), and acetylcholine have been implicated, either directly, or through interactions with dopaminergic systems. How multiple neurotransmitters and risk genes interact to produce the positive symptoms of schizophrenia is poorly understood.

Hallucinations and smoking

Recent research has focused on the fact that schizophrenic subjects have an auditory sensory-gating deficit which could be corrected by tobacco use. The prevalence of smoking among schizophrenic subjects is higher than in the general population. Schizophrenic smokers have higher psychotic symptoms scores (including hallucinations) than nonsmokers, and the intensity of symptoms is positively correlated to tobacco consumption. These findings suggest a form of self-medication, considering that tobacco could counteract the sensory deficit. Eighty percent of schizophrenic patients have an impaired auditory sensory transmission of repeated auditory stimuli (P50 wave inhibition deficit), which is transiently improved by nicotine. Current theories imply that the P50 wave inhibition prevents schizophrenic patients from filtering unimportant auditory stimulation, thus facilitating the emergence of auditory hallucinations and delusional interpretations.

Hallucinations and Bipolar Disorders

Few studies are devoted to hallucinations in the course of bipolar disorders. Compared with those of schizophrenia,

hallucinations in bipolar disorders are less severe, more often visual, and less often auditory. Characteristics of hallucinations seem to be similar among manic and both bipolar- and unipolar-depressed subjects. Among patients with major affective disorders, those with hallucinations are less well-educated, have higher anxiety scores, less insight into the illness, and longer hospitalizations. Recent researches have shown that childhood sexual abuse and other early traumas are associated with serious mental illness and more specifically positive symptoms, particularly hallucinations. In one study, about half of the bipolar patients had experienced hallucinations (mostly auditory followed by visual) and 16% revealed sexual abuse. These findings suggest that childhood sexual abuse could increase the vulnerability of bipolar patients to later experience auditory hallucinations.

Posttraumatic Stress Disorders and Borderline Personality Disorders

Several studies suggest that patients with posttraumatic stress disorders (PTSDs) have perceptual disturbances, and are predisposed to hallucinations and paranoia. Psychotic symptoms, especially hallucinations, are frequently experienced by survivors of early (e.g., sexual abuse) and later (e.g., exposure to military combat) trauma. The nature of delusional and hallucinatory symptoms in borderline personality disorder (known to have experienced trauma in childhood) is not well documented. Psychotic episodes are common among patients with borderline personality disorder, narrowly due to concomitant disorders. However, the nature of the relationship between trauma and hallucinations is poorly understood from a psychological perspective. As previously stated, hallucinations may result from the misattribution of mental events to an external source: this is likely to occur when experiencing mental events that are automatic and associated with low cognitive effort, such as intrusive memories of trauma. The latter may be experienced as hallucinations by individuals whose source-monitoring abilities are compromised by severe mental illness. This mechanism may be reinforced during stressful periods, for instance, when an adult survivor of abuse suffers additional negative experiences. In line with this hypothesis, many patients experiencing hallucinations report that hallucinations began following a retraumatising experience.

Ekbom Syndrome: the Delusional Parasitosis

In this condition, the subject has the strong delusional belief of being infested with parasites. Patients give detailed descriptions of the activity of the parasites (crawling, biting, burrowing), translating tactile hallucinations. Delusional parasitosis is referred to as the Ekbom's syndrome, after the Swedish neurologist, who published seminal cases in 1937, or as 'delusional disorder, somatic type' in the DSMIV criteria. Secondary functional delusional parasitosis can occur in psychiatric conditions such as schizophrenia or depression.

Hallucinogens and Alcohol

Hallucinogenic Substances

Hallucinogens include natural substances extracted from plants, such as mescaline and psilocybin, and synthetic substances such as lysergic acid diethylamide (LSD), 3,4-méthylène-dioxy-méthylamphétamine (MDMA, or ecstasy), and phencyclidine (PCP). The perceptual, cognitive, and psychological effects of these compounds are unpredictable, and are heavily dependent on the expectations of the user and the environment. The effects also depend on the dose, with differences in nature, and not only in intensity, with higher or lower doses. The hallucinations induced by these compounds are mainly auditory and visual, and are associated with, or preceded by, intensification of perceptions, synesthesias, illusions, and derealization. Visual hallucinations often consist of geometric patterns, sometimes persons or objects. Geometric patterns have been classified into four groups, called 'form constants.' It has been postulated that these hallucinations arise in the primary visual cortex (V1), and that the form of the retino-cortical map and the micro-architecture of V1 determine their geometry. In most cases, insight on the hallucinatory nature of the phenomenon is maintained. Perceptual symptoms may be re-experienced in the absence of any recent hallucinogen intoxication (hallucinogen persisting perception disorder, or flashbacks).

The drug category of hallucinogens encompasses many compounds, which exhibit a wide range of pharmacological properties. The three prototypical drugs – mescaline, psilocybin, and LDS – are agonists at 5-HT_{2A} (serotoninergic) receptors. Recent research has confirmed that 5-HT_{2A} receptors are an important site of action for the hallucinogens, and have also directed attention on the modulatory roles of 5-HT_{2C} (for the phenethylamines) and $5HT_{1A}$ receptors (for the tryptamines).

Other drugs may act through different mechanisms such as cannabinoid agonism (tetrahydrocannabinol), *N*-methyl-D-aspartate (NMDA) antagonism (phencyclidine), muscarinic receptor antagonism (scopolamine), and mixed action monoamine release (MDMA).

Alcohol

Hallucinations occur in up to 10% of alcohol withdrawal patients. They are commonly visual, though they may be

auditory, tactile, and olfactory. They usually occur early, in the first 24 h following the last drink, and are associated with insomnia, agitation, and enacting-dream behaviors with partial or absent awareness of reality. Polysomnographic studies have shown the presence of an atypical transitional state between REM-sleep and wake (status dissociatus, see above).

Alcoholic hallucinosis is a much rarer condition of acute onset, occurring after one or more decades of heavy alcohol consumption. The clinical picture includes hallucinations, generally auditory, often accompanied by delusions of reference and persecution, persisting for variable periods of time, regardless of whether the patient is abstinent. The toxic effect of alcohol on frontal lobe functions is well known, suggesting that alcohol hallucinosis may share mechanisms with the positive symptoms of schizophrenia.

Therapeutic Aspects

Antipsychotic Drugs

Antipsychotic drugs are the first-line treatment for patients suffering from hallucinations occurring in the course of psychiatric conditions, especially schizophrenia. In line with the dopamine theories of schizophrenia mentioned above, antipsychotics inhibit the actions of dopamine by acting on D2 and D3 dopaminergic receptors. Although it has been assumed that antipsychotics are antagonists at the D2/D3 receptors in the brain, *in vitro* assays suggest that they are in fact inverse agonists at these receptors. Recently, a D2/D3 partial agonist drug (aripiprazole) has also shown antipsychotic properties. Action at serotonin receptors ($5HT_{1A}$, $5HT_{2A}$) might also be important for the action of some second-generation (atypical) antipsychotics. However, the exact characteristics that make these new antipsychotics atypical are a matter of debate, and there may be significant differences between the drugs within this class. The atypical antipsychotic effect could, at the molecular level, be due to a fast dissociation of the drug from the D_2 receptor, rather than to a high 5-HT_2 occupancy. All these drugs treat primarily the positive symptoms of schizophrenia, including the hallucinations. A meta-analysis has shown that some (but not all) of the second-generation antipsychotic drugs are most efficacious than first-generation drugs for treatment of positive (and negative) symptoms. However, the effect on hallucinations, among other positive symptoms, was not specifically assessed. Due to the side effects associated with the use of conventional (first- or second-generation) antipsychotics, there is a need for alternative pharmacological treatment. Preliminary studies suggest that metabotropic glutamate receptor agonists could represent a promising new class of antipsychotics.

Repetitive Transcranial Magnetic Stimulation

Recently, repetitive transcranial magnetic stimulation (rTMS) has emerged as a possible alternative treatment of hallucinations in schizophrenic patients resistant to antipsychotic drugs. Several studies and recent meta-analysis of controlled studies suggest that low-frequency rTMS delivered to the left temporo-parietal cortex induce a significant, although modest-to-moderate, reduction of overall positive symptoms in patients receiving active treatment. However, the effect size is higher and more robust when only auditory hallucinations are taken into account, thus confirming that the temporal association cortex plays a crucial role in the pathophysiology of auditory hallucinations.

See also: Hallucinogens; Parkinson's Disease; Schizophrenia; Sleeping, Waking, and Dreaming; Vision.

Further Reading

Allen P, Larøi F, McGuire PK, and Aleman A (2008) The hallucinating brain: A review of structural and functional neuroimaging studies of hallucinations. *Neurosciences and Biobehavioral Reviews* 32: 175–191.

Baethge C, Baldessarini RJ, Freudenthal K, Streeruwitz A, Bauer M, and Bschor T (2005) Hallucinations in bipolar disorder: Characteristics and comparison to unipolar depression and schizophrenia. *Bipolar Disorders* 7: 136–145.

Collerton D, Perry E, and McKeith I (2005) Why people see things that are not there: A novel perception and attention deficit model for recurrent complex visual hallucinations. *Behavioral and Brain Sciences* 28: 737–794.

Diederich N, Fénelon G, Stebbins G, and Goetz CG (2009) Hallucinations in Parkinson disease. *Nature Reviews Neurology* 5: 331–342.

ffytche DH (2009) Visual hallucinations in eye disease. *Current Opinion in Neurology* 22: 28–35.

Frith CD (1992) *The Cognitive Neuropsychology of Schizophrenia*. Hove: Erlbaum.

Griffith TD (2000) Musical hallucinosis in acquired deafness. Phenomenology and brain substrate. *Brain* 123: 20652076.

Hugdahl K, Løberg EM, Specht K, Steen VM, van Wageningen H, and Jørgensen HA (2007) Auditory hallucinations in schizophrenia: The role of cognitive, brain structural and genetic disturbances in the left temporal lobe. *Frontiers in Human Neuroscience* 1(6): 1–10.

Larøi F (2006) The phenomenological diversity of hallucinations: Some theoretical and clinical implications. *Psychologica Belgica* 46: 163–183.

Mauguière F (1999) Scope and presumed mechanisms of hallucinations in partial epileptic seizures. *Epileptic Disorders* 1: 81–91.

Nichols DE (2004) Hallucinogens. *Pharmacology and Therapeutics* 101: 131–181.

Strange PG (2008) Antipsychotic drug action: Antagonism, inverse agonism or partial agonism. *Trends in Pharmacological Sciences* 29: 314–321.