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# Auditory Hallucinations and Its Mechanism

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**Abstract**

Auditory hallucinations are one of the most frequent and reliable symptoms of psychosis. However, the neurocognitive and neurophysiological bases of auditory and verbal hallucinations remain obscure. These hallucinations are thought to result from disordered monitoring of inner speech. In this article, the synaptic and psychopathological mechanisms for the auditory hallucinations are discussed. Auditory hallucinations might be occurred due to a failure of synaptic connectivity. The disturbances of the spine are caused by temporary abnormal neuronal excitations and failure of synaptic connectivity will be observed. The abnormality in the neurotransmission of glutamic acid and GABA will cause a musical hallucinations, heightened auditory awareness and "Les eidolies hallucinosiques" (which are hallucinations without delusions). By adding the abnormal neurotransmission of dopamine and /or serotonin to GABA and glutamate abnormalities, the delusions will be applied to the "Les eidolies hallucinosiques" and it will become paranoid hallucinations ("Les hallucinations délirantes"). The valproic acid that inhibits the GABA degrading enzyme and agonist of the NMDA receptor will be the first choice for "Les eidolies hallucinosiques" from immediately after onset. If the patient complains the paranoid symptoms, the dopamine and serotonin receptor antagonist will be desirable.

**Keywords**: Auditory hallucinations; Neuronal excitations; Neurotransmission; GABA

## Introduction

Auditory hallucinations are one of the most frequent and reliable symptoms of psychosis [1]. However, the neurocognitive and neurophysiological bases of auditory and verbal hallucinations remain obscure [2]. These hallucinations are thought to result from disordered monitoring of inner speech [3]. Direct stimulation or disease of Wernicke's area produces auditory and verbal hallucinations without subvocal speech [4]. Penfield and Perot reported that electrical stimulation of the brain produces elementary hallucination-like phenomena but these do not resemble schizophrenic hallucinations [5]. Furthermore, surface and depth electroencephalogram (EEG) recordings in patients during hallucinations do not reveal consistent abnormalities [6,7].

## Symptomatology of Schizophrenia [8]

Here, we consider how auditory hallucinations are occurred as the dissolutive process of the mind. Clinical picture of the early schizophrenia will be discussed, but it may be a common process to mental dissolution. The mental dissolution begins with neurosis-like state consisting of psychosomatic malaises. Patients gradually become reticent and inactive. They are inclined to stay at home all the time. The following symptoms may be recognized. First, the autochthonous experiences are described. It is following kind of experiences.

1) Autochthonous thinking: It is the condition where the various idle thoughts are arising autochthonously.

2) Autochthonous recollection: The scenes that had been experienced in the past are revived autochthonously regardless of the current situation.

3) Autochthonous fantasy images: It is fantastic phenomenon that is developed like a narrative.

4) Autochthonous music images: Sound and music are resounded in one's head. It is also considered as the musical hallucinations.

The heightened awareness state is also observed in the patient with an early schizophrenia. It appears particularly in the auditory sense. The patients are sensitive to a variety of trivial hearing stimuli other than the stimuli that are paying attention. Troubles are to come out in everyday life because of the heightened auditory awareness.

In addition, the kind of tension that something comes being imminent appears in autochthonously. It baffled the patients. They have a tense and perplexed mood and a vague sense of being watched.

The patients sometimes feel as if someone is in his own side, in rear, or to be on.

This is a substantive awareness of Jaspers (Leibhaftige Bewußtheit) [9]. They also have a suspicion of being observed and commented on by the people around. This is not a delusion of injury or observation because it will be passing away and they could not quite believe it. And a disorder of immediate understanding, judgment or memory could be also observed.

It is said that hallucinatory-paranoid state will be observed from 1-2 weeks to several years after when these symptoms that is described above have been observed.

There is a possibility that the above symptoms are not specific to schizophrenia, but will be commonly observed in the process of mental dissolution [10].

## Classification of Auditory Hallucinations

Here, we'll try to think about what is the illusion.

Esquirol [11] was discriminated between the illusion and

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hallucination from the ambiguous definition with the presence or absence of external stimuli. He was redefined hallucination as "belief from mind that they are actually perceived even though there is no external object to stimulate the perception".

Esquirol considered that the hallucinations were caused by the pathology of ideas rather than the problems of a matter of sense.

Esquirol regarded delusions and hallucinations as almost a synonymous.

On the contrary, Kahlbaum [12] considered that a sensory excitement was always the starting point of hallucination. And it was experienced as hallucinations through the mental deformation.

Tamburini [13] considered that the psychiatric symptoms of the epilepsy were a model of the hallucinations. He understood the hallucination as a convulsion of the sensory center.

Ball [14] was defined hallucinations as the "perception sans objet" (perception without object).

Baillarger [15] considered that the essence of hallucinations was a psycho-sensory hallucination. He assumed that poor sensory hallucinations (psycho hallucinations) were incomplete.

Jackson [16] was focused on the similarities between dreams and hallucinations. He considered that dreams and hallucinations were positive symptoms associated with the mental dissolution. He hypothesized that the difference in the degree of disturbances of thought and perception depended on the difference in the degree of strength of the neuronal discharge.

Jaspers [17] defined a true hallucination as an only experience that does not depend on the will and is localized at the outside world clearly. And he called the hallucinations that close to the representation as the pseudo hallucinations. Bleuler [18] defined hallucination as the representation that was given a perceptual value by the subject.

Janet [19] considered as follows on the basis of the observation of hallucinations during the dissociation. The delusional thinking was come from the dissociation of real function or attenuation of psychological tension. Hallucination was the representation that was given a real value to subjective material [19].

De Clérambault [20] assumed that there was a neutral and sensory primary experience (le petit automatisme mental) in the foundation of all hallucinations. It became a hallucination ("automatisme mental") when a certain degree of delusional processing was applied to this meaningless experience and developped into delusional system.

Ey [21] reconsidered the hallucinations by integrating the hierarchic theory of Jackson and Janet's psychogenic theory. He re-defined the hallucinations as the "perception sans objet à percevoir "(perception without object to perceive). He classified hallucinations into two large groups, "Les hallucinations délirantes" (which is hallucinations with delusions) and "Les eidolies hallucinosiques" (which is hallucinations without delusions). In addition, Ey divided "les eidories" between "protéidolie "(which was archetypal element image) and "phantéidolie" (which was a scene imagery composite image, similar to the experience of the dream).

## Abnormality of Neurotransmitters in Schizophrenia

The abnormalities of neurotransmission of GABA (γ-aminobutyric acid) and glutamate are observed in schizophrenia. And these abnormalities are existed from an early stage.

There is also a change in EEG, which is considered to reflect the neurotransmission of GABA and glutamate in the brain.

### γ oscillations

The EEG is measured the electric field that is generated by synaptic potentials of pyramidal cells in the cerebral cortex. Pyramidal cells receive a projection from GABAergic interneurons. Its firing rate is regulated through the synaptic GABA receptor. When this is measured from extracellular space, it becomes cyclic electric potential changes (α, β, γ and θ oscillations). The γ oscillations are associated with GABA neurotransmission. In schizophrenia, the abnormalities of γ oscillations are observed [18]. Abnormality of the GABA synthetic enzyme, the abnormality of GABA transporter and abnormality of the GABA receptor are considered as a cause [22]. In the onset of schizophrenia, abnormalities of γ oscillations already are observed [23]. It correlates with clinical symptoms [24,25].

### Mismatch-negativity (MMN)

The MMN is one of the event-relatedpotential. When PCP (phencyclidine) that is the antagonist of the NMDA (N-methyl-D-aspartate) receptor is prescribed to the monkey and MMN is measured with the primary auditory area, MMN amplitude was attenuated as compared with prior to administration [26]. In addition, the administration of ketamine that is the antagonist of the NMDA receptor was attenuated MMN amplitude in humans [27]. From the above, MMN is considered to be related with abnormalities of neurotransmission of glutamate. The MMN amplitude in very early phase of schizophrenia is same as healthy person. But 1.5 years later, the amplitude is attenuated than the onset time in schizophrenia. This MMN amplitude attenuation was also correlated with gray matter volume loss of Heschl's gyrus (part of the auditory cortex) [28]. Therefore there is a possibility that there is an abnormality in the neurotransmission of glutamate from immediately after onset of schizophrenia.

## Case

Then we'd like to consider the mechanism of auditory hallucinations through cases that are considered auditory hallucinations has caused a hardness of hearing. Mr. G was a 69-year-old Japanese man who worked as a banker. He was neglectful because of auditory hallucinations and delusions and often made mistakes in his work, as a result of which he lost his job within a year. He consulted a psychiatrist because of insomnia, autism, inexpressiveness and monologue speech. At the time of consultation, he had delusions of persecution as well as auditory and verbal hallucinations in which 11 unknown women reproached him for his stubbornness and tenaciousness. He could not understand the necessity for his hospitalization. Therefore, he was admitted without consent at the age of 23 and was diagnosed with paranoid schizophrenia. He was prescribed 18 mg haloperidol, 150 mg thioridazine hydrochloride, 12 mg perphenazine and 1200 mg sulpiride. His EEG was normal, and he did not complain of hearing impairment. A computed tomography scan of the head indicated slight frontal and temporal atrophy (left dominant). Later, he complained of sudden hearing impairment. According to him, the impairment occurred because of a loud auditory hallucination and because a nurse who had cared for him 3 years ago had spoken to him maliciously in a loud voice. An audiogram showed a 65-Db hearing impairment on both sides (the frequency of Japanese language is from 150 Hz to 1500 Hz. The hearing ability at 500–1000 Hz was studied, and an average was calculated). An EEG showed spike abnormalities at the frontal and temporal lobes. Although consultation with an otolaryngologist was considered at that time, the hallucinations suddenly diminished and his

hearing ability was recovered. He believed that he regained his hearing because the nurse forgave him. At this time, his EEG was normal and a hearing ability of 35 dB on both sides was recorded on an audiogram. Subsequently, he complained of loud auditory hallucinations and hearing impairment. At this time, a hearing ability of 67.5 dB on both sides was recorded on an audiogram. The 100 mg of lamotrigine was prescribed initially. The hallucinations diminished after 200 mg of lamotrigine was prescribed, thereby improving his hearing ability (35 dB on both sides). The patient has not shown any signs of impairment since then.

## The Mechanism of Auditory Hallucinations

### Psycopathological level

Auditory and verbal hallucinations have been attributed to aberrant activity in the primary auditory cortex (Heschl's gyrus) and are usually triggered by emotionally charged and stressful situations [2]. Several hypotheses have been proposed to explain the mechanism of auditory hallucinations [29]. In this study, the explanation for auditory hallucinations was based on Henri Ey organodynamism [30], with reference to the perceptual expanded model of Hugdahl's hypothesis [29]. In an integrated cortical network, the peri-Sylvian region connects ventrally with anterior parts of the temporal lobe to generate auditory hallucinations as perceptual misrepresentations, with prefrontal regions for top-down inhibitory control and dorsally with parietal regions for attention to the voice. A defining feature of auditory hallucinations is a strong attention shift towards the voice [29]. In schizophrenia, prefrontal cortex for up-down inhibitory system as superior function is impaired (negative symptom). And this causes a release from inhibitions for the generation of auditory hallucinations as perceptual misrepresentations in the left peri-Sylvian region and for the attentions towards the voice in the parietal cortex. Thus, the auditory hallucinations are generated and attended to in this manner (positive symptom). The inner voice experienced in healthy individuals can be explained in the same manner. The function to inhibit attention towards the voice in the parietal cortex works normally, while that to inhibit the generation of auditory hallucinations as perceptual misrepresentations in the left peri-Sylvian region is released. Therefore, the frequency of inner voice generation may increase but will not be perceived as an auditory hallucination. Penfield and Perot reported that electrical stimulation of the brain produces elementary hallucination-like phenomena, but these do not resemble schizophrenic hallucinations [5]. This may be the inner voice. Our patient had auditory hallucinations and delusions for 30 years and was diagnosed with paranoid schizophrenia. Atrophy of the perisylvian regions was observed. Gaser et al. reported that the severity of auditory hallucinations is significantly correlated with volume loss in Heschl's gyrus [31]. Activation of Heschl's gyrus is observed during auditory hallucinations [32]. The volume loss in Heschl's gyrus may disconnect the neural network that inhibits auditory hallucinations. The distinguished feature of this case was that the sudden and loud auditory and verbal hallucinations caused a hearing impairment that diminished spontaneously. The spike abnormalities detected in his EEG during these symptoms disappeared after the loud auditory hallucinations diminished, suggesting that the hallucinations may have been caused by abnormal excitations around the auditory hallucination inhibitory neural network.

Psychopathology of the case listed above is as follows.

Henri Ey classified hallucinations into two large groups: 'les hallucinations délirantes' (hallucinations with delusions) and 'les eidolies hallucinosiques' (hallucinations without delusions) [21].

His auditory hallucinations were classified as 'les hallucinations délirantes' during normal times. However, during times of hearing impairment, they were 'les eidolies hallucinosiques,' which are produced by abnormal firing around the auditory hallucination inhibitory network. Thus, 'les hallucinations délirantes' coexisted with 'les eidolies hallucinosiques' within a patient with schizophrenia. In fact, the patient stated that he was unable to interpret the loud voices and even wondered about their presence.

### Synaptic level

About 80% of the neurons in the cerebral cortex are excitatory neurons. The majority of excitatory synapses are formed in a dendrite as the spines that are mushroom-like structures [33]. The spinal connective strength will vary depending on the stimulus and synaptic transmission efficiency changes dramatically [34].

There is a possibility that forming an abnormal neural circuits cause schizophrenia [35]. Loss of volume of the gray matter in cerebral cortex with a focus on the frontal and temporal area has been repeatedly reported in schizophrenia, but there is no obvious change in glial cell number and number of neuron [36].

In the view of the fact that the volume of cell body is correlative to the sum of neurites [37,38], the loss of volume in gray matter in schizophrenia may be due to decrease a synaptic density and neurites. The degree of aggravation of schizophrenia may be depended on a degree of failure of synaptic connectivity [35].

At the time of onset of schizophrenia, the abnormality in the neurotransmission of glutamic acid and GABA will be observed. And the disturbances of the spine may occur by the transient hyper-excitability in neurotransmission pathways of glutamate and GABA.

As a result, the MMN amplitude attenuation and abnormal γ oscillations might be occurred.

And it will cause a musical hallucinations, heightened auditory awareness and "Les eidolies hallucinosiques" (which is hallucinations without delusions).

By adding the abnormal neurotransmission of dopamine and /or serotonin to GABA and glutamate abnormalities, the delusions will be applied to the "Les eidolies hallucinosiques" and it will become paranoid hallucinations ("Les hallucinations délirantes").

In our case, the patient experienced "Les eidolies hallucinosiques" because a new abnormal GABA and glutamate neurotransmission was applied in a state of controlled paranoid hallucinations.

## Proposition of Concrete Remedy Strategy

The valproic acid that inhibits the GABA degrading enzyme and agonist of the NMDA receptor will be the first choice for "Les eidolies hallucinosiques" from immediately after onset. If the patient complains the paranoid symptoms, the dopamine and serotonin receptor antagonist will be desirable.

## Conclusion

Auditory hallucinations might be occurred due to a failure of synaptic connectivity.

The disturbance of the spine is caused by temporary abnormal neuronal excitations and the failure of synaptic connectivity will be observed.

The abnormality in the neurotransmission of glutamic acid and

GABA will cause a musical hallucinations, heightened auditory awareness and "Les eidolies hallucinosiques"(which is hallucinations without delusions).

By adding the abnormal neurotransmission of dopamine and /or serotonin to GABA and glutamate abnormalities, the delusions will be applied to the "Les eidolies hallucinosiques" and it will become paranoid hallucinations ("Les hallucinations délirantes").

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