The low-frequency oscillation model of hallucinations in neurodegenerative disorders and in delirium

Grzegorz R. Juszczak

Department of Animal Behaviour, Institute of Genetics and Animal Breeding, Jastrzebiec, Poland.
Jastrzebiec, ul. Postępu 1
05-552 Wolka Kosowska, Poland
Phone: +48 (22) 756 17 11
Fax: +48 (22) 756 14 17
E-mail: g.juszczak@ighz.pl, g.juszczak@yahoo.com

Received: 23 May 2011
Accepted: 02 Sep 2011
Published: 17 Sep 2011

Iran J Med Hypotheses Ideas, 2011, 5:11

Abstract

Electroencephalography (EEG) found in dementia with Lewy bodies, Parkinson’s disease, Alzheimer’s disease and delirium, is characterized by increased power of delta and theta frequencies with the degree of EEG slowing parallel to the frequency of hallucinations occurrence. According to the proposed model of hallucination, pathological low-frequency oscillations may interfere with information processing in two different ways leading to hallucinations. First, pathological low-frequency oscillations may be a source of signal noise, which is next transformed into emotionally charged signal. The filtering of the signal noise may depend on differences in synaptic weights between networks storing representations of emotionally charged and neutral objects. Initially filtered signal can be next reinforced by attention leading to hallucinations. Second, there is growing body of evidence that theta oscillations in distributed cortical networks participate in mechanism of working memory. Therefore, pathological low-frequency oscillations may interfere with the mechanisms of working memory leading to excessive activation of memory traces and to the intrusion of memories into consciousness. The assumption that neuronal representations of emotionally relevant and neutral objects differ in synaptic strengths is supported by studies showing enhanced memory for emotional stimuli. The model is also supported by experiments showing that perception of feared object is facilitated by stimulus-driven, involuntary and automatic recruitment of attention. Consistently with the model, hallucinations are most often unpleasant and emotionally irrelevant objects are rarely hallucinated in neurodegenerative disorders. Proposed disturbances of visual working memory are consistent with the high incidence of palinopsia (perseveration of previously viewed objects after a certain time) in demented patients. The significance of the model for understanding hallucinations that occur in schizophrenia is also discussed. The proposed model predicts that we should search for treatments decreasing the power of cortical delta and theta oscillations or reshaping synaptic plasticity in order to prevent the occurrence of hallucinations.

Keywords
Hallucinations, Delirium, Dementia with Lewy bodies, Parkinson’s disease, Alzheimer’s disease, Delta, Theta

Introduction
Hallucinations are common in many disorders including schizophrenia, neurodegenerative disorders and eye disorders. They are considered as significant medical problem because hallucinations are often frightening and distressing for patients (1). Number of hypotheses and models have been proposed to explain occurrence of hallucinations, including illusionary misperceptions and misidentifications, cortical irritation, cortical release and hyperexcitability or unbalanced top-down activation, dream intrusion, and interactive information processing models (1). Unfortunately, they can neither fully explain the phenomenology of hallucinations, nor the variation in the frequency of hallucinations in different disorders (1). As noted by Collerton et al., (1) hallucinations observed in conditions such as dementia with Lewy bodies, Parkinson’s disease, Alzheimer’s disease and delirium, share phenomenological similarities, although they occur with different frequencies. To explain both the phenomenology and differences in frequency of hallucinations in different disorders, Collerton et al. (1) proposed the perception and attention deficit (PAD) model of hallucinations. According to the PAD model, hallucinations occur when incorrect proto-objects are incorporated into visual scene as a result of impaired attention and visual perception leading to incorrect attentional binding (1). They also propose that hallucinations in neurodegenerative disorders are caused by cholinergic dysfunction (1). Unfortunately, the PAD model does not explain exactly how hallucinations are created at the level of neuronal network. Therefore, herein the low-frequency oscillation model of hallucination is proposed, that is based on electrophysiological findings in basic and clinical research.

Low-frequency oscillations (delta/theta; 1-8 Hz) are composed of prolonged periods of hyperpolarization, associated with decreased responsiveness of neurons to excitatory inputs, and with periods of depolarization, associated with increased excitability of neurons and increased firing rate. Consistent finding in the electroencephalographic studies of dementia with Lewy bodies (2, 3), Parkinson’s disease (3-8), Alzheimer’s disease (9-15), and delirium (16-21) is electroencephalographic slowing in widespread cortical areas including occipital, parietal, temporal, and frontal regions of the head with increased power of delta and theta frequencies (1-8 Hz) (Table 1). Furthermore, the degree of electroencephalographic slowing parallels the frequency of occurrence of hallucinations. The degree of electroencephalography (EEG) slowing is higher in dementia with Lewy bodies compared with Alzheimer’s disease and Parkinson’s disease with dementia (2, 3) and the degree of slowing in Parkinson’s disease with dementia is higher compared with Alzheimer’s disease (3) consistently with differences in frequency of hallucinations (Table 2). In case of Parkinson’s disease there is progressive electroencephalographic slowing in following order:

healthy control group < Parkinson’s disease without cognitive impairments < Parkinson’s disease with mild cognitive impairments < Parkinson’s disease with dementia (5-8). These differences in EEG are also consistent with differences in frequency of hallucinations between cognitively unimpaired and demented patients suffering from Parkinson’s disease (Table 2). The same pattern of electroencephalographic changes characterized by increased power in delta and theta frequencies in widespread cortical areas (occipital, parietal, temporal, and frontal lobes) have been found in humans injected with anticholinergic drugs (22-27), which are known to induce hallucinations in healthy subjects (24-26). As noted by Collerton et al., (1) it is important to explain both the frequency and the phenomenology of anomalous experiences. Visual hallucinations in neurodegenerative disorders and in delirium have several important features. First, they do not typically contain simple geometric shapes or amorphous objects (1, 28). Second, hallucinated objects are not fragmented or distorted (1). Third, hallucinated images are seen in normal locations known from everyday life and have correct orientation in space (1). The characteristic of hallucinations occurring in neurodegenerative disorders suggests that they result from activation of preexisting and shaped by experience neuronal representation of external objects. Therefore, it is important to consider the mechanism of neuronal representation of external objects in the scientific account of hallucinations. According to the model proposed by Damasio, objects are represented by distributed networks composed of reciprocally connected neurons located at different levels of sensory and association cortices (29). He also suggested that activation of these networks is necessary for both perception and recall (29). Recently, this model has received growing support from neuropsychological and neuroimaging studies (29) and therefore it has been incorporated into the low-frequency model of hallucinations.

**Hypothesis**

The model proposes that the pathological low-frequency oscillations can interfere with the mechanisms of long- and short-term memory (Figure 1). First, the low-frequency oscillations may be a source of a signal noise in the brain; and synaptic plasticity shaped by emotions may participate in transforming the noise into meaningful signal. Second, low-frequency oscillations may interfere with the mechanism of working memory.

**Transformation of signal noise induced by low-frequency oscillations**

1) Prolonged depolarization, associated with low-frequency oscillations, randomly activates neurons without the external stimulation in corresponding visual field (Figure 2A). The increased probability of firing during positive
phase of slow oscillations can result from combination of different factors. Opening of hyperpolarization-activated cation channels during positive phase brings the resting membrane potential close to the firing threshold (30). Furthermore, during positive phase of slow oscillations there is also decreased inhibitory drive (31-33) and decreased input resistance (34). In this situation any additional factor such as the presence of extracellular electric fields, generated during strongly synchronized activity (35, 36), can trigger action potential in neurons without the external stimulation.

2) Activated neurons send impulses by forward and backward connections to other neurons belonging to the networks storing representations of different external objects. Emotionally charged targets are memorized better then neutral targets (37-40) and therefore it is expected that neuronal representations of emotionally relevant and neutral objects differ in synaptic strengths. The stronger object representation, the higher probability that random activation, constituting a noise, will activate the entire network by means of reciprocal connections (Figure 2B).

3) Neuronal representation of emotionally relevant object activates in turn attentional system. This leads to further reinforcement of activity in the network storing representation of emotionally relevant object and to silencing the activity in networks representing other objects (Figure 2C).

4) Representation of emotionally relevant object reinforced by attention wins competition with other networks and the winning representation enters the content of consciousness leading to hallucination (Figure 2D).

5) The activity in the network underlying hallucinated percept is susceptible for extinction because it is not supported by consistent visual stimulation and depends only on random activation underlying signal noise. Networks activated by visual input can attract attention and, as a result, the activity of the network underlying the hallucination will be silenced.

Interference of low-frequency oscillations with mechanism of working memory

Working memory is a limited capacity system allowing the temporary storage and manipulation of information and it is assumed to participate in feeding information into and retrieving information from episodic long-term memory (41). Electrophysiological experiments revealed that neurons in parietal, temporal and frontal cortex display persistent spiking activity after the brief presentation of a stimulus, what is thought to underlay neuronal mechanism of working memory (42). This sustained spiking is thought to depend on reverberating neuronal activity through the system of recurrent networks (42) and on subthreshold low-frequency (5-12 Hz) oscillation (43). Electrophysiological experiments in humans and monkeys showed that theta oscillations in visual cortex are enhanced during maintenance of visual working memory (44-47) and that occipital, parietal, temporal, and frontal theta oscillations play an important role in the dynamics of memory retrieval (48-50).

It has been found that discharge of single neurons is phase locked to the theta oscillations, and that the activity reflecting the identity of the remembered stimulus is greater near the preferred theta angle (44). For many neurons stimulus-selective signals occurred only near the preferred theta angle (44); confirming the theoretical model proposed by Lisman and Idiart (43). The overlap between neuronal mechanism of working memory and pathological low-frequency oscillations may lead to excessive activation of working memory traces and to the intrusion of previously viewed objects or recollected memories into consciousness. On the other hand, constantly increased theta oscillations in demented patients will lead to cluttering the working memory and will disrupt proper memorizing the selected new information.

Evaluation of the Hypothesis

Content of hallucinations

According to the model, the neuronal network with the strongest synaptic connections between neurons that store representation of emotionally relevant object, wins competition with other networks. Subsequently, the winning representation enters the content of consciousness. Consistently with the model, emotionally irrelevant objects such as pieces of furniture are rarely hallucinated in neurodegenerative disorders and in delirium (1, 28, 51). Most often the hallucinations are unpleasant and frightening (28, 52). Common motives are spiders, snakes, mice, rats, distorted and frightening faces, and fire (28, 51, 52). Very common in hallucinations are also people (28, 51, 52). Many older people suffer from loneliness and it can be expected that constant thinking about the loneliness can reinforce the neuronal representation of people. The role of emotions has been also noticed in case of experiential phenomena of temporal lobe epilepsy such as visual and auditory hallucinations and memory flashbacks (53). Gloor et al. (53) reported that most of the perceptual phenomena observed in temporal lobe epilepsy are emotionally charged. They suggested that attaching affective valence to the percept may be a prerequisite for conscious perception (53). Also experiments using attentional blink task suggest that the fear salience of the stimulus enhances its probability to be consciously perceived (54, 55). These data supports the idea that emotions affect perception and that they can shape the content of hallucinations.

Consistently with the idea that random noise triggers hallucinations of objects with the strongest brain representations in defined patients, hallucina-
tions are often constant and they do not change one into another (28). Typically, the same image repeats itself on different occasion and patients usually hallucinate one kind or limited number of different kinds of objects over time (1, 56). Another consistent fact is that when there are many objects simultaneously hallucinated they belong usually only to one category such as people, nuns, gypsies, soldiers, children, rats, snakes, spiders, insects, flames (28, 52, 57, 58).

The idea that plasticity related to the long-term memory plays an important role in generation of hallucinations is consistent with the assumption that disruption of plasticity is responsible for the therapeutic effect of transcranial magnetic stimulation applied in treatment of hallucinations (59). The possible effects of transcranial magnetic stimulation include long-term depression, depotentiation and homeostatic metaplasticity (59, 60). It can be expected that any treatment remodeling synaptic plasticity can decrease the ability of neuronal networks to generate hallucinations. First, the therapeutic remodeling can result from resetting the synaptic weights to baseline level (depotentiation), which is expected to affect mainly networks with the strongest synaptic weights. Second, the remodeling can be achieved through potentiation of the synaptic plasticity, which can be expected to affect mainly networks with the weakest synaptic weights because of the ceiling effect (61) limiting further increase in synaptic weights in networks with the strongest synaptic connections.

**Multimodal hallucinations**

Visual hallucinations in significant number of cases are associated with contextually correct hallucinations in other modalities (1, 56). For example, hallucinations of people can be associated with auditory hallucinations of human voices (56). This finding is consistent with the model of neuronal representation proposed by Damasio (29), which was incorporated into the low-frequency oscillation model of hallucinations. According to the model proposed by Damasio, activation of object representation in one modality can activate associated representations in other modalities by backward connections (29).

**Context-associated hallucinations**

As noted by Collerton et al. (1), hallucinations in neurodegenerative disorders occur usually in the same and contextually correct location. For example, hallucinations of visitors are often exclusively associated with the living room (1). The sight of a defined place can activate neuronal representations of objects by means of recurrent connections shaped by experience consistently with the model proposed by Damasio (29). Activated memory traces may be further reinforced by the low-frequency oscillations leading to hallucinations. Therefore, the context-associated hallucinations can be explained by combination of mechanism underlying memory formation and the low-frequency model of hallucinations.

**Palinopsia**

Mosimann et al. (28) found high incidence of temporal palinopsia (perseveration of previously viewed objects after a certain time) in Parkinson’s disease with dementia and in dementia with Lewy bodies. This observation supports the hypothesis that pathological low-frequency oscillations may interfere with mechanism of working memory leading to excessive activation of memory traces and to the intrusion of previously viewed objects into consciousness. Recent studies employing transcranial magnetic stimulation showed that excessive activation of residual working memory traces in visual cortex can bring content of short-term memory into visual consciousness (62, 63). For example, Jolij and Lamme (63) showed that transcranial magnetic stimulation induced a perception of previously seen image in 33% of trials.

**Discussion**

The aim of this paper is to point to the possible functional significance of pathologically increased oscillatory activity in the cortex. Although oscillatory EEG activity may be associated with perception or behavior only as an epiphenomenon, there are recent studies showing that oscillatory activity has a causal effect on neuronal activity and human performance. A recent study showed that even weak extracellular electric fields induce changes in somatic membrane potential independently of synapses and that these fields, especially at the frequency below 8 Hz, strongly entrain action potentials (35). It has been also found that repeated long trains of transcranial electric stimulation with a 0.8 – 1.7 Hz sinusoid current generate stable neuronal entrainment over time in widespread cortical areas (64) and that successive hyperpolarizing pulses induce increasingly higher rates of tonic firing that remain stable for tens of seconds (30). Also recent modeling study showed that the modulation of membrane potential by low-frequency oscillation (5 Hz) produce more action potentials than fast oscillations (50 Hz) with identical amplitudes (33). In human studies it has been found that transcranial alternating-current stimulation of the motor cortex at 20 Hz entrained beta-band activity and impaired concurrent voluntary movements in contrast to 5 Hz stimulation, which affected neither beta-band activity nor the motor performance (65). This study shows that the extracellular fields applied at defined frequency can functionally affect human performance (65). Similarly, Marshall et al. (66) found that application of transcranial oscillating potentials at 0.75 Hz to the frontal cortex during Non-rapid eye movement (NREM) sleep induced an increase in cortical slow wave oscillations (0.5 – 1 Hz) and
enhanced retention of declarative memories, whereas theta stimulation (5 Hz) (67) produced a decrease in slow oscillatory activity (0.5 - 4 Hz) and a decrement in memory consolidation suggesting again a causal role of the oscillatory activity. Oscillating potentials at 0.75 Hz applied to frontal cortex during wakefulness also increased slow oscillations (0.4-1.2 Hz) and theta frequency (4-8 Hz) and enhanced memory encoding (68). These studies show that electrical oscillations change the neuronal activity and that they exert functional effects on human performance.

Although the low-frequency oscillation model differs in many respects from the perception and attention deficit (PAD) model (1), it applies the same approach based on phenomenology and frequency of hallucinations in different disorders and in fact is consistent with main observations of Collerton and co-workers (1). The PAD model (1) proposes that hallucinations emerge as a result of incorrect attentional binding occurring in the case of impaired attention and visual perception. The association between the degree of visual impairment and the frequency of hallucinations (1) can be explained however by the EEG slowing. During the low-frequency oscillations cortical neurons may discharge to excitatory inputs only during depolarizing phases of membrane potential fluctuations and therefore they display poor responsiveness to afferent stimuli (69). The association of attentional impairments with hallucinations in neurodegenerative disorders (1) can result from increased signal noise and resulting perceptual impairments. In the low-frequency oscillation model of hallucinations the visual impairment is not a main causal factor. Nonetheless, associated visual impairments can facilitate the occurrence of hallucinations because visual impairments decrease competition between real and hallucinated percepts.

According to the low-frequency oscillation model, the content of hallucinations depends on the structure of neuronal networks storing representations of external objects. These networks are shaped by experience and it is expected that emotionally relevant objects are represented by neuronal networks with stronger synaptic connections compared with networks storing representations of emotionally neutral objects. This assumption is supported by studies showing enhanced memory for emotional stimuli (37-40). It has been shown for example that both spider phobic and non-anxious controls memorize spiders more successfully than positive and neutral targets (40, 70). There are also data showing the effect of emotions on perception. Spider phobics, in comparison to non-phobic controls, are more prone to see spiders in morphed stimuli that gradually transform from a schematic picture of a flower into a schematic picture of a spider (71).

The model proposes also that neuronal representation of emotionally relevant object activates attentional system, which facilitates further processing of the emotionally charged signal. This assumption is consistent with psychological experiments in humans. It has been shown that detection of threatening targets is privileged over detection of nonthreatening targets (72). Perception of the feared object is facilitated by stimulus-driven, involuntary and automatic recruitment of attention, which is independent of prior expectations (54, 55, 73-75). Therefore, threatening information is processed in a facilitated and automatic manner (73) and is less affected by the distractors (55, 72).

Collerton et al. (1) suggested that the content of hallucinations can be shaped by expectations directing the attention to hallucinated proto-objects in line with the proposition of learned top-down expectations inducing hallucinations in the model proposed by Grossberg (76). The expectations affecting attentional processes (1) and synaptic plasticity shaped by emotions can be considered as a complementary mechanism affecting the content of hallucinations.

The low-frequency model of hallucinations is consistent with the observation of cholinergic dysfunction associated with hallucinations in neurodegenerative disorders and in delirium (1) because decrease in activity of cholinergic system plays a crucial role in generation of cortical low-frequency waves (69, 77). It has been also found that anticholinergic drugs increase power in delta and theta frequencies in widespread cortical areas (22-27) and that these drugs induce hallucinations in healthy subjects (24-26). Cholinergic system affects cortical low-frequency activity directly by projection from nucleus basalis to the cortex and indirectly through thalamus (34). The direct effects of acetylcholine on cortical activity are complex and the emergence of cortical low-frequency waves during reduced cholinergic activity results probably from combination of long-lasting hyperpolarizations of cortical pyramidal neurons (77, 78), subsequent depolarization resulting from opening of the hyperpolarization-activated cation channels (79) and reduced inhibitory drive mediated by GABAergic interneurons (31, 32).

Increased low-frequency oscillations can contribute also to the mechanism of hallucinations occurring at the sleep onset and in schizophrenia. In healthy population the most common are hypnagogic hallucinations experienced at sleep onset (80), which is associated with increased delta EEG activity (81). Therefore, the occurrence of hallucinations during transition from wakefulness to sleep is consistent with the low-frequency oscillation model. Furthermore, the amplitude of delta oscillations during the sleep onset is higher in narcoleptics than normal sleepers (81), what is consistent with higher frequency of hypnagogic hallucinations experienced by narcoleptics (82). Auditory hallucinations which are most common in schizophrenia share some basic similarities with visual hallucinations experienced during delirium and in neurodegenerative disorders.
Importantly, simple hallucinations of elemental sounds such as clicks and bangs were reported only by 16% of patients, whereas all studied subjects experienced complex hallucinations of voices (83). Furthermore, the most common were emotionally charged hallucinations of abusive voices expressing personal insults specific for the subject (83). It has been also found that schizophrenic patients exhibit increased slow wave activity in temporal region containing auditory cortex (84-86). According to the commonly accepted disconnection hypothesis, the core pathology of schizophrenia is an impaired neuromodulation of synaptic plasticity leading to abnormal functional integration (87, 88). This idea has been combined with Bayesian model of perceptual interference to explain the occurrence of hallucinations (87). According to the hierarchical Bayesian model of perceptual interference, each level of the hierarchy in the brain adjusts the top-down expectations to the sensory input in order to minimize the prediction error (87). This perceptual learning depends on synaptic plasticity and the hallucinations occur when perceptual learning is disrupted through abnormal modulation of plasticity (87). In such situation the predictions are not adjusted to the bottom-up sensory signal and too much weight is afforded to the expectations (87). The increased slow oscillatory activity can contribute to the Bayesian model of perceptual interference by increasing the signal noise, and as a result, decreasing the mismatch between bottom-up signal and top-down expectations. Furthermore, the long-term memory shaped by emotions may contribute to generation of emotionally charged hallucinations in schizophrenia. Schizophrenic subjects display impaired social cognition (89, 90) leading to school failures, peer problems and social isolation starting in childhood (91, 92). Therefore, frequent social and school failures can lead to excessive reinforcement of memory traces for personal insults explaining characteristic content of auditory hallucinations in schizophrenia.

It should be mentioned that previously also other authors implicated slow oscillatory activity in generation of hallucinations (93-95) but the proposed mechanisms are completely different from the present model. Sperling et al. recently proposed that auditory hallucinations in schizophrenia result from increased beta activity constituting intermittent compensation mechanism for increased delta activity observed in schizophrenic patients (94). However, transient increase in beta activity during auditory hallucinations can be an electrophysiological correlate of neuronal processing of auditory information triggered by the low-frequency oscillations according to proposed here model. Kavanau (93) proposed that abnormal slow waves cause long-lasting weakening or dysfunction of synapses and activation of resulting incompetent circuits during waking leads to hallucinations, whereas Llinas et al., (95) suggested that positive clinical symptoms can result from ectopic gamma band activation resulting from inhibitory asymmetry between high- and low-frequency thalamocortical modules at the cortical level. Finally, Ffytche proposed that hallucinations may result from change in firing of LGN neurons from tonic to burst mode causing transient thalamic blindness (96). The main weakness of these hypotheses (93-96) is that they do not explain the phenomenology of hallucinations mainly composed of emotionally charged objects.

**Conclusions**

The model contains three main ideas which are combined together (Figure 1) but can also be applied separately. First, the low-frequency oscillations may be a source of a signal noise in the neuronal system. Second, synaptic plasticity shaped by emotions may participate in transforming noise into meaningful signal. Third, low-frequency oscillations may interfere with the mechanisms of short-term memory. Multimodal hallucinations can result from occurrence of hallucinations in one modality and subsequent activation of associated percepts in other modalities by backward connections. The proposed model predicts that we should search for treatments decreasing the power of cortical delta and theta oscillations or reshaping synaptic plasticity.

**Acknowledgments**

I am grateful to Ms. Malgorzata Kilanowska for bibliographic assistance, to Prof. Artur Swiergiel for critical reading of the manuscript and for editorial assistance and to anonymous reviewer for comments.

**Conflict of Interest**

The author declares no conflict of interest.
**First Question:** What do we already know about the subject?
Number of hypotheses and models has been proposed to explain occurrence of hallucinations but they can neither explain the phenomenology of hallucinations, nor the variation in the frequency of hallucinations in different disorders.

**Second Question:** What does your proposed theory add to the current knowledge available, and what benefits does it have?
The model explains phenomenology of hallucinations occurring in neurodegenerative disorders and in delirium and can be also relevant for hallucinations experienced in schizophrenia. The model predicts that we should search for treatments decreasing the power of cortical delta and theta oscillations or reshaping synaptic plasticity.

**Third question:** Among numerous available studies, what special further study is proposed for testing the idea?
First, the hypothesis can be evaluated by application of transcranial electric stimulation with sinusoid current to induce or disrupt low-frequency oscillations in distributed networks including sensory and association areas of the cortex. Second, interviewing patients and their families should reveal whether the content of hallucinations is related to previous emotional events or phobias.

---

**Table 1:** Spatial distribution of significant changes in power of delta (1-3.9 Hz) and theta (4-8 Hz) oscillations in neurodegenerative disorders and delirium based on quantitative EEG reports, which provided data for separate EEG channels.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Ref.</th>
<th>Eyes</th>
<th>DELTA Occipital</th>
<th>Parietal</th>
<th>Temporal</th>
<th>Frontal</th>
<th>THETA Occipital</th>
<th>Parietal</th>
<th>Temporal</th>
<th>Frontal</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alzheimer’s disease</strong></td>
<td>(2)</td>
<td>C</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>(10)</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(3)</td>
<td>C</td>
<td>O1, O2</td>
<td>NS</td>
<td>NS</td>
<td>F3, F4, F7, F8</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(13)</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Early onset Alzheimer’s disease</strong></td>
<td>(11)</td>
<td>C</td>
<td>O1</td>
<td>P3, P4</td>
<td>T5, T6</td>
<td></td>
<td>NS</td>
<td>P3, P4</td>
<td>T5, T6</td>
<td></td>
</tr>
<tr>
<td><strong>Late onset Alzheimer’s disease</strong></td>
<td>(12)</td>
<td>C</td>
<td>O1, O2</td>
<td>P3, P4</td>
<td>T5, T6</td>
<td></td>
<td></td>
<td>P3, P4</td>
<td>T5, T6</td>
<td></td>
</tr>
<tr>
<td><strong>Frontal dementia of the Alzheimer Type</strong></td>
<td>(15)</td>
<td>C</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>F7, F9</td>
<td>NS</td>
<td>P4</td>
<td>T5, T6</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Parkinson’s disease with REM sleep behaviour disorder</strong></td>
<td>(8)</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Parkinson’s disease without REM sleep behaviour disorder</strong></td>
<td>(5)</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Parkinson’s disease without cognitive impairments</strong></td>
<td>(4)</td>
<td>C</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Parkinson’s disease with mild cognitive impairments</strong></td>
<td>(5)</td>
<td>C</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Parkinson’s disease with dementia</strong></td>
<td>(5)</td>
<td>C</td>
<td>O1, O2</td>
<td>P3, P4, P2</td>
<td>T5, T6</td>
<td></td>
<td></td>
<td>P3, P4</td>
<td>T5, T6</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Parkinson’s disease with non-fluctuating dementia</strong></td>
<td>(3)</td>
<td>C</td>
<td>O1, O2</td>
<td>NS</td>
<td>NS</td>
<td>F3, F4, F7, F8</td>
<td>NS</td>
<td>P3, P4</td>
<td>T5, T6</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Parkinson’s disease with fluctuating dementia</strong></td>
<td>(3)</td>
<td>C</td>
<td>O1, O2</td>
<td>NS</td>
<td>NS</td>
<td>F3, F4, F7, F8</td>
<td>NS</td>
<td>P3, P4</td>
<td>T5, T6</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Dementia with Lewy bodies</strong></td>
<td>(2)</td>
<td>C</td>
<td>O1, O2</td>
<td>P3, P4, P2</td>
<td>T5, T6</td>
<td>T5, T6</td>
<td>F3</td>
<td>F4</td>
<td>T5, T6</td>
<td>T5, T6</td>
</tr>
<tr>
<td><strong>Delirium</strong></td>
<td>(19)</td>
<td>C</td>
<td>O1, O2</td>
<td>P3, P4, P2</td>
<td>T5, T6</td>
<td>F3</td>
<td></td>
<td>F4</td>
<td>T5, T6</td>
<td>T5, T6</td>
</tr>
</tbody>
</table>

Ref. - references; C - analyzed EEG traces were recorded in subjects resting with closed eyes; O - analyzed EEG traces were recorded in subjects resting with open eyes; red color - increased power of oscillations; blue color - decreased power; NS - not significant changes; white and empty cells - data not provided by authors; O1, O2, P3, P4, Pz, T3-T6, F3-F8, Fz - positions of EEG electrodes provided by authors.
Table 2: Frequency of hallucinations. * - at least 1 hallucinatory experience in a month.

<table>
<thead>
<tr>
<th>% of patients experiencing hallucinations</th>
<th>General population (80)*</th>
<th>Parkinson’s disease without dementia (51)</th>
<th>Alzheimer’s disease (97-99)</th>
<th>Parkinson’s disease with dementia (51, 100)</th>
<th>Dementia with Lewy bodies (51, 56)</th>
<th>Delirium (101)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any modality</td>
<td>6.2%</td>
<td>14%</td>
<td>-</td>
<td>45% - 54%</td>
<td>76% - 93%</td>
<td>32%</td>
</tr>
<tr>
<td>Visual</td>
<td>0.3%</td>
<td>8%</td>
<td>8 – 23%</td>
<td>50%</td>
<td>72%</td>
<td>27%</td>
</tr>
<tr>
<td>Auditory</td>
<td>0.2%</td>
<td>7%</td>
<td>3 – 8 %</td>
<td>21%</td>
<td>38%</td>
<td>12%</td>
</tr>
<tr>
<td>Tactile</td>
<td>0.6%</td>
<td>1%</td>
<td>-</td>
<td>0%</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Olfactory</td>
<td>3.5%</td>
<td>1%</td>
<td>-</td>
<td>6%</td>
<td>8%</td>
<td>-</td>
</tr>
</tbody>
</table>

Figure 1: Possible effects induced by pathological low-frequency oscillations.
**Figure 2:** The low-frequency model of hallucinations. The network on the left side denotes the neuronal representation of a tree (emotionally neutral object). The network on the right side is a neuronal representation of the spider (emotionally relevant object). The thickness of the arrows represents the strength of synaptic connections between neurons represented by black dots. The circles denote neuronal activation. The depolarization period of low-frequency oscillation is depicted at the top of the figure. Further explanations can be found in the main text.

### References


22. Sannita WG, Maggi L, Rosadini G. Effects of scopolamine (0.25-0.75 mg i.m.) on the quantitative EEG and the neuropsychological status of healthy volunteers. Neuropsychobiology 1987;17:199-205.


34. Steriade M. Acetylcholine systems and rhythmic activities during the waking--sleep cycle. Prog Brain Res 1999;110:1831-1837.