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Phosphene phenomenon: A new concept

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Abstract

This paper proposes a new biopsychophysical concept of phosphene phenomenon. Namely, visual sensation of phosphenes is due to the intrinsic perception of ultraweak bioluminescent photon emission of cells in the visual system. In other words, phosphenes are bioluminescent biophotons in the visual system induced by various stimuli (mechanical, electrical, magnetic, ionizing radiation, etc.) as well as random bioluminescent biophotons firings of cells in the visual pathway. This biophoton emission can become conscious if induced or spontaneous biophoton emission of cells in the visual system exceeds a distinct threshold. Neuronal biophoton communication can occur by means of non-visual neuronal opsins and natural photosensitive biomolecules. Our interpretation is in direct connection with the functional roles of free radicals and excited biomolecules in living cells.

Keywords: Phosphenes; Functional free radicals; Bioluminescent biophotons

1. Introduction

Our visual system not only mediates information about the visual environment but also is capable of generating pictures/lights of nonexistent visual worlds within the brain as afterimages, illusions, phosphenes, dream pictures, visual hallucination, and visual imagery. Bókkon (2005, 2006) suggested that features of homeotherm state made the development of explicit memory possible, and the brain can operate by weak pictures during informational processes (dreams and thinking), which is due to the weak coherent (bio)photon emission of the brain's cells. It was also raised that exact thermoregulation is of high importance in the brain, and weak biophotons are originated from molecular processes.

Here we suggest that phosphene phenomenon supports Bókkon's concept. Namely, the brain can internally generate ultraweak lights signals by bioluminescent biophoton processes of neuronal cells. This ultraweak light (biophoton) emission can become conscious if induced or spontaneous biophoton emission of cells in the visual system exceeds a distinct threshold. In other words, phosphenes can be mechanically, electrically, magnetically, etc., induced bioluminescent electromagnetic visible photons (biophotons) of the visual system as well as random bioluminescent biophoton firings of cells in the visual system.

2. Bioluminescent Biophotons From Living Cells

Ultraweak biophoton emission appears as a general feature of all living organisms (Quickenden and Que Hee, 1974; Popp et al., 1984; Tilbury and Cluickenden, 1988; Scott et al., 1991; Isojima et al., 1995; Takeda et al., 1998; Kobayashi et al., 1999a; Mansfield, 2005; Yoon et al., 2005; Yoshinaga et al., 2006). Ultraweak photon emission from unicellular and multicellular organisms is termed by several diverse names as dark luminescence, low-intensity chemiluminescence, ultraweak electromagnetic light, ultraweak bioluminescence, ultraweak photons, biophotons, etc. Sometimes the prefix bio is added to indicate its biological connection. The origin of coherent and incoherent biophotons is due to the different coherent and incoherent dynamical reactions especially bioluminescent radical and non-radical reaction, as well as the simple cessation of excited states. This ultraweak electromagnetic photon emission includes various ranges of wavelength including ultraviolet, visible, and infrared ranges. Natural oxidative metabolism of cells is the main source of ultraweak visible biophotons, i.e., biophotons derive mostly from reactions of reactive oxygen species (ROS) and reactive nitrogen species (RNS). For examples: non-enzymatic and enzymatic

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lipid peroxidation, mitochondrial respiration chain and peroxisomal reactions, oxidation of catecholamines, oxidation of tyrosine and tryptophan residues in proteins, etc. (Kruk et al., 1989; Hideg et al., 1990; Watts et al., 1995; Nakano, 2005).

A great deal of experiments provided strong evidence that generation of ROS and RNS is not an unwanted random process, but rather a very precise mechanism used in signaling pathways during physiological processes in cells and the brain (Contestabile, 2000; Prast and Philippu, 2001; Dröge, 2002; Knapp and Klann, 2002; Thiels and Klann, 2002; Gordeeva et al., 2003; Matsumoto et al., 2003; Tejada-Simon et al., 2005; Touyz, 2005; Kishida et al., 2006; Ullrich and Kissner, 2006; Valko et al., 2007). Therefore, ultraweak photon emission is not a byproduct of biochemical processes but it is linked to precise signaling pathways of ROS and RNS. Namely, under oxidative metabolism, regulated generation of ROS and RNS is in connection with the ultraweak photon emission of cells. Consequently, electrical (redox) signals of neurons can be converted into biophoton signals by bioluminescent radical and non-radical processes in the brain.

2.1. Biophoton Emission Within The Brain

Isojima et al. (1995) reported activity-dependent ultraweak photon emission from hippocampal slices of rat brain. Spontaneous ultraweak biophoton emission from neural tissue depended on the neuronal membrane depolarization and Ca^{2+} entry into the cells (Kataoka et al., 2001). This spontaneous biophoton emission could be facilitated by the membrane depolarization of neurons by a high concentration of K^+ and could be attenuated by removal of extracellular Ca^{2+} (Kataoka et al., 2001). In experiments of Kobayashi et al. (1999a,b) in vivo imaging of spontaneous ultraweak biophoton emission from a rat's brain correlated with cerebral energy metabolism, EEG activity, cerebral blood flow and oxidative stress. Biophoton emission intensity from the brain slices was dependent on temperature and oxygen concentrations. Therefore, we can conclude that ultraweak biophoton emission from neurons is in direct connection with biochemical processes of neurons. Namely, there is a neural activity-dependent ultraweak photon emission in the brain.

Up to this point, we can summarize:

- A great deal of experiments provided strong evidence that generation of ROS and RNS is not an unwanted random process, but rather a very precise mechanism used in signaling pathways during physiological processes in cells and the brain.
- Ultraweak photon (biophoton) emission is due to the natural reactions of reactive oxygen and nitrogen species of cells.
- Neuronal electrical signals can be converted into biophoton (ultraweak optical signal) signals by bioluminescent radical and non-radical processes in the brain.
- There is a neural activity-dependent ultraweak biophoton emission in the brain.

3. Phosphenes

Phosphenes represent the perceived sensation of flashes of light in the absence of visual stimulation. Phosphenes can be points, spots, bars or chaotic structures of colorless or colored light (Oster, 1970; Walker, 1981). Phosphenes are caused by various stimuli (mechanical, electrical, magnetic, etc.) of cells in the visual pathway as well as random firing of cells in the visual system (Reznikov, 1981; Lindenblatt and Silny, 2002; Merabet et al., 2003). Phosphenes are an early symptom in a variety of diseases of the retina or of the visual pathways, but healthy individuals can perceive them as well (Onofrj et al., 1998; Brigatti and Maguluri, 2005). Phosphenes can also be associated with emotional factors, drugs, alcohol, stress, fever or psychotic conditions (Cervetto et al., 2007). Induction of phosphenes is dependent on the type of stimulation (electrical or magnetic stimulation), stimulation parameters, and the neural structure of individuals (Merabet et al., 2003; Tehovnik et al., 2005). Furthermore, phosphenes are only perceived by blind subjects who have prior visual experience, suggesting that early visual exposure is essential to maintain any level of residual visual function (Merabet et al., 2003). The perceived phosphene lies within the visual hemifield contra-lateral to the stimulated cortical hemisphere, at a location reflecting the retinotopic organization of the visual cortex. The minimum magnetic or electric intensity needed to induce a conscious phosphene is widely held to provide a measure of visual cortex excitability (Boroojerdi et al., 2000; Delbeke et al., 2001).

3.1. Phosphenes As Electrically Or Magnetically Induced Bioluminescent Biophotons

It is well known that electrical stimulation of the visual cortex (from a few micro-amperes to a few milli-amperes) with electrodes is able to elicit phosphenes in sighted and blind subjects (Tassiker, 1956; Brindley and Lewin, 1968; Dobelle et al., 1974; Tehovnik et al., 2005). Phosphene induction by electrical stimulation of the visual pathway with implanted electrodes is regarded as a promising method for making the blind see again (Dobelle et al., 1974; Schmidt et al., 1996; Zrenner, 2002). Depending on the type of vision impairment, there are different types of implants. Different types of visual implants are named according to their locations: subretinal, epiretinal, optic nerve, lateral geniculate nucleus and cortical (Cohen, 2007).

Similarly but less invasively phosphenes can be elicited by transcranial magnetic stimulation (TMS) of the visual cortex (Merabet et al., 2003). Direct electrical or transcranial magnetic stimulation of the visual cortex causes a brief reversible disruption in cortical function and induces spiking activity in excitatory and inhibitory neurons of regional cortical layers. These electrical and transcranial magnetic stimulations have several similar effects on neuronal processes as: modulation of nonlinear ion currents, neuronal membrane potentials, neuronal metabolic (oxidative) processes, neurotransmitters release, etc. (Caramia et al., 1991; Rosenthal and Sick, 1992; You et al., 1998; Juckel et al., 1999; Oliviero et al., 1999; Walsh and Cowey,

2000; Strafella et al., 2001; Kanno et al., 2003; Jelenković et al., 2006).

Reactive oxygen species and nitric oxide are important participants in neural signal transduction that can provide the cellular basis for activity-dependent regulation of neuronal excitability (Yermolaieva et al., 2000; Knapp and Klann, 2002; Kishida and Klann, 2007). There is a tight coupling between neuronal activity and oxygen consumption. It has been demonstrated that oxygen consumption increases as a function of synaptic activity, i.e., functionally active neurons show increased metabolic activity and oxygen consumption, resulting in higher levels of ROS and RNS (Yermolaieva et al., 2000; Sheth et al., 2004; Offenhauser et al., 2005). Furthermore, electrically or magnetically induced spiking activity in excitatory and inhibitory neurons of regional cortical layers in the visual cortex can trigger the opening of calcium-selective channels at the synaptic membrane. Then, mitochondria produce ROS in response to increases in cellular calcium concentrations (Kamsler and Segal, 2007).

As we could see above, biochemical reactions of ROS and RNS are the main source of ultraweak visible biophotons during physiological circumstances, and this ultraweak photon emission is dependent on the neural activity and oxygen concentrations in the brain (Isojima et al., 1995; Kobayashi et al., 1999b; Kataoka et al., 2001). Therefore, electrically or magnetically induced production of free radicals and excited species can cause a transient increase of bioluminescent biophoton emission in the stimulated neuronal tissue. This transiently increased emission of local biophotons can appear as phosphene lights in our mind. Taken all round, during electrical or transcranial magnetic stimulation of cells in the visual pathway, intrinsic visual perception of phosphene lights is due to the electrically or magnetically induced and locally increased emission of biophotons in the visual system.

3.2. Mechanical Phosphenes As Bioluminescent Biophotons

The most common phosphenes are pressure phosphenes, caused by rubbing the closed eyes. This pressure mechanically stimulates the retinal cells (Grüsser et al., 1989). Pressure phosphenes can persist briefly after the rubbing stops and the eyes are opened, allowing the phosphenes to be seen on the visual scene. Furthermore, a blow to the head, resulting in pressure of the visual cortex against the inside of the skull, can also elicit phosphenes (the effect often described as seeing stars) (Oster, 1970). Both a pressure on the eye or a blow to the brain can cause a stretch-induced mitochondrial dysfunction and surprisingly high overproduction of reactive oxygen species (Perlman et al., 1999; Arundine et al., 2004). ROS generation in response to mechanical forces can originate from many various sources as NAD(P)H oxidase system, nitric oxide synthase or other oxidase systems (Arundine et al., 2004; Harrison et al., 2006; Suzuma et al., 2007).

Mechanosensitive ion channels play a critical role in transducing physical stresses at the cell membrane into an electrical and/or chemical intercellular signal response (Martinac, 2004). Pressure causes changes in trans-membrane nonlinear ion fluxes, currents and subsequent downstream processes such as neural transmission. Potassium channels are very important in setting the membrane potential of most cells. TRAAK is a novel two-pore mammalian K^+ mechanosensitive channel that is widely expressed in the brain, spinal cord, and retina (Martinac, 2004). TRAAK produces baseline K^+ currents that are strongly stimulated by mechanical stretch. It has been suggested that mechanical force can be transmitted directly to the channel via the lipid bilayer (Patel et al., 1998).

Under mechanical stretch, mechanosensitive potassium channels alter the membrane potential and cellular oxidative metabolism of cells. Changing the membrane potential is an important element in the signal transduction cascade leading from membrane receptor ligation to an increase in NADPH oxidase activity (Jones et al., 1981). We could see above that the emission of biophotons can be facilitated by a high concentration of K^+ (Kataoka et al., 2001).

In brief, under mechanical stress, a transient overproduction of reactive oxygen and excited species in cells of the visual system can also cause an excess bioluminescent biophoton emission. These pressure induced excess biophotons can appear as phosphene lights in our conscious mind.

3.3. Drug And Stress Induced Phosphenes As Bioluminescent Biophotons

Several factors as drugs, alcohol, stress, psychotic conditions, various diseases, etc., can cause visual hallucinations (Fountain, 2002). According to Cervetto et al. (2007), a wide variety of causal agents can induce phosphenes either by a nonspecific direct stimulation of the visual system or by changing the neuronal excitability or by suppressing noise filtering processes.

Almost a half-century ago, Karreman et al. (1959) proposed involvement of electrochemical phenomena of the electron charge transfer type during drug action in the central nervous system. Recently, a unifying theme for toxicity of abused and therapeutic drugs was suggested based upon electron transfer, reactive oxygen species, and oxidative stress (Kovacic and Cooksy, 2005).

Over 300 drugs are known to cause visual hallucinations (Fountain, 2002). Abused drugs as nicotine, cocaine, ecstasy, amphetamines, morphine, tetrahydrocannabinol, etc., can induce a nonphysiological overproduction of free radicals in the brain and can interact with the visual system. Oxidative damage plays a significant role in cocaine-induced disruption of the central nervous system (Poon et al., 2007). Psychostimulants as morphine and methamphetamine induce oxidative stress resulting in generation of free radicals and lipid peroxidation (Sharma et al., 2007). Methamphetamine causes its neurotoxic effects via the production of peroxynitrite radicals (Imam et al., 2001). MDMA (Ecstasy, 3,4-methylenedioxymethamphetamine) induces decreases in catalase activity in the caudate-putamen and hippocampus, decreases in glutathione peroxidase activity in the frontal cortex, increases in lipid peroxidation in the frontal cortex, caudate-putamen, and hippocampus of wild-type mice (Jayanthi et al., 1999). Under alcohol intoxication, accumulation of superoxide

radical-generating agents, inactivation of superoxide dismutase, and increase in nitric oxide concentration were shown in the brain cortex of albino rats (Museridze et al., 2006).

There is a large amount of convincing data demonstrating that unregulated reactive oxygen and nitrogen species are involved in initiation and development of many different forms of neuropsychiatric and neurodegenerative disorders (Lohr and Browning, 1995; Halliwell, 2001; Akyol et al., 2004; Calabrese et al., 2006). The pharmacological and biochemical results indicate that free radicals can be involved in stress-induced neurobehavioural effects (Chakraborti et al., 2007). Neurotization provokes a stable activation of lipid peroxidation in homogenates and synaptosomes of the rat brain cortex (Taranova et al., 1994).

In summary, drugs, psychotic conditions, neuropsychiatric disorders perturb the redox state of neuronal cells and induce unregulated overproduction of free radicals in the brain. This uncontrolled overproduction of free radicals causes an increased production of bioluminescent biophoton emission in different parts of the visual pathway, which can appear as phosphene lights in our mind.

3.4. Phosphenes As Bioluminescent Biophotons And Optic Nerve Diseases

Optic neuropathy refers to damage to the optic nerve due to any cause. Phosphenes can be an early symptom in a variety of diseases of the retina, but healthy individuals can perceive them as well (Swerdloff et al., 1981; Onofrj et al., 1998; Brigatti and Maguluri, 2005). Both non-regulated overproduction of reactive species and dysfunction of antioxidant systems play a pivotal role in the pathogenesis of different optic neuropathy. Glaucoma is a special type of optic neuropathy, usually associated with high intraocular pressure and retinal oxidative stress (Moreno et al., 2004; Tezel et al., 2007). Optic neuritis is an inflammation, with accompanying demyelination of the optic nerve. Dysregulated overproduction of reactive oxygen species, such as superoxide, peroxynitrite and hydrogen peroxide, has key role in peroxidation of myelin lipid and demyelination of the optic nerve (Guy et al., 1993, 1994; Wu et al., 1997). However, non-enzymatic and enzymatic lipid peroxidation and dysregulated mitochondrial respiration chain are the main sources of biophoton emission of cells (Miyazawa et al., 1989; Devaraj et al., 1997). Consequently, optic neuropathy can cause a non-regulated excess production of free radicals, which can also generate an excess bioluminescent biophoton emission in the visual system. Then, this random excess biophoton emission can also appear as phosphene lights in our mind.

3.5. Phosphenes As Bioluminescent Biophotons During Space Travel

Ionizing radiation consists of electromagnetic radiation as X-rays and gamma rays, and particulate radiation, such as electrons, protons, and neutrons. Light flashes (phosphenes) are abnormal visual sensations caused by the interaction of high-energy ionizing particles with the human visual apparatus in space travel (Fuglesang et al., 2006). It is well known, that ionizing radiation changes the chemistry of matter along its passage and produces ions and free radicals in the body (Todorović et al., 2005). Exposure to ionizing radiation produces oxygen-derived free radicals in the tissue environment as hydroxyl radicals, superoxide anion radicals and hydrogen peroxide (Casadesus et al., 2004; Guelman et al., 2005; Matsumoto et al., 2005). Therefore, high-energy ionizing particles can also generate a transient increase of free radicals. This transient overproduction of free radicals produces an excess biophoton emission in the visual system during space travel. Therefore, during space travel, phosphene perception is also due to the temporary increases of biophoton emission generated by ionizing particle induced free radical reactions in the visual system.

4. Endogenous Photoperception of Bioluminescent Biophotons by Non-Visual Photoreceptors And Photosensitive Biomolecules

Visual phototransduction is specifically retinal, but non-visual phototransduction also occurs in many extraretinal sites. Since the first sequence of an opsin, bovine rhodopsin, more than 1000 opsins have been identified, but some opsins have unknown functions (Terakita, 2005). Most opsins act as pigments that activate G proteins in a light-dependent manner in both visual and non-visual systems. Phototransduction can occur in the pineal complex, the brain, the iris, melanocytes of the skin, and possibly other sites (Terakita, 2005). Non-visual photoreceptor cells play important roles in diverse physiological responses as photoentrainment of circadian rhythms, detection of seasonal changes in the photoperiod, regulation of pineal melatonin production, regulation of body color.

Encephalopsin (Opn3, the first extraocular opsin identified in mammals) is expressed at high levels in several regions of the mouse brain, including the diencephalon, the cerebellum, and the cerebral cortex (Blackshaw and Snyder, 1999). Besides, neural specific expression of neuropsin (Opn5) was detected in the retina, brain, spinal cord derived from human and mouse tissues (Tarttelin et al., 2003). Why have photoreceptors in the deep brain regions where there is no light?

It has been suggested that extraretinal opsins may form some essential component of the circadian clock (Terakita, 2005). However, Purkinje cells of the cerebellum and various neurons in the cerebral cortex and elsewhere have no known relationship to circadian photoreception. Phosphenes can also be produced by electrically stimulating the lateral geniculate nucleus (LGN) (Pezaris and Reid, 2007). LGN is an area deep in the centre of the brain that relays visual signals from the retina to the cortex. However, both encephalopsin and neuropsin are expressed at high levels in several regions in the deep brain among them in the lateral geniculate nucleus. It seems that non-visual photoreceptors in the brain can contribute to many more aspects of mammalian physiology than previously suspected.

Biophoton absorption of neuronal cells is not restricted to various non-visual opsins. Biophotons generated within cells can also be absorbed by natural photosensitive chromophores (Thar and Kühl, 2004; Kato et al., 1981; Karu, 1999). For example, the electron transport chains on the inner membrane of mitochondria

contain photosensitive chromophores (cytochromes and porphyrins). Bioluminescent biophotons in the visible range can be absorbed by these mitochondrial chromophores (porphyrin ring, flavinic or pyridinic rings). Absorbed biophotons can induce conformation changes in natural photosensitive biomolecules (Cilento, 1988; Cilento and Adam, 1995; Mei, 1994). Then, conformation changes can trigger complex signal processes in cells.

In brief, neuronal biophoton communication can occur by means of non-visual neuronal photoreceptors and natural photosensitive biomolecules within the brain.

5. Summary

We have suggested a biopsychophysical (redox molecular) interpretation of phosphene lights. Our interpretation is in direct connection with the functional role of free radicals and excited species in living cells. It is well documented that the main source of ultraweak visible photons (biophotons) originates from oxidative metabolism of living cells, i.e., from biochemical reactions of reactive oxygen and nitrogen species as well as excited biomolecules. Furthermore, ultraweak photon emission is dependent on the neural activity in the brain. We have seen that several factors – *as electrical or magnetic stimulation of the visual system, mechanical effects on the visual system, various drugs, stress, high-energy ionizing radiation and high-energy particles, optic nerve diseases, etc.* – can induce phosphenes. However, these factors have a common feature, i.e., all of them can cause an unregulated overproduction of free radicals and excited biomolecules in various parts of the visual system and can change the neural activity in the brain. This unregulated overproduction of free radicals and excited species can generate a transient increase of ultraweak biophotons in different regions of the visual system. This non-specific overproduction of free radicals and excited species can elicit an excess ultraweak photon emission in the visual system. If this excess biophoton emission exceeds a distinct threshold, it can appear as phosphene lights in our mind. Neuronal biophoton communication can occur by means of non-visual neuronal opsins and natural photosensitive biomolecules within the brain. Taken all round, phosphene lights are due to the intrinsic perception of induced or spontaneous increased biophoton emission of cells in various parts of the visual system (from retina to cortex).

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