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A Theoretical Framework for Photosensitivity: Evidence of Systemic Regulation

Ewing G.W

Montague Healthcare, Mulberry House, 6 Vine Farm Close, Cotgrave, Nottinghamshire NG12 3TU, England

Abstract

There is not yet a precise understanding of why flashing lights could be used to induce photosensitive migraine and epilepsy or why flashing lights could be used with therapeutic effect.

Most Proteins and enzymes are activated by light. The chemiluminescence arising from protein-substrate reactions influences visual perception which can measured. This can be adapted diagnostically. Each protein-substrate reaction releases biophotons of light, commonly known as autofluorescence or chemiluminescence, the colour being unique to each protein-substrate reaction and the intensity being a measure of the rate of reaction. The degree of activation or deactivation of such reactions is dependent upon the prevailing reaction conditions i.e. the influence of systemic parameters (pH, temperature, levels of minerals, etc).

Knowledge of the nature and structure of the physiological systems enables a wider understanding of systemic dysfunction and pathology(s). Specific neural (EEG) frequencies can be associated with visual perception. This can be adapted therapeutically i.e. to photostimulate inhibited protein-substrate reactions thereby regulating the function of each physiological system. By such biofeedback technique(s) it may be possible to treat, in a person-specific manner, the dysfunction associated with specific physiological and psychological disorders.

Keywords: Light; Enzymes; Proteins; Mathematical modelling; Physiological systems; Autonomic nervous system; Visual perception; Virtual scanning

Introduction

Light is an essential requirement for life. It may be supplied by the absorption of sunlight and/or it may be generated by chemiluminescent processes. The precise selection of colour and its intensity are linked to the function of the autonomic nervous system (Krakov, 1941) e.g. it is essential for cellular respiration (Warburg, 1931). Light-based therapies are used in the treatment of neonatal hyperbilirubinemia (Cremer et al., 1958; Sisson, 1976), seasonal affective disorder (Lam et al., 2006; Oren et al., 1991; Wirz-Justice et al., 1996; Wileman et al., 2001), hormonal imbalance (Hollwich and Dieckhues, 1980), etc. Many technologies have been developed which use light although without a precise understanding of the mechanisms involved. Flashing lights at specific frequencies have been shown to induce migraines and/or epileptic fits and, at different frequencies, they have been shown to have a therapeutic benefit. Over 100 medical conditions are known to respond to the therapeutic influence of light. It influences immune function and the morbidity associated with viral infections (Finsen, 1895; Finsen, 1903; Moller-Sorensen and Brade, 1995; Møller et al., 2005). Its influence is context dependent i.e. disease is more prevalent at higher latitudes (multiple sclerosis (Goldacre et al., 2004), cancer(s) (Garland et al., 2006; Kent et al., 2009), depression (Gonzalez and Aston-Jones, 2008), chronic fatigue syndrome, etc) where there is lower levels of natural sunlight. The influence of light upon the body's physiology: immune response (Roberts, 1995), hormonal system (Hollwich and Dieckhues, 1980) and neurotransmitters (Shealy, 1990), etc; is widely reported.

The body absorbs light but it also emits light (Kobayashi et al., 2009). The absorption of light is widely studied however the emission of light is less well understood and is known variously as autofluorescence, chemiluminescence, bioluminescence, biophoton emission, etc (Shimomura et al., 2008). Such emission of light is associated with the activation of enzymes and proteins and their subsequent reaction or interaction with reactive substrates. Under normal circumstances the absorption and emission of light are in an apparent equilibrium however the consequences of stress, and of subsequent oxidative stress reactions, create pathological processes which influence this balance and alter the nature and emission of photon emission (Rattemeyer and Popp, 1981; Grasso et al., 1992). This influences visual perception (Ewing and Parvez, 2008; Ewing and Ewing, 2008) i.e. such changes to visual perception are the consequence of of altered biochemistry arising from pathologies and the use of drugs.

Intensity and colour of light

In order to excite the circadian system it is considered that the prevailing light intensity should be approximately 1000 lux. Melanopsin, a key protein in the function of the body clock, is excited by blue light (Avery et al., 2001; Avery et al., 2001; Rea et al., 2004). Morning light brings about a more rapid end to melatonin secretion; exposure to sunlight increases serotonin production; whilst the decline of natural sunlight later in the day stimulates melatonin production, the onset of sleep and

***Corresponding author:** Ewing G.W, Montague Healthcare, Mulberry House, 6 Vine Farm Close, Cotgrave, Nottinghamshire NG12 3TU, England, E-mail: graham.ewing@montaguediagnostics.co.uk, graham.ewing@montague-diagnostics.co.uk

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Sleep	Temperature	Breathing	Digestion
Blood pressure	Blood volume	Blood Glucose	Blood Cell Content
pH	Sexual function	Osmotic Pressure	Excretion (Urination)
Posture & Locomotion			

Table 1: Physiological Systems.

production of Human Growth Hormone (HGH). Sleep on its own has not been recognised to perform a function although the quality and quantity of light and sleep influences cognitive function (Tonks, 1999), morbidity and mortality.

Sleep facilitates the production of HGH

Nearly fifty percent of HGH secretion occurs during the third and fourth REM sleep stages (Takahashi et al., 1968). This indicates that Sleep provides a regenerative, regulatory or coordinating role facilitating the production of key biochemicals which are necessary for other systems and organs (cardiovascular, endocrine, pancreas, etc) to function properly (Shannahoff-Khalsa et al., 1996; Shannahoff-Khalsa et al., 1997; Shannahoff-Khalsa and Yates, 2000; Shannahoff-Khalsa et al., 2001) and hence that lack of sleep influences the function of other systems.

HGH and its various isomers are considered essential for growth, cell reproduction and regeneration in humans. It is implicated in regulation of body fat, muscle mass, bone density, energy levels, sexual function and immune function. It is produced in a pulsed manner of typically 3-5 hour intervals. The production of HGH is age-related. Teenagers produce HGH at typically 700µg/day whilst adults produce at typically 400µg/day. In general, the rate of HGH production declines with age. Stress in its many and various manifestations influences all aspects of autonomic (ANS) function including sleep, HGH production (Shannahoff-Khalsa et al., 1997), immune function (Kiecolt-Glaser and Glaser, 2002), the speed of recovery following illness, etc.

Circadian rhythms

There is evidence of cycles influencing almost every aspect of the body's function e.g. changes at puberty, pregnancy (9 months), menstruation (28 days), circadian cycle (24 hours), the sleep cycle (90 minutes) and many lesser ultradian cycles; each being evidence of significant biochemical changes (and their rate) in the body at the systemic, organ/cellular and molecular levels e.g. pancreatic cycles which are typical of a feedback control loop which monitors insulin release and blood glucose levels. This is necessary because insulin is highly reactive and internal manufacture of insulin by the pancreas is relatively slow. Circadian rhythms are common to many lifeforms and are a feature of the body's basic biochemistry (Sweeney and Borgese, 1989; Kondo et al., 1993; Halberg et al., 1965; Katinas et al., 2002). Light influences the autonomic nervous system (Krakov, 1941) and is essential to the regulation and stability of the circadian rhythms (Halberg et al., 1970; Sanchez de la Pena et al., 1989; Hillman et al., 1994), the body's timing, and its systemic function.

What is not yet known is how the body regulates its function. Is this by light or by biochemistry alone i.e. the autonomic nervous system, or does it involve frequency or a combination of all or some of these factors?

Systemic Function

The nature and structure of the physiological systems (revised)

The Russian researcher I.G. Grakov has mathematically modelled the relationship between cognition, the autonomic nervous system and physiological systems. This includes a revised understanding of the physiological systems (see Table 1) and a revised understanding of the role performed by sleep.

Of these physiological systems only sleep has an apparently unexplained function. Each system performs an essential physiological function and is regulated by a network of organs. Extremes of system function are recognised and referred to as *hyper* function or *hypo* function. Such a viewpoint is not new to the GP who routinely assesses the stability of the physiological systems, albeit in an empirical manner, however Grakov's revised understanding differs in the following respects: (Krakov, 1941) the inclusion of sleep, temperature, osmotic pressure and pH as physiological systems; (Warburg, 1931) the revised understanding of the cardiovascular system as breathing, blood glucose, blood pressure, blood volume and blood cell content; (Cremer et al., 1958) the exclusion of an immune system i.e. its inherent presence in other systems (e.g. digestion, pH, sleep, blood cell content, etc); (Sisson, 1976) the inclusion of locomotion and posture as a physiological system. Such an explanation is inclusive of all functional systems in the body by comparison with the conventional explanation which excludes consideration of vital aspects of the body's physiology and function.

Examples of synchronised function between organs

That the body's complex multi-systemic function is regulated is evident by considering the digestive system i.e. that the taste and chewing processes forewarn the digestive system: fermentation by the stomach, preparation of gastric juices and their synchronised and regulated input into the digestive system by the gall bladder, absorption of nutrients by a suitably functioning set of intestines (and hence of appropriate blood quality), neutralisation of excess acids, and ultimately the storage and release of excrement. Poor quality or quantity of pancreatic juices/bile salts, digestive acidity or blood, or their desynchonised function (e.g. premature or delayed addition of pancreatic juices), influences digestive function and the degree of absorption of specific nutrients.

Another example is that of heart function mathematically modelled at the biochemical level (Noble, 2008) however, apart from the practical limitations of such models there is the significant lack of consideration that sensory input/stress could influence the function and stability of the visceral organs (Zagulova et al., 2001) or that there could be a mechanism which regulates the function and stability of physiological systems and inherent organ networks (Ewing and Ewing, 2008).

The Significance of Sensory Input and Sense Perception

There is no evidence to support the contention that the eyes take snap shots or photographs of the world or that the brain has an internal cinema to view the world in a holographic manner. The evidence indicates that the eyes and brain receive information on an almost continuous basis and that this information is stored in neuronal structures. Moreover, the brain does not react to every individual stimulus. It responds to sequences of sensory input which have specific significance (intensity) and/or which compare with stored memories. We note from the phenomena 'subliminal imaging' that the brain sees or processes information abt once every cycle and that the rate of visual cycles is typically 40 hz (i.e. within the gamma frequency range (30-60 hz) or every c25 milliseconds). This indicates that the sensory perception or neural representation of a particular object is encoded by the prevailing biochemistry and by the electrochemical activity associated with differing frequencies (Gray et al., 1989; Eckhorn et al., 1988).

If the brain worked by taking a series of pictures there would be a significant chance that a great deal of visual input would be out of phase therefore the brain must continuously be in phase, or must receive data sufficiently quickly that phasing is not a significant impediment, therefore sensory input and the brain waves, must operate continuously i.e. in a seamlessly overlapping mode. It is also worth noting that our view of a particular object is not one 'photo' but instead the summation of a huge amount of visual information comprising shape, colour, visual contrast, and the time to observe the object i.e. we continuously assimilate visual input. Accordingly the presentation of light as a frequency or flashing light will influence the absorption of specific colours of light and of its intensity every cycle. It requires several exposures for a short-term memory to be created i.e. for the first such memory there is no residual memory. There cannot be. It is the first exposure which creates the memory. If the colour alters the effect will be random, however if the same colour is continuously presented this will amplify the absorption of this colour and hence its therapeutic effect upon the body's biochemistry. It indicates that the rate of receiving and processing sensory information, in particular of visual information, is related to pathologies, age and weight. It explains why response times slow down with increased age and weight. It illustrates that age-related cognitive decline is the physiological consequence of biochemical changes (Ambatipudi et al., 2009) which cease to support the proper function of the neuronal structures and, as a consequence, the creation of memories. The evidence also illustrates that the eyes do not function independently of the other senses but instead function as part of a multi-sensory data processing matrix. Under normal circumstances the eyes are responsible for an estimated 85% of sensory input with verification being provided by the other senses. This is supported by considering how, in the visually impaired, the brain is able to compensate and amplify non-visual input.

There is no evidence that the neuronal structures store complex pieces of information but instead that each stores simple pieces of information and that it is the context in which such information is stored which, when accessed and decoded, is interpreted as a distinct memory i.e. as sensory input is converted into biochemical and electrochemical impulses the brain must store data as complex biochemical and/or electrochemical signatures. Furthermore the ability to store memories is influenced by the prevailing neuronal biochemistries and brain wave frequencies. This illustrates the influence of biochemistry i.e. including the function of the visceral organs, upon memory formation. The process of 'long-term potentiation' (Lynch and Baudry, 1984) is considered essential for the formation and storage of new memories and the recall of old memories. This illustrates the potential to use frequency to stimulate the production of specific neurotransmitters e.g. of serotonin, melatonin, catecholamines, etc. It does not however consider the wider implications of the varying EEG frequencies i.e. the multi-level nature of memory and of events of differing physiological significance i.e. of lower (delta/coma) or higher (theta/pain, alpha/thought/shouting, beta/physical activity) EEG frequencies.

We never forget issues which have the greatest significance e.g. the result of harm, injury or disease; and which are indelibly imprinted in the body through the formation of scar tissue(s) or by the memory of pain. The greater the extent and/or significance of our cumulative, multi-sensory, experience(s) the lower will be the prevailing EEG frequency and the greater will be the ability to recall the memory. Similarly the influence of stress e.g. when tired, reduces our ability to store memories.

The brain regulates the release of neurotransmitters by light and frequency. Pathologies or the accumulation of toxins influence the brain wave frequencies which are appropriate for each physiological system i.e. organ and system function are stimulated by frequencies and light e.g. how photosensitive migraine and epilepsy can be initiated by flashing lights. Similarly migraine, dyslexia and other conditions can be treated by the selective use of brain frequencies i.e. there is a positive therapeutic effect which can be employed using knowledge of this relationship between colour and frequency.

The implications of such findings are significant. It indicates that the use of drugs may not be able to create health i.e. drugs may eliminate the progress of pathology and hence reduce the symptoms of disease but their use relies upon the body being able to recover its original stable state. That disease can exist in a stable state i.e. in the case of 'chronic' illness and/or of subsequent biochemical change e.g. of demyelination in Multiple Sclerosis, suggests that the assumption that drugs improve health and wellbeing may have significant limitations.

Linking the Function of Proteins and Enzymes to Chemiluminescence and Visual Perception

That protein and enzyme function involves the releases of chemiluminescence (Martinek and Berezin, 1979; Hug et al., 1980; Yousuf-Azeemi et al., 2008; Yousuf-Azeemi et al., 2009) is not a new phenomena however linking this release of light to (i) oxidative stress (Cadenas, 1984; Cadenas and Sies, 1985; Cadenas and Sies, 1984; Kobayashi et al., 1999; Nakano, 1989; Nwose and Ewing, 2009) and pathology and to (ii)visual perception (Ewing and Parvez, 2008) is a significant development. Light raises the enzyme to an activated state (Sytina et al., 2008) in which a more favourable conformation of the

enzyme and its active site facilitates the enzymatic conversion of its substrate i.e. the precise selection of colour (Vojisavljevic et al., 2007), can be used rather than general exposure to sunlight.

Enzymes are catalysts for many biochemical reactions (Bairoch, 2000). They are highly specific and catalyse reactions by providing an alternative reaction pathway with lower activation energy. Their efficiency and specificity is due to the shape of the enzyme molecule. They operate efficiently in a narrow range of environmental conditions i.e. the intra- and intermolecular bonds involved in protein conformation are disrupted by changes to temperature, pH, and the influence of cofactors and inhibitors.

The influence of light upon Bilirubin is notable for several reasons: (i) the isomers of bilirubin (an unresolved mixture of its E, Z and Z, E isomers) produced by exposure to light (and/or UV) are more soluble than the unilluminated isomer. These are excreted by the liver (Sisson, 1981). (ii) Irradiation by visible light catalyses the reaction (Sisson, 1981). (iii) pH influences the rate of reaction and improves albumin's ability to bind to bilirubin (Kozuki et al., 2008).

Light activates many biochemical reactions. This phenomena is now being intensively researched for its potential to improve the understanding of neuronal pathways and firing mechanisms (Miller, 2006; Airan et al., 2007; Banghart et al., 2004), conceivably linked to protein conformation and the degree of coiling of DNA, which are considered to be implicated in Alzheimers disease and other neurological conditions. This leads to an improved understanding of: the visual pathways (Bitensky et al., 1978; Arshavsky et al., 1985; Arshavsky and Bownds, 1992; Binder et al., 1990; Nicol GD, Bownds, 1989); specific physiological processes and an improved understanding of the physiological processes of repair (Alilain et al., 2008); the neurosensory pathways (Cardin et al., 2009); techniques to activate specific drugs (Xu et al., 1985); techniques to activate or inhibit specific biochemical reactions (Binder et al., 1980; Seeman et al., 1985); and influence behaviour (Lima and Miesenböck, 2005). Current research is focussed upon manipulating the function of neurons to be responsive to light in order to alter ion-channels i.e. specific minerals (Sodium, Calcium, Potassium) stimulate firing of neurons (Banghart et al., 2004; Nicol and Bownds, 1989). Others are researching natural phenomena i.e. the natural light-sensitive ion channel channelrhodopsin-2 (Boyden et al., 2005).

It has been illustrated that light activates enzymes and hence influences the rate and completeness of biochemical reactions. This has an influence upon behaviour. It influences memory (Vandewalle et al., 2007), sleep (Duffy et al., 1996; Neumeister et al., 1996), mood (Golden et al., 2005; Kasper et al., 1989), physical strength (Hamid and Newport, 1989), personality (Schaie, 1966), aggressive behaviour (Schauss et al., 1985), and mental illness such as bipolar disorder (Benedetti et al., 2005; Deltito et al., 1991), eating disorders (Goel et al., 2009), seasonal affective disorder and depression (Tuunainen et al., 2004; Martiny et al., 2004), etc. It influences many, if not all, aspects of the body's function (Daw, 1984; Meer, 1985; Trevor-Roper et al., 1969). Multisensory therapies are used to treat multisensory dysfunction (Wolfarth H, Sam, 1982; Lancioni et al., 2002; Chung and Lai, 2002; Hotz et al., 2006). As drugs help only circa 40% of people with mood disorders and only circa 50% of disease (Spear et al., 2001) we are left to conclude that (i) the understanding and assumptions upon which drugs are based remains significantly deficient, and/or (ii) that light (and/or sensory input) may play a more significant role than hitherto imagined. The role performed by light is associated with the regulation of the body's function i.e. of the autonomic nervous system and physiological stability, by contrast with that of drugs which seek to eradicate the symptoms of disease. They are two distinctly different mechanisms, each with a different significance and potential benefit depending upon circumstances. They are mutually compatible. These are the different roles performed by the doctor and (a) the nurse, or (b) the health psychologist, and/or (c) which perplex researchers of 'placebo' effect.

Is Internal Timing the Key to Physiological Stability?

It is inconceivable that there is not a mechanism to coordinate the function of the organs and systems which regulate the body's biochemistry. It is the coordinated function of our eyes, limbs and visceral organs which enables our movement. The coordination of sensory function is necessary for the body's multi-level function i.e. its appreciation of danger.

There are clear precedents that timing of internal events is a significant factor in systemic function e.g. from the first taste and visual input the digestive system is primed to receive food. The processing of this food requires the coordinated function of numerous organs. Whilst the normal flow is that of oesophagus, stomach, duodenum, large intestine, small intestine; in particular it requires coordination with the function of the duodenum in which the digestive juices from pancreas, liver, bile duct and gall bladder mix together and are fed into the digestive stream.

The coordinated function of neurons is regulated by voltage, chemicals, temperature and frequency which influence mental (Bhattacharjee, 2007) and physiological stability. Orthodox medicine (Fell, 1997) considers the body's biochemistry and fails to recognise the multi-level and multi-systemic nature of the body's physiology (Noble, 2007; Ewing and Parvez, 2008; Ewing and Ewing, 2008). It overlooks that (i) the body's function is regulated by the influence of sensory input i.e of light, upon the autonomic nervous system and its subsequent influence upon the physiological systems (Ewing and Ewing, 2008) and (ii) the role of EEG frequency.

Multi-Sensory Functionality

Our senses work in a coordinated manner, as a data processing matrix, each conveying different information to the brain. Information of multi-level significance is linked to the brain by different EEG brain frequencies i.e involving differing biochemistries. Sight enables the vision of events but it requires the coordination of visual input and sound (and other forms of sensory input) to convey meaning, distance, and danger. Sight is used primarily to observe therefore this must be related to memory and to the EEG frequencies in order to give significance and meaning.

Sight is associated with perception; Sound conveys meaning, danger; Touch conveys pain, damage and sensuality; Smell conveys danger, sensuality, maternalism; Taste conveys the pleasure of nutritious food or the danger from rancid or poisonous foods; the movement of hairs on the skin, associated with touch, convey information of temperature changes, etc. Each acts at different levels of the body's function (EEG frequencies and the associated biochemistries). There is evidence that sound (Holmes-Atwater, 1997) and smell (Schuett et al., 2000; Schuett et al., 2000) function at delta frequency and are related to consciousness and behaviour. Significant defects associated with sensory dysynchronisation include prosopagnosia, autism, dyslexia and related autistic spectrum disorders, etc (Ewing et al., 2009).

There is evidence that cognitive processes are related to the degree of firing synchronisation of neural networks (Gray et al., 1989; Gray, 1994; Fries et al., 2001; Fries, 2005; Sejnowski and Paulsen, 2006; Schoffelen et al., 2005) and are linked to the coherence or synchronisation of EEG frequency (König et al., 1995). Gamma band synchronisation is related to cognitive function (Bragin et al., 1995) and similarly for other EEG frequencies (Canolty et al., 2006; Tsodyks et al., 2000; Salansky et al., 1998). If exposed to a visual stimulus e.g. at 40 or 50 hz, in the gamma band (30-60 hz) the brain will record the image but will ignore its significance. It is only the repeat exposure to the visual stimulus, its visual recognition and hence its similarity to a stored memory (short-term or long-term) which determines its significance (deCharms and Merzenich, 1996). This may occur by a synchronisation process which enables firing of neurons and hence the fixation of the memory. Similarly the intensity or nature of the exposure will also determine its significance – (Krakov, 1941) through visual comparison with past events and (Warburg, 1931) by aural comparison to past sounds and to the degree of its exposure (loudness). The coordination of sensory input acts to determine its physiological significance, each acting at different EEG bands and recording differing levels of sensory input e.g. by touch, firmness, pain and damage. The body's function, its receipt of sensory input, is rapid – different species having differing EEG patterns (Bullock et al., 2005) – however the body's function involves feedback loops to assimilate the data by comparison to past memories e.g. it takes time following physical injury for the pain to develop (up to 30 seconds). The body cannot react instantaneously otherwise physiological stability (regulated by the theta and delta EEG frequencies) would be difficult to achieve. This explains why it takes time for the association with pain to develop following severe injury/ trauma. Existing precedents illustrate an association between (i) physiological damage (comatose state) with delta frequency, (ii) pain and the theta frequencies, (iii) thought/neural processing and the alpha frequencies, (iv) physiological responses and the beta, and (v) visual function and the gamma wave frequencies. Accordingly therapies involving lower EEG frequencies can be expected to have greater therapeutic effect than those at higher EEG frequencies (Achmon et al., 1989).

The rate of synchronization or firing must also be related to biochemistry i.e. declining with advancing age (Ambatipudi et al., 2009), the influence of excess weight or of pathology. Through the process of age-related decline the body's biochemistry ceases to support the production of neurons and their normal neuronal function. This illustrates that the brain is continually scanning its environment (Womelsdorf et al., 2007) i.e. that neuronal synchronization contributes to cognitive function and that neural desynchronisation is associated with reduced cognitive function i.e. arising from the influence of pathologies.

The Dynamic Relationship between Cognition and Physiology

Grakov's methodology is consistent with a central governor theory (Hill et al., 1924; Bassett, 2002; Noakes et al., 2005 Noakes et al., 2001) i.e. that the brain is continuously assimilating data from its external and internal environments as a set of interacting data processing matrices (via the neural networks and physiological systems (Red'ko et al., 2004; Anokhin, 1975)) which advises the nature of threats and of the body's condition and preparedness for actions of specific types and intensities.

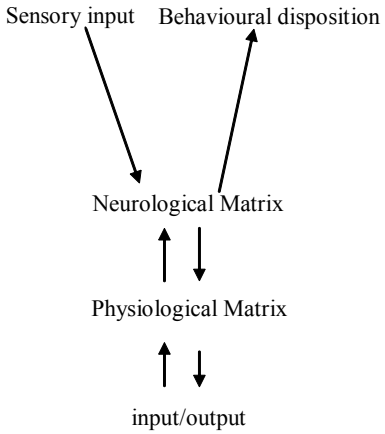

Figure 1

That the brain's function involves neural networks to regulate the network of visceral organs is increasingly evident (Rózsa, 1987; Massabuau and Meyrand, 1996; Suzuki et al., 2005; Silva et al., 2005; Büschges, 2005). In cases of pathology this systemic stability may alter i.e. as a 'pathological functional system' in which the most dysfunctional systems work at an EEG frequency which is stable, involves other organs, and hence differs from normal EEG frequency (Kryzhanovskii et al., 1995; Sudakov, 1987; Anokhin, 1975). We recognise this as the *chronic* disease state.

Such observations illustrate that there are neural mechanisms which regulate the function of the visceral organs. By contrast, in cases of severe trauma (stroke, coma) brain function may not, in the short term, be necessary to regulate the body's function. This illustrates the body's memory may be able to exert a compensatory influence.

Flashing Light Therapies

Flashing lights have been shown to have growth or therapeutic benefit in plants (Sassenrath-Cole et al., 1994) and humans (Dewan et al., 1978; Anderson et al., 1997; Anderson, 1989; Noton, 1997; Noton, 2000; Liddle et al., 2005, Nakao et al., 2003). To consider why a migraine or epilepsy could be

induced by photostimulation it is necessary to have an understanding of what causes a migraineous event or an epileptic fit. The results obtained by Virtual Scanning (Nwose et al., 2009; Ewing and Ewing, 2009; Ewing et al., 2009) illustrate that migraines (and perhaps also epilepsy) are caused by a lack of oxygen being supplied to the brain, arising from the condition of the spine/neck, the quality of the blood (viscosity, iron content, blood glucose and blood cell content i.e. the autonomic nervous system), and the ability of the blood vessels and heart to convey oxygenated blood through the lungs to the brain. This is consistent with known observations and illustrates that systemic dysfunction is a significant factor in migraines. It explains why complex migraine medications are not significantly more effective than simple analgesic combinations. It explains the apparent effectiveness of drugs designed to reduce blood viscosity i.e. that such drugs have a systemic action upon blood cell content and blood glucose.

Frequency is used in flashing light therapies with variable effect, perhaps because of the poor level of understanding of the phenomena. Nevertheless it has been shown to have a beneficial influence upon the Human Menstrual Cycle (Dewan et al., 1978; Anderson et al., 1997), Migraine (Anderson, 1989; Noton, 1997; Noton, 2000), Dyslexia (Liddle et al., 2005), regulation of blood pressure (Nakao et al., 2003) and many other conditions. It is linked to the coherent function of neurons (Fields, 2006) and the regulation of physiological systems. Furthermore the greater the physiological need for synchronised function i.e. at the organ level, the lower will be the frequencies required to support the action of brain waves and of neuronal interaction (Bullock et al., 2005).

Virtual scanning: case studies

Studies of the therapeutic value of such technologies, conducted in Russia and UK and verified by medical professionals, illustrate the powerful nature of such a technology (Vysochin et al., 2000; Nwose et al., 2009; Ewing et al., 2009 Ewing and Ewing, 2009). Case studies reported by doctors and consultants at various Russian hospitals (Vysochin et al., 2000) include the successful treatment of eneuresis (involuntary urination), amenorrhea (absence of menstruation), impaired cardiac rhythm, depression, trigeminal neuralgia, epilepsy, slipped disc, endometriosis, plexitis, infertility, tinnitus, latex allergy, migraine, high blood pressure, excess weight, night phobias, the stabilisation of blood glucose in patients with diabetes mellitus, etc.

Discussion

There are many inconsistencies with the orthodox approach which prevails in current medical research and medicine e.g.

- it assumes that EEG frequencies are the consequence and manifestation of the body's biochemistry yet fails to consider phenomena which manipulate the EEG frequencies and consequently the body's biochemistry.
- it overlooks the significance of the different EEG categories which illustrate the multi-level nature of the body's function i.e. it is not a chance observation but instead a significant phenomenon.
- it recognises that the body's function is multi-systemic yet fails to consider the significance of phenomena linked to systemic function and dysfunction.
- it assumes that the body's function is regulated from the bottom up i.e. from its biochemistry, when there are clear indications that stress acts at the neural level and influences the body's biochemistry – a top down approach. The evidence suggests that the body's function is dynamic i.e. involving both the top down and bottom up approaches. Both are correct.
- it steadfastly ignores the influence of sensory input upon neural function and organ function when there are clear indications that stress (experienced mainly through visual input) influences the function of many organs including heart, pancreas, duodenum, intestines, lungs, etc.
- it overlooks that the body's biochemistry alters throughout human development i.e. from birth until death.
- it assumes that the disciplines of psychology and physiology differ i.e. seeking differing neurobiological explanations for what we perceive as psychology and physiology. It overlooks the plausibility, increasingly recognised by neuroscience, that the body's function and hence its psychology (our health, wellbeing, personality, emotions, consciousness, etc) are manifestations of the body's multi-level physiology and function.
- it assumes that upon treatment of disease by drugs that the body will re-establish its natural stability i.e. health and wellbeing.

Such issues can be explained by considering that the body's function is dynamic, hierarchical, multi-systemic, multi-level and context dependent. There is a dynamic relationship which exists between the brain and the body (psychology and physiology), neurons and neural networks, the brain waves and the visceral organs (incl cellular and molecular biochemistry). Such understanding has been developed by I.G. Grakov, (1985) who identified patterns of biological response to the influence of specific frequencies and subsequently mathematically modeled the consequences of visual perception, upon the physiological systems, and upon cellular and molecular biochemistry (Kandel, 2006). In addition he has mathematically modelled the parameters of a flashing light therapy (i.e. of the colour and intensity of light and the appropriate resonant frequencies) which are specific for each patient. This is now the fundamental basis of the commercialized technology – 'Virtual Scanning'.

Such methodology establishes the systemic consequences of biochemical dysfunction by contrast with what is mislabeled as 'systems biology' - which seeks to determine the biology of systemic function and dysfunction. It addresses the limitations of the reductionist approach and takes into account the role of sensory input upon the body's physiology whereas by comparison biochemical reductionist research often completely ignores such fundamental and significant influences (Kohl and Noble, 2009).

Any explanation for the body's function must be based upon

an understanding of the body's structures, the prevailing biochemistry and of related biochemical phenomenae. The photostimulation of specific neurons is linked to specific behavioural traits which involves the body's cellular and molecular biochemistry. Light (of specific colour and intensity) acts to coordinate the firing of neurons across neural networks. The chemiluminescence (colour and intensity) released by specific protein-substrate reactions is not the same as the light absorbed. The release of light from one reaction activates that of associated reactions. The use of frequency, delivering colour of specific intensity, acts to coordinate the firing of neurons across neural networks and coordinating the function of organ systems, organs, and cells.

The energy from light activates proteins. Specific wavelengths (colours) activates specific proteins. This induces the migration of stem cells (Biener et al., 2009) and translocation of proteins (Levskaya et al., 2009) to the cell membrane. It has also been shown to have a positive therapeutic effect re treatment of diabetes (Ramdawon, 2001). Furthermore, the use of stem cells to treat diabetes mellitus has encountered problems. Initial studies have shown promise however the effectiveness of such therapies has declined with time, conceivably because the stem cells are being exposed to the same biochemical environment which caused their original demise (Ewing and Ewing, 2008). Light has been shown to influence many, if not all, of the body's key physiological functions. It influences the autonomic nervous system and is associated with all aspects of the body's function including the migration of stem cells (Horowitz et al., 1999), the production of Nitric Oxide (Nagase et al., 2005), the function of the lymphatic system, regulation of intercellular pH balance, improved wound healing (Horowitz et al., 1999), etc. Light influences the autonomic nervous system and consequently the prevailing phenotype (Speck and Rosenkranz, 1975).

That conditions can be treated by the application of light, colour and frequencies indicates that the brain generates frequencies which are responsible for the synchronised function of networks of organs. Depending upon the parameters selected it may stabilise or destabilise each of the physiological systems. The general exposure to light and colour acts indiscriminately. The wrongful selection of colour, light intensity or frequency will stimulate the sympathetic nervous system or the parasympathetic nervous system. An empirical approach will lead to variable outcomes and hence to controversy over the alleged benefits and claims. In the case of migraines, which has multiple origins, this may lower blood pressure and lead to the occurrence of headaches and migraines. Consequently, and as outlined in this article, phototherapy has more considerable consequences and broader applicability than was originally considered to be possible. A superior understanding of the principles which the body uses to regulate its stability will lead to improved therapeutic outcomes in many areas of medicine.

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Competing Interests

Graham Ewing is a Director of Montague Healthcare, a company dedicated to the future commercialisation of Virtual Scanning.

References

1. Achmon J, Granek M, Golomb M, Hart J (1989) Behavioural treatment of essential hypertension: A comparison between cognitive therapy and biofeedback of heart rate. Psychosomatic Medicine 51: 152-164. » CrossRef » PubMed » Google Scholar
2. Alilain WJ, Li X, Horn KP, Dhingra R, Dick TE, et al. (2008) Light-induced rescue of breathing after spinal cord injury. J Neurosci 28: 11862-70. » CrossRef » PubMed » Google Scholar
3. Airan RD, Hu ES, Vijaykumar R, Roy M, Meltzer LA, et al. (2007) Integration of light-controlled neuronal firing and fast circuit imaging. Curr Opin Neurobiol 17: 587-592. » CrossRef » PubMed » Google Scholar
4. Ambatipudi KS, Lu B, Hagen FK, Melvin JE, Yates JR (2009) Quantitative Analysis of Age Specific Variation in the Abundance of Human Female Parotid Salivary Proteins. J Proteome Res 8: 5093-5102. » CrossRef » PubMed » Google Scholar
5. Anderson DJ (1989) The Treatment of Migraine with Variable Frequency Photo Stimulation. Headache 29: 154-155. » CrossRef » PubMed » Google Scholar
6. Anderson DJ, Legg NJ, Ridout DA (1997) Preliminary Trial of Photic Stimulation for Premenstrual Syndrome. J Obstet Gynaecol 17: 76-79. » CrossRef » PubMed » Google Scholar
7. Anokhin PK (1975) The summary about physiology of functional systems. Medicine P: 448. » CrossRef » PubMed » Google Scholar
8. Arshavsky VY, Bownds MD (1992) Regulation of deactivation of photoreceptor G protein by its target enzyme and cGMP. Nature 357: 416-417. » CrossRef » PubMed » Google Scholar
9. Arshavsky VY, Dizhoor AM, Shestakova IK, Philippov PP (1985) The effect of rhodopsin phosphorylation on the light-dependent activation of phosphodiesterase from bovine rod outer segments. FEBS Letters 181: 264-266. » CrossRef » PubMed » Google Scholar
10. Avery DH, Kizer D, Bolte MA, Hellekson C (2001) Bright light therapy of subsyndromal seasonal affective disorder in the workplace: morning vs. afternoon exposure. Acta Psychiatrica Scandinavica 103: 267-274. » CrossRef » PubMed » Google Scholar
11. Avery DH, Eder DN, Bolte MA, Hellekson CJ, Dunner DL, et al. (2001) Dawn simulation and bright light in the treatment of SAD: a controlled study. Biol Psychiatry 50: 205-216. » CrossRef » PubMed » Google Scholar
12. Bairoch A (2000) The Enzyme database in 2000. Nucleic Acids Res 28: 304-5. » CrossRef » PubMed » Google Scholar
13. Banghart M, Borges K, Isacoff E, Trauner D, Kramer RH (2004) Light-activated ion channels for remote control of neuronal firing. Nat Neurosci 7: 1381-6. » CrossRef » PubMed » Google Scholar
14. Bassett DR (2002) Scientific Contributions of A.V. Hill: Exercise Physiology Pioneer. J Appl Physiol 93: 1567-1582. » CrossRef » PubMed » Google Scholar
15. Benedetti F, Barbini B, Fulgosi MC, Colombo C, Dallaspezia S, et al. (2005) Combined total sleep deprivation and light therapy in the treatment of drug-resistant bipolar depression: acute response and long-term remission rates. J Clin Psychiatry 66: 1535-40. » CrossRef » PubMed » Google Scholar
16. Bhattacharjee Y (2007) Is Internal Timing Key to Mental Health? Science 317: 1488-1490. » CrossRef » PubMed » Google Scholar
17. Biener G, Vrotsos E, Sugaya K, Dogariu A (2009) Optical Torques Guiding Cell Motility. Optics Express 17: 9724-32. » CrossRef » PubMed » Google Scholar
18. Binder BM, Biernbaum MS, Bownds MD (1990) Light activation of one rhodopsin molecule causes the phosphorylation of hundreds of others. A

reaction observed in electropermeabilized frog rod outer segments exposed to dim illumination. J Biol Chem 265: 15333-15340. » CrossRef » PubMed » Google Scholar

19. Bitensky MW, Wheeler GL, Aloni B, Vetury S, Matuo Y (1978) Light- and GTP-activated photoreceptor phosphodiesterase: regulation by a light-activated GTPase and identification of rhodopsin as the phosphodiesterase binding site. Adv Cyclic Nucleotide Res 9: 553-572. » CrossRef » PubMed » Google Scholar

20. Boyden ES, Zhang F, Bamberg E, Nagel G, Deisseroth K (2005) Millisecond-timescale, genetically targeted optical control of neural activity. Nat Neurosci 8: 1263-8. » CrossRef » PubMed » Google Scholar

21. Bragin A, Jando G, Nadasdy Z, Hetke J, Wise K, et al. (1995) Gamma (40-100 Hz) oscillation in the hippocampus of the behaving rat. J Neurosci 15: 47-60. » CrossRef » PubMed » Google Scholar

22. Bullock TH, Bennett MV, Johnston D, Josephson R, Marder E, et al. (2005) The Neuron Doctrine, Redux. Science 310: 791-3. » CrossRef » PubMed » Google Scholar

23. Büschges A (2005) Sensory Control and Organization of Neural Networks Mediating Coordination of Multisegmental Organs for Locomotion. Neurophysiol 93: 1127-1135. » CrossRef » PubMed » Google Scholar

24. Cadenas E (1984) Biological Chemiluminescence. Photochem Photobiol 40: 823-830. » CrossRef » PubMed » Google Scholar

25. Cadenas E, Sies H (1984) Low-level chemiluminescence as an indicator of singlet molecular oxygen in biological systems. Methods Enzymol 105: 221-31. » CrossRef » PubMed » Google Scholar

26. Cadenas E, Sies H (1985) Oxidative stress: excited oxygen species and enzyme activity. Adv Enzyme Regul 23: 217-37. » CrossRef » PubMed » Google Scholar

27. Cremer RJ, Perryman PW, Richards DH (1958) Influence of Light on the Hyperbilirubinemia in Infants. Lancet 1: 1094-1097. » CrossRef » PubMed » Google Scholar

28. Canolty RT, Edwards E, Dalal SS, Soltani M, Nagarajan SS, et al. (2006) High Gamma Power is Phase-Locked to Theta Oscillations in Human Neocortex. Science 313: 1626-8. » CrossRef » PubMed » Google Scholar

29. Cardin JA, Carlén M, Meletis K, Knoblich U, Zhang F, et al. (2009) Driving fast-spiking cells induces gamma rhythm and controls sensory responses. Nature 459: 663-7. » CrossRef » PubMed » Google Scholar

30. Chung JCC, Lai CKY (2002) Snoezelen for dementia. The Cochrane Database of Systematic Reviews 4: Art No CD003152. » CrossRef » PubMed » Google Scholar

31. Daw N (1984) The Psychology and Physiology of Colour Vision. Trends in Neuroscience 7: 330-335. » CrossRef » PubMed » Google Scholar

32. deCharms RC, Merzenich MM (1996) Primary cortical representation of sounds by the coordination of action-potential timing. Nature 381: 610. » CrossRef » PubMed » Google Scholar

33. Deltito JA, Moline M, Pollack C, Martin LY, Maremmani I (1991) Effects of phototherapy unpon non-seasonal unipolar and bipolar depressive spectrum disorders. J Affective Disorders 23: 231-7. » CrossRef » PubMed » Google Scholar

34. Dewan EM, Menkin MF, Rock J (1978) Effects of Photic Stimulation on the Human Menstrual Cycle. Photochem Photobiol 27: 581-585. » CrossRef » PubMed » Google Scholar

35. Duffy JF, Kronauer RE, Czeisler CA (1996) Phase-shifting human circadian rhythms: influence of sleep timing, social contact and light exposure. Journal of Physiology 495: 289-97. » CrossRef » PubMed » Google Scholar

36. Eckhorn R, Bauer R, Jordan W, Brosch M, Kruse W, et al. (1988) Coherent oscillations: a mechanism of feature linking in the visual cortex? Multiple electrode and correlation analyses in the cat. Biol Cybern 60: 121. » CrossRef » PubMed » Google Scholar

37. Ewing GW, Ewing EN (2008) Cognition, the Autonomic Nervous System and the Physiological Systems. J Biogenic Amines 22: 140-163. » CrossRef » PubMed » Google Scholar

38. Ewing GW, Ewing EN (2008) NeuroRegulation of the Physiological Systems by the Autonomic Nervous System – their relationship to Insulin Resistance and Metabolic Syndrome. J Biogenic Amines 22: 99-130. » CrossRef » PubMed » Google Scholar

39. Ewing GW, Ewing EN (2009) Virtual Scanning – a new generation of medical technology – beyond biomedicine? ISBN 978-0-9556213-0-7 pub Montague Healthcare books pp 256-264. » CrossRef » PubMed » Google Scholar

40. Ewing GW, Ewing EN, Parvez SH (2009) The Multi-systemic Origins of Migraine. J Biogenic Amines. » CrossRef » PubMed » Google Scholar

41. Ewing GW, Ewing EN, Parvez SH (2009) The Regulatory Significance of the Autonomic Nervous System and the Physiological Systems, and their relationship to Dyslexia. J Biogenic Amines. » CrossRef » PubMed » Google Scholar

42. Ewing GW, Nwose EU, Ewing EN (2009) Obstructive Sleep Apnoea management with Alternative and Complementary Medicine: case reports. J Altern Complement Med. » CrossRef » PubMed » Google Scholar

43. Ewing GW, Parvez SH (2008) Systemic Regulation of Metabolic Function. J Biogenic Amines 22: 179-194. » CrossRef » PubMed » Google Scholar

44. Fell D (1997) Understanding the control of metabolism. Published by Portland Press. » CrossRef » PubMed » Google Scholar

45. Fields RD (2006) Beyond the Neuron Doctrine. Scientific American Mind 17: 20-27. » CrossRef » PubMed » Google Scholar

46. Finsen NR (1895) The Red Light Treatment of Smallpox. Br Med J 7: 1412-1414. » CrossRef » PubMed » Google Scholar

47. Finsen NR (1903) Lysets. Ind- virkninger paa Huden, Hospitalstidende, July 5th, 1893. Br Med J 1: 1298-1304. » CrossRef PubMed » Google Scholar

48. Fries PA (2005) Mechanism for cognitive dynamics: Neuronal communication through neuronal coherence. Trends in Cognitive Sciences 9: 474-480. » CrossRef » PubMed » Google Scholar

49. Fries P, Reynolds JH, Rorie AE, Desimone R (2001) Modulation of oscillatory neuronal synchronization by selective visual attention. Science 291: 1560. » CrossRef » PubMed » Google Scholar

50. Garland CF, Garland FC, Gorham ED, Lipkin M, Newmark H, et al. (2006) The Role of Vitamin D in cancer prevention. Am J Public Health 96: 252-261. » CrossRef » PubMed » Google Scholar

51. Gasparyan L, Brill G, Makela A (2006) Influence of laser radiation on migration of stem cells. Progress in biomedical optics and imaging 7: 61400P.1-61400P.6. » CrossRef » PubMed » Google Scholar

52. Goel N, Stunkard AJ, Rogers NL, Van Dongen HPA, Allison KC, et al. (2009) Circadian Rhythm Profiles in Women with Night Eating Syndrome. J Biol Rhythms 24: 85-94. » CrossRef » PubMed » Google Scholar

53. Goldacre MJ, Seagrott V, Yeates D, Acheson ED (2004) Skin cancer in people with Multiple Sclerosis: record linkage study. J Epidemiol Community Health 58: 142-4. » CrossRef » PubMed » Google Scholar

54. Golden RN, Gaynes BN, Ekstrom RD, Hamer RM, Jacobsen FM, et al. (2005) The efficacy of light therapy in the treatment of mood disorders: a review and meta-analysis of the evidence. Am J Psychiatry 162: 656-662. » CrossRef » PubMed » Google Scholar

55. Gonzalez MMC, Aston-Jones G (2008) Light deprivation damages monoamine neurons and produces a depressive behavioral phenotype in rats. Proc Natl Acad Sci USA 105: 4898-4903. » CrossRef » PubMed » Google Scholar

56. Grakov IG (1985) Strannik Diagnostic and Treatment System: a Virtual Scanner for the Health Service. *Minutes of Meeting No. 11 of the* Praesidium of the Siberian of the Academy of Medical Sciences of the USSR (AMN) held in Novosibirsk. » CrossRef » PubMed » Google Scholar

57. Grasso F, Grillo C, Musumeci F, Triglia A, Rodolico G, et al. (1992) Pho-

ton Emission from Normal and Tumor Human Tissues. Experientia 48: 10-13. » CrossRef » PubMed » Google Scholar

58. Gray CM (1994) Synchronous oscillations in neuronal systems: Mechanisms and functions. J Comp Neurosci 1: 11-38. » CrossRef » PubMed » Google Scholar

59. Gray CM, König P, Engel AK, Singer W (1989) Oscillatory responses in cat visual cortex exhibit inter-columnar synchronization which reflects global stimulus properties. Nature 338: 334. » CrossRef » PubMed » Google Scholar

60. Halberg F, Engeli M, Hamburger C, Hillman D (1965) Spectral resolution of low-frequency, small-amplitude rhythms in excreted 17-ketosteroid; probable androgen induced circaseptan desychronization. Acta endocrinol 103: 5-54. » CrossRef » PubMed » Google Scholar

61. Halberg F, Reinberg A, Haus E, Ghata J, Siffre M (1970) Human biological rhythms during and after several months of isolation underground in natural caves. Nat Speleol Soc Bull 32: 89-115. » CrossRef » PubMed » Google Scholar

62. Hamid P, Newport A (1989) Effect of Color on Physical Strength and Mood in Children. Percept Mot Skills 1989;69:179-185. » CrossRef » PubMed » Google Scholar

63. Hill AV, Long CNH, Lupton H (1924) Muscular exercise, lactic acid and the supply and utilisation of oxygen. Parts I–III. Proc R Soc Lond 97: 438-475. » CrossRef » PubMed » Google Scholar

64. Hillman DC, Siffre M, Milano G, Halberg F (1994) Free-running psychophysiologic circadians and three-month pattern in a woman isolated in a cave. New Trends in Experimental and Clinical Psychiatry 10: 127-133. » CrossRef » PubMed » Google Scholar

65. Hollwich F, Dieckhues B (1980) The Effect of Natural and Artificial Light via the Eye on the Hormonal and Metabolic Balance of Animal and Man. Ophtalmologica 180: 188-197. » CrossRef » PubMed » Google Scholar

66. Horowitz LR, Burke TJ, Carnegie DH (1999) Augmentation of Wound Healing Using Monochromatic Infrared Energy. Advances in Wound Care 12: 35-40. » CrossRef » PubMed » Google Scholar

67. Hotz GA, Castelblanco A, Lara IM, Weiss AD, Duncan R, et al. (2006) Snoezelen: a controlled multi-sensory stimulation therapy for children recovering from severe brain injury. Brain Inj 20: 879-88. » CrossRef » PubMed » Google Scholar

68. Holmes-Atwater F (1997) Accessing anomalous states of consciousness with a binaural beat technology. Journal of Scientific Exploration 11: 263-274. » CrossRef » PubMed » Google Scholar

69. Hug DH, O'Donnell PS, Hunter JK (1980) Light activation of enzymes. Photochem Photobiol 32: 841-848. » CrossRef » PubMed » Google Scholar

70. Katinas G, Hillman D, Siegelova J, Dusek J, Svacinova H, et al. (2002) About-weekly changes in electrical potential, chloroplast migration and oxygen production in acetabularia grown under continous exposure to light. Scripta Medica 75: 309-314. » CrossRef » PubMed » Google Scholar

71. Kandel E (2006) Essay:The New Science of Mind. Scientific American Mind 17: 62-69. » CrossRef » PubMed » Google Scholar

72. Kasper S, Rogers SL, Yancey A, Schulz PM, Skwerer RG, et al. (1989) Phototherapy in Individuals With and Without Subsyndromal Seasonal Affective Disorder. Arch Gen Psychiatry 46: 837-844. » CrossRef » PubMed » Google Scholar

73. Krakov SV (1941) Color vision and the autonomic nervous system. J Opt Soc Am 31: 335-337. » CrossRef » PubMed » Google Scholar

74. Kent ST, McClure LA, Crosson WL, Arnett DK, Wadley VG, et al. (2009) Effect of sunlight exposure on cognitive function among depressed and non-depressed participants: a REGARDS cross-sectional study. Environ Health 8: 34. » CrossRef » PubMed » Google Scholar

75. Kiecolt-Glaser JK, Glaser R (2002) Depression and immune function: Central pathways to morbidity and mortality. J Psychosom Res 53: 873-876. » CrossRef » PubMed » Google Scholar

76. Kobayashi M, Takeda M, Sato T, Ito KL, Kato H, et al. (1999) In vivo imaging of spontaneous ultraweak photon emission from a rat's brain correlated with cerebral energy metabolism and oxidative stress. Neurosci Res 34: 103-113. » CrossRef » PubMed » Google Scholar

77. Kobayashi M, Kikuchi D, Okamura H (2009) Imaging of Ultraweak Spontaneous Photon Emission from Human Body Displaying Diurnal Rhythm. PLoS ONE 4: e6256. » CrossRef » PubMed » Google Scholar

78. Kohl P, Noble D (2009) Systems biology and the Virtual Physiological Human. Mol Syst Biol 5: 292. » CrossRef » PubMed » Google Scholar

79. Kondo T, Strayer CA, Kulkarni RD, Taylor W, Ishiura M, et al. (1993) Circadian rhythms in prokaryotes: luciferase as a reporter of circadian gene expression in cyanobacteria. Proc Natl Acad Sci USA 90: 5672-5676. » CrossRef » PubMed » Google Scholar

80. König P, Engel AK, Singer W (1995) Relation between oscillatory activity and long-range synchronization in cat visual cortex. Proc Natl Acad Sci USA 92: 290-294. » CrossRef » PubMed » Google Scholar

81. Kozuki K, Oh W, Widness J, Cashore WJ (2008) Increase in Bilirubin Binding to Albumin with Correction of Neonatal Acidosis. Acta Paediatrica 68: 213-7. » CrossRef » PubMed » Google Scholar

82. Kryzhanovskii GN, Adrianov OS, Bekhtereva NP, Negovskii VA, Sudakov KV, et al. (1995) Integrative activity of the nervous system in health and in disease. Vestnik Rossiiskoi akademii meditsinskikh nauk / Rossiiskaia akademiia meditsinskikh nauk. » CrossRef » PubMed » Google Scholar

83. Lam RW, Levitt AJ, Levitan RD, Enns MW, Morehouse R, et al. (2006) The Can-SAD Study: a randomized controlled trial of the effectiveness of light therapy and fluoxetine in patients with winter seasonal affective disorder. Am J Psychiatry 163: 805-812. » CrossRef » PubMed » Google Scholar

84. Lancioni GE, Cuvo AJ, O'Reilly MF (2002) Snoezelen: an overview of research with people with developmental disabilities and dementia. Disabil Rehabil 24: 175-84. » CrossRef » PubMed » Google Scholar

85. Levskaya A, Weiner OD, Lim WA, Voigt CA (2009) Spatiotemporal control of cell signaling using a light-switchable protein interaction. Nature [Epub ahead of print]. » CrossRef » PubMed » Google Scholar

86. Liddle E, Jackson G, Jackson S (2005) An evaluation of a visual biofeedback intervention in dyslexic adults. J Dyslexia 11: 61-77. » CrossRef » PubMed » Google Scholar

87. Lima SQ, Miesenböck G (2005) Remote control of behavior through genetically targeted photostimulation of neurons. Cell 121: 141-52. » CrossRef » PubMed » Google Scholar

88. Lynch G, Baudry M (1984) The Biochemistry of Memory: A New and Specific Hypothesis. Science 224: 1057-63. » CrossRef » PubMed » Google Scholar

89. Martinek K, Berezin I (1979) Artificial Light-Sensitive Enzymatic Systems as Chemical Amplifiers of Weak Light Signals. Photochem Photobiol 29: 637-649. » CrossRef » PubMed » Google Scholar

90. Martiny K (2004) Adjunctive bright light in non-seasonal major depression. Acta Psychiatr Scand 110: 7-28. » CrossRef » PubMed » Google Scholar

91. Massabuau JC, Meyrand P (1996) Modulation of a Neural Network by Physiological Levels of Oxygen in Lobster Stomatogastric Ganglion. J Neurosci 16: 3950-9. » CrossRef » PubMed » Google Scholar

92. Meer J (1985) The Colors of Behavior. Psychology Today 9: 66-67. » CrossRef » PubMed » Google Scholar

93. Moller-Sorensen IM, Brade AE (1995) Niels Finsen's treatment of tuberculosis of the skin. Dan Medicinhist Arbog 228-99. » CrossRef » PubMed » Google Scholar

94. Møller KI, Kongshoj B, Philipsen PA, Thomsen VO, Wulf HC (2005) How Finsen's light cured lupus vulgaris. Photodermatol Photoimmunol Photomed 21: 118-124. » CrossRef » PubMed » Google Scholar

95. Miller G (2006) Optogenetics. Shining new light on neural circuits. Science 314: 1674-6. » CrossRef » PubMed » Google Scholar

96. Nagase S, Hirayama A, Ueda A, Oteki T, Takada K, et al. (2005) Light-Shielded Hemodialysis Prevents Hypotension and Lipid Peroxidation by

Inhibiting Nitric Oxide Production. Clin Chem 51: 2397-2398. » CrossRef » PubMed » Google Scholar

97. Nakano M (1989) Low-level chemiluminescence during lipid peroxidations and enzymatic reaction. J Biolum Chemilum 4: 231-240. » CrossRef » PubMed » Google Scholar

98. Nakao M, Yano E, Nomura S, Kuboki T (2003) Blood-pressure lowering effects of biofeedback treatment in hypertension: a meta-analysis of randomised control trials. Hypertension Research – Clinical & Experimental 26: 37-46. » CrossRef » PubMed » Google Scholar

99. Neumeister A, Goessler R, Lucht M, Kapitany T, Bamas C, et al. (1996) Bright light therapy stabilizes the antidepressant effect of partial sleep deprivation. Biol Psychiatry 39: 16-21. » CrossRef » PubMed » Google Scholar

100. Nicol GD, Bownds MD (1989) Calcium regulates some, but not all, aspects of light adaptation in rod photoreceptors. J Gen Physiol 94: 233-259. » CrossRef » PubMed » Google Scholar

101. Noakes TD, Peltonen JE, Rusko HK (2001) Evidence that a central governor regulates exercise performance during acute hypoxia and hyperoxia. J Exp Biol 204: 3225-3234. » CrossRef » PubMed » Google Scholar

102. Noakes TD, St Clair Gibson A, Lambert EV (2005) From catastrophe to complexity: a novel model of integrative central neural regulation of effort and fatigue during exercise in humans: summary and conclusions. Br J Sports Med 39: 120-124. » CrossRef » PubMed » Google Scholar

103. Noble D (2007) Claude Bernard, the first systems biologist, and the future of physiology. Exp Physiol 93: 16-26. » CrossRef » PubMed » Google Scholar

104. Noble D (2008) Computational models of the heart and their use in assessing the actions of drugs. J Pharmacol Sci 107: 107-17. » CrossRef » PubMed » Google Scholar

105. Noton D (1997) PMS, EEG and Photic Stimulation. J Neurotherapy 2: 8-13. » CrossRef » PubMed » Google Scholar

106. Noton D (2000) Migraine and photic stimulation: report on a survey of migraineurs using flickering light therapy. Complement Ther Nurs Midwifery 6: 138-42. » CrossRef » PubMed » Google Scholar

107. Nwose EU, Ewing GW (2009) Computer diagnosis in cardiology: oxidative stress hypothesis. North Amer J Med Sci 1: 152-159. » CrossRef » PubMed » Google Scholar

108. Nwose EU, Ewing GW, Ewing EN (2009) Migraine can be managed with Virtual Scanning: case report. The Open Complementary Medicine Journal 1: 16-18. » CrossRef » PubMed » Google Scholar

109. Oren DA, Brainard GC, Johnston SH, Joseph-Vanderpool JR, Sorek E, et al. (1991) Treatment of Seasonal Affective Disorder with Green Light and Red Light. Am J Psychiatry 148: 509-511. » CrossRef » PubMed » Google Scholar

110. Ramdawon P (2001) Bioresonance information Laser Therapy of Diabetes Mellitus: a first Clinical Experience. In: Laser Florence 2001: a window on the laser medicine world. Proceedings: Longo.L, Hofstetter A, Pascu M.L, Waidelich W. Editors. Progress in Biomedical Optics and Imaging 4903: 146-153. » CrossRef » PubMed » Google Scholar

111. Rattemeyer M, Popp F (1981) Evidence of Photon Emission from DNA in Living Systems. Naturwissenschaften 68: 572-573. » CrossRef » PubMed » Google Scholar

112. Rea MS, Bullough JD, Figuero MG, Bierman A (2004) Spectral opponency in human circadian phototransduction: implications for lighting practice. Commission Internationale de l'Eclairage Expert Symposium on Light and Health. » CrossRef » PubMed » Google Scholar

113. Roberts J (1995) Visible Light Induced Changes in the Immune Response through an Eye-Brain Mechanism. J Photochem Photobiol 29: 3-15. » CrossRef » PubMed » Google Scholar

114. Red'ko VG, Prokhorov DV, Burtsev MS (2004) Theory of Functional Systems, Adaptive Critics and Neural Networks. Proceedings of the IEEE International Joint Conference on Neural Networks 3: 1787- 1792. » CrossRef » PubMed » Google Scholar

115. Rózsa KS (1987) Organization of the multifunctional neural network regulating visceral organs in *Helix pomatia* L (Mollusca, Gastropoda). Cellular aand Molecular Life Sciences 43. » CrossRef » PubMed » Google Scholar

116. Salansky N, Fedotchev A, Bondar A (1998) Responses of the Nervous System to Low Frequency Stimulation and EEG Rhythms: Clinical Implications. Neurosci Biobehav Re 22: 395-409. » CrossRef » PubMed » Google Scholar

117. Sanchez de la Pena S, Halberg F, Galvagno A, Montalbini M, Follini S, et al. (1989) Circadian and circaseptan (about-7-day) free-running physiologic rhythms of a woman in social isolation. Proc 2nd Ann IEEE Symp on Computer-Based Medical Systems pp273-278. » CrossRef » PubMed » Google Scholar

118. Sassenrath-Cole GF, Pearcy RW, Steinmaus SJ (1994) The role of enzyme activation state in limiting carbon assimilation under variable light conditions. Photosynthesis Research 41: 295-302. » CrossRef » PubMed » Google Scholar

119. Schaie W (1966) On the Relation of Color and Personality. Journal of Projective Techniques 30: 512-524. » CrossRef » PubMed » Google Scholar

120. Schauss A (1985) Tranquilizing Effect of Color Reduces Aggressive Behavior and Potential Violence. International Journal of Biosocial Research 7: 55-64. » CrossRef » PubMed » Google Scholar

121. Schoffelen JM, Oostenveld R, Fries P (2005) Neuronal coherence as a mechanism of effective corticospinal interaction. Science 308: 111-113. » CrossRef » PubMed » Google Scholar

122. Schuett A, Bullock TH, Basar E (2000) Odorant-induced low frequency activities of the Helix pedal ganglionare odorant-specific and related to behaviour. Comparative Biochemistry and Physiology. A 124: 297-311. » CrossRef » PubMed » Google Scholar

123. Schuett A, Bullock TH, Basar E (2000) Odor input generates ~ 1.5 Hz and ~ 3 Hz spectral peaks in the Helix pedal ganglion. Brain Research 879: 73-87. » CrossRef » PubMed » Google Scholar

124. Seeman JR, Berry JA, Freas SM, Krump MA (1985) Regulation of ribulose bisphosphate carboxylase activity *in vivo* by a light-modulated inhibitor of catalysis. Proc Natl Acad Sci USA 82: 8024-8028. » CrossRef » PubMed » Google Scholar

125. Sejnowski TJ, Paulsen O (2006) Network oscillations: Emerging Computational Principles. J Neurosci 26: 1673-6. » CrossRef » PubMed » Google Scholar

126. Shealy N (1990) Effects of the Lumatron upon Neurochemicals. 6th International Rehab Med Ass Congress, Madrid. » CrossRef » PubMed » Google Scholar

127. Shannahoff-Khalsa DS, Kennedy B, Yates FE, Ziegler MG (1996) Ultradian rhythms of autonomic, cardiovascular, and neuroendocrine systems are related in humans. Am J Physiol 270: R873-R887. » CrossRef » PubMed » Google Scholar

128. Shannahoff-Khalsa DS, Kennedy B, Yates FE, Ziegler MG (1997) Low-frequency ultradian insulin rhythms are coupled to cardiovascular, autonomic, and neuroendocrine rhythms. Am J Physiol 272: R962-R968. » CrossRef » PubMed » Google Scholar

129. Shannahoff-Khalsa DS, Yates FE (2000) Ultradian sleep rhythms of lateral EEG, autonomic, and cardiovascular activity are coupled in humans. Int J Neurosci 101: 21-43. » CrossRef » PubMed » Google Scholar

130. Shannahoff-Khalsa DS, Gillin JC, Yates FE, Schlosser A, Zawadzki EM (2001) Ultradian rhythms of alternating cerebral hemispheric EEG dominance are coupled to rapid eye movement and non-rapid eye movement stage 4 sleep in humans. Sleep Med 2: 333-346. » CrossRef » PubMed » Google Scholar

131. Shimomura O, Chalfie M, Tsien R (2008) The Nobel Prize in Chemistry. http://nobelprize.org/nobel_prizes/chemistry/laureates/2008/chalfie-lecture.html. » CrossRef » PubMed » Google Scholar

132. Silva A, Cortez P, Santos M, Gomes L, Neves J (2005) Multiple Organ Failure Diagnosis using Adverse Events and Neural Networks. In: Seruca

I. et al. (eds), Enterprise Information Systems VI. » CrossRef » PubMed » Google Scholar

133.Sisson T (1976) Visible Light Therapy of Neonatal Hyperbilirubinemia. Photochemical and Photobiological Reviews 1: 241-268. » CrossRef » PubMed » Google Scholar

134.Sisson TRC (1981) Molecular Basis of Hyperbilirubinemia and Phototherapy. J Invest Dermatol 77: 158-161. » CrossRef » PubMed » Google Scholar

135.Spear B, Heath-Chiozzi M, Huff J (2001) Clinical Applications of Pharmacogenetics. Trends in Molecular Medicine 7: 5: 201-204. » CrossRef » PubMed » Google Scholar

136.Speck WT, Rosenkranz HS (1975) The Bilirubin-induced Photodegradation of Deoxyribonucleic Acid. Pediatr Res 9: 703-5. » CrossRef » PubMed » Google Scholar

137.Sudakov KV (1987) The basic principles of the general theory of functional systems/functional system bodies Mechanism. Manual. Medicine S: 26-49. » CrossRef » PubMed » Google Scholar

138.Suzuki M, Kimura T, Aonuma H, Kitamura Y, Ogawa H, et al. (2005) Neural Networks Controlling Squid Chromatophore Organs in Local Skin Area. Zool Sci 22: 1489. » CrossRef » PubMed » Google Scholar

139.Sweeney BM, Borgese MB (1989) A circadian rhythm in cell division in a prokaryote, the cyanobacterium Synechococcus WH7803. J Phycol 25: 183-186. » CrossRef » PubMed » Google Scholar

140.Sytina OA, Heyes DJ, Hunter CN, Alexandre MT, van Stokkum IHM, et al. (2008) Conformational changes in an ultrafast light-driven enzyme determine catalytic activity. Nature 456: 1001-1004. » CrossRef » PubMed » Google Scholar

141.Takahashi Y, Kipnis D, Daughaday W (1968) Growth hormone secretion during sleep. J Clin Invest 47: 2079-90. » CrossRef » PubMed » Google Scholar

142.Tonks A (1999) Children who sleep with light on may damage their sight. BMJ 318: 1369A. » CrossRef » PubMed » Google Scholar

143.Trevor-Roper P (1969) Psychopathology of Colour. Transactions of the Ophtalmologists Society UK 89: 251-257. » CrossRef » PubMed » Google Scholar

144.Tsodyks M, Uziel A, Markram H (2000) Synchrony generation in recurrent networks with frequency-dependent synapses. J Neurosci 20: 1-5. » CrossRef » PubMed » Google Scholar

145.Tuunainen A, Kripke DF, Endo T (2004) Light therapy for non-seasonal depression. Cochrane Database Syst Rev 2: CD004050. » CrossRef » PubMed » Google Scholar

146.Vandewalle G, Schmidt C, Albouy G, Sterpenich V, Darsaud A, et al. (2007) Brain Responses to Violet, Blue, and Green Monochromatic Light Exposures in Humans: Prominent Role of Blue Light and the Brainstem. PLoS ONE 2: e1247. » CrossRef » PubMed » Google Scholar

147.Vojisavljevic V, Pirogova E, Cosic I (2007) Influence of Electromagnetic Radiation on Enzyme Kinetics. Engineering in Medicine and Biology Society, 2007. EMBS 2007. 29th Annual International Conference of the IEEE 22: 5021-5024. » CrossRef » PubMed » Google Scholar

148.Vysochin YV, Lukoyanov VV, Yaichnikov IK, Tkachuk MI, Chyev VA, et al. (2000) Methodology and Technology of Invigoration of Different Population Orders. In: Consolidated 5 year Research Plan of Physical Training, Sports and Tourism State Committee of the Russian Federation. 2000. English translation available at: http://www.montaguehealthcare.co.uk/files/Vysochin/Vysochin.pdf. » CrossRef » PubMed » Google Scholar

149.Warburg O (1931) The oxygen-transferring ferment of respiration. The Nobel Prize in Medicine. » CrossRef » PubMed » Google Scholar

150.Wileman SM, Eagles JM, Andrew JE, Howie FL, Cameron IM, et al. (2001) Light therapy for seasonal affective disorder in primary care. Randomised controlled trial. Br J Psychiatry 178: 311-316. » CrossRef » PubMed » Google Scholar

151.Wirz-Justice A, Graw P, Krauchi K, Sarrafzadeh A, English J, et al. (1996) Natural Light Treatment of Seasonal Affective Disorder. J Affect Disord 37: 109-120. » CrossRef » PubMed » Google Scholar

152.Wolfarth H, Sam C (1982) The Effects of Color Psychodynamic Environment Modification upon Psycho-Physical and Behavioral Reactions of Severely Handicapped Children. International Journal of Biosocial Research 3: 10-21. » CrossRef » PubMed » Google Scholar

153.Womelsdorf T, Schoffelen JM, Oostenveld R, Singer W, Desimone R, et al. (2007) Modulation of Neuronal Interactions Through Neuronal Synchronization. Science 316: 1609-1612. » CrossRef » PubMed » Google Scholar

154.Xu J, Hadjiconstantinou M, Neff NH (1985) Exposure to Light Accelerates the Formation of Dopamine from Exogenous L-DOPA in the Rat Retina. J Ocul Pharmacol 1: 177-181. » CrossRef » PubMed » Google Scholar

155.Yousuf-Azeemi ST, Raza SM, Yasinzai M (2008) Colors as Catalysts in Enzymatic Reactions. Journal of Acupuncture and Meridian Studies 1: 139- 142. » CrossRef » PubMed » Google Scholar

156.Yousuf-Azeemi ST, Raza SM, Yasinzai M, Samad A (2009) Effects of Different Wavelengths on Superoxide Dismutase. Journal of Acupuncture and Meridian Studies 2: 236-8. » CrossRef » PubMed » Google Scholar

157.Zagulova DV, Podkopaeva TI, Vasil'ev VN, Medvedev MA (2001) Effect of audiovisual stimulation on heart rhythm variability. Bull Exp Biol Med 131: 273-5. » CrossRef » PubMed » Google Scholar