

Historical and cultural aspects of the pineal gland: comparison between the theories provided by Spiritism in the 1940s and the current scientific evidence

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Abstract

Significance has been attached to the pineal gland in numerous different cultures and beliefs. One religion that has advanced the role of the pineal gland is Spiritism. The objective of the present study was to compile information on the pineal gland drawing on the books of Francisco Cândido Xavier written through psychography and to carry out a critical analysis of their scientific bases by comparing against evidence in the current scientific literature. A systematic search using the terms “pineal gland” and “epiphysis” was conducted of 12 works allegedly dictated by the spirit “André Luiz”. All information on the pineal having potential correlation with the field of medicine and current studies was included. Specialists in the area were recruited to compile the information and draw parallels with the scientific literature. The themes related to the pineal gland were: mental health, reproductive function, endocrinology, relationship with physical activity, spiritual connection, criticism of the theory that the organ exerts no function, and description of a hormone secreted by the gland (reference alluding to melatonin, isolated 13 years later). The historical background for each theme was outlined, together with the theories present in the Spiritist books and in the relevant scientific literature. The present article provides an analysis of the knowledge the scientific community can acquire from the history of humanity and from science itself. The process of formulating hypotheses and scientific theories can benefit by drawing on the cultural aspects of civilization, taking into account so-called non-traditional reports and theories.

INTRODUCTION

The pineal, formerly called the epiphysis, is a structure with a mass of around 0.5 g which protrudes from the posterior aspect of the diencephalon. This definition, taken from one of most respected books on medical physiology available today (Guyton & Hall 2006), seriously underestimates the importance of the pineal, providing scant information on this gland and its known physiological effects as well as those under study.

In the space of little over a decade (1954–1965), the pineal gland was revealed as an active neuroendocrine transducer, particularly following the isolation of melatonin by Aaron Lerner at Yale University in 1958 (Lerner *et al.* 1958). Currently, this tiny structure is one of the most studied by modern science and knowledge regarding its structure and functions is growing at an impressive pace. Up to our last review (performed on 7th of June, 2013 using the uniterms “pineal OR melatonin”), there were a total of 27173 indexed articles available on the Pubmed/MEDLINE database, 8957 of which were published within the last 10 years, while the SCOPUS database yielded 36488 articles, 14475 of which were published within the last decade.

Considered the most controversial organ of the body, it has been conceived as anything from a rudimentary vestigial remnant to the “principal seat of the soul” (López-Muñoz *et al.* 2010b). Today, in light of new knowledge, the pineal gland is recognized for chronobiology (Webb & Puig-Domingo 1995b), but even more so as a source of melatonin, which is a potent anti-oxidant (Galano *et al.* 2011; Galano *et al.* 2013) and anti-inflammatory agent (Mauriz *et al.* 2013).

Thus, significance has been attached to the pineal gland in numerous different cultures and beliefs and its role has been described by thinkers, mystics, philosophers and religious figures alike. One religion that has advanced the role of the pineal gland is Spiritism.

Spiritism consists of a collection of philosophical and scientific ideas and religious doctrines founded in France by Allan Kardec in 1857, author of the book entitled “The Book of the Spirits” (Lucchetti *et al.* 2011). Briefly, Spiritism adopts a dualistic concept of human beings: it postulates that we are essentially immortal spirits that temporarily inhabit physical bodies for several necessary incarnations to attain moral and intellectual improvement. It also implies a possible beneficent or maleficent influence of the spirits over incarnate humans (Moreira-Almeida *et al.* 2005; Lucchetti *et al.* 2011).

Although of European origin, Spiritism spread widely in Brazil, where it is currently the third most popular religion in number of followers (Lucchetti *et al.* 2012), owing to several factors, especially the work of a medium called Francisco Cândido Xavier who, despite limited schooling, penned over 460 books attributed to various spirits.

This study focuses attention on this work, particularly the books attributed to the “spirit” called André

Luiz, allegedly a physician in a past life in Brazil, who authored books containing information of a scientific nature in the field of medicine through the hands of the medium. The most notable of these books is “Missionaries of the Light”, published in Brazil in 1945 (Xavier 1945) and translated into English (Xavier 2009/1945), whose second chapter is entitled “The Pineal Gland”.

According to “André Luiz”, the pineal gland “*secretes the ‘psychic hormones’ or ‘power units’, which act positively on the generative energies*”, suggesting the role of a hormone produced by the pineal gland, some 13 years prior to the isolation of melatonin by Lerner *et al.* in 1958 (Lerner *et al.* 1958). Throughout the works of Francisco Cândido Xavier, the “spirit” dictates further statements pointing to the role of the pineal gland in the human body.

The objective of the present study was to compile information on the pineal gland drawing on the psychographed books by Francisco Cândido Xavier and to carry out a critical analysis of their scientific bases by comparing against evidence in the relevant scientific literature.

METHODS

A review of the works allegedly authored by the spirit “André Luiz” written through psychography by Francisco Cândido Xavier was carried out. This “spirit” was chosen for having produced several publications on the mechanisms and functions of the pineal gland.

Books were selected based on a search of the spiritist literature and subsequently leaders of the spiritist community were consulted on those books containing information about the gland.

It was decided to include all the titles included in the “Life in the Spirit World” collection, comprising a total of 13 volumes, all allegedly dictated by the spirit “André Luiz”, namely: *Nosso Lar* (Our Home), *Os Mensageiros* (The Messengers), *Missionários da Luz* (Missionaries Of The Light), *Obreiros da vida eterna* (Workers Of The Life Eternal), *No Mundo Maior* (In the Greater World), *Libertação* (Freedom), *Entre a Terra e o Céu* (Between Heaven and Earth), *Nos Domínios da Mediunidade* (In the Realms of Mediumship), *Ação e Reação* (Action and Reaction), *Evolução em Dois Mundos* (Evolution On Two Worlds), *Mecanismos da Mediunidade* (Mechanisms of Mediumship), *Sexo e Destino* (Sex and Destiny), and *E a Vida Continua* (And Life Goes On). Although originally written in Portuguese, all these titles have since been translated into English (Xavier 2009/1945).

Analysis of the book passages containing information referring to the pineal gland was carried out by scanning collection contents using the search function provided by Adobe Acrobat Reader with the uniterms “pineal” or “epiphysis”.

After selection and counting uniterm matches, the authors opted to read all chapters in which the terms

appeared, for subsequent analysis of the information. All information potentially related with the field of medicine and current studies was included.

Finally, endocrinologists, neurologists, neuroscientists, general clinicians and scholars of the spiritist theme were recruited to compile the information and draw parallels with evidence in the scientific literature.

RESULTS

Table 1 shows results of the systematic search for the uniterms in the different books from the “A Vida no Mundo Espiritual” (Life in the Spirit World) collection.

The book containing the greatest number of uniterms related to the theme of the pineal gland was the book “Missionários da Luz” (Missionaries of the Light) (1945) with 20 uniterms matches, followed by the book “No Mundo Maior” (In the Greater World) (1947), and “Evolution On Two Worlds” (1958). Six out of the 13 books (46.1%) in the collection yielded some information related to the pineal gland.

The themes addressed by the “spirit” author were: information on the spiritual connection of the pineal gland (7 passages), mental health (6 passages), reproductive function (4 passages), endocrine function (4 passages), criticism of the theory that the organ exerts no function (2 passages), physical activity (1 passage), and description of a hormone secreted by the gland (1 passage). A total of 6 passages reporting visualizations of light emitted from the pineal gland by the spirits were rejected because they lacked correlations with current evidence. Tables 2–4 contain passages related to each theme.

DISCUSSION

Based on these findings, the books by Francisco Cândido Xavier written through psychography, yield numerous statements pointing to the roles of the pineal gland in the human body. The results in the ensuing section are stratified by subtheme, allowing parallels to be drawn with current scientific evidence.

A: Mental Health

Historical background: The role of melatonin in mental health was first seen in early reports from the XVII and XVIII centuries linking this gland to “madness” (Miles & Philbrick 1988). In 1920, the first extracts from the pineal gland for treating schizophrenia were assessed with controversial results (Kitay & Altschule 1954). Only after isolation of melatonin in 1958 (Lerner *et al.* 1958) did experimental studies start to confirm this link between melatonin and mental health (Cardinali *et al.* 2012; Sanchez-Barcelo *et al.* 2010).

Vision held by Spiritism in the 1940s: The passages analysed point to a strong relationship between the pineal gland and an individual’s mental health. The “spirit” André Luiz makes clear that the pineal gland “*is the gland of mental life*”, that “*it presides over the neural phenomena of the emotions*”, acting as “*the controller of the world of the emotions*” and “*the most advanced laboratory of a human being’s psychic elements*” (Xavier 1945).

Current scientific evidence: This relationship, a remote and futuristic notion for the 1940s, has been increas-

Tab. 1. Results of the systematic search for the uniterms in the different books from the “A Vida no Mundo Espiritual” (Life in the Spirit World) collection.

Book title	Year of publication	Epiphysis	Pineal gland
Nosso Lar (Our Home)	1943	0	0
Os Mensageiros (The Messengers)	1944	0	0
Missionários da Luz (Missionaries of the Light)	1945	16	4
Obreiros da vida eterna (Workers of the Life Eternal)	1946	0	0
No Mundo Maior (In the Greater World)	1947	3	0
Libertação (Liberation)	1949	0	0
Entre a Terra e o Céu (Between Heaven and Earth)	1954	0	0
Nos Domínios da Mediunidade (In the Realms of Mediumship)	1954	1	0
Ação e Reação (Action and Reaction)	1957	1	0
Evolução em Dois Mundos (Evolution On Two Worlds)	1958	2	1
Mecanismos da Mediunidade (Mechanisms of Mediumship)	1959	1	0
Sexo e Destino (Sex and Destiny)	1963	0	0
E a Vida Continua (And Life Goes On)	1968	0	0

ingly proposed recently based on a number of studies investigating melatonin. In fact, psychiatric diseases (bipolar disorder, depression, schizophrenia) are related to sleep disorders; and insomnia is a symptom commonly associated with decompensation and recurrence of these diseases (Maldonado *et al.* 2009b).

It has been shown that melatonin exerts an antidepressant-like action when assessed in animal models predictive of antidepressant action of drugs in humans (Raghavendra *et al.* 2000). Similarly, recent studies have shown that melatonin receptors are elevated in the suprachiasmatic nucleus of depressed patients and may rise during the disease course (Wu *et al.* 2013). Some authors (Maldonado *et al.* 2009b; Maldonado *et al.* 2009a) have also proposed that melatonin might play an important role as an adjuvant therapy for depression, due to other properties including its anti-inflammatory, anticonvulsant, sedative, anxiolytic and protective actions against osteoporosis, among others.

In schizophrenia, biological rhythms, including that of melatonin, are altered and treatments based on

exogenous melatonin used in association with antipsychotics can reduce the collateral effects (Webb & Puig-Domingo 1995a).

Eating disorders are also associated with changes in melatonin level: in bulimia levels are high during the day; in anorexia high during the day/night; in panic syndrome high at night, whereas in obsessive compulsive disorder (OCD) concentrations are low at night (López-Muñoz *et al.* 2011).

Recently, studies have also shown effects of melatonin in improving dementia-related changes in behavior (such as depression, anxiety, apathy, as well as lower prevalence of hallucinations, delirium, agitation, irritability and appetite disorders), according to evidence compiled in a recent Cochrane systematic review (Jansen 2011).

According to Verster (2009), developments have proven the efficacy of melatonin receptor agonism in synergy with serotonin antagonism. Possible applications in the treatment of other neuropsychiatric conditions have been suggested, and further investigation

Tab. 2. Passages from books psychographed by Francisco Cândido Xavier mirroring current scientific findings.

Theme	Book title	Passage
Mental Health	Missionários da Luz (Missionaries Of The Light) – page 17	<u>“It’s the gland of mental life. During puberty it awakens the creative forces in the human organism, and thereafter it continues to function as the most advanced laboratory of a human being’s psychic elements. Regular neurologists don’t understand it very well. Someday, psychiatrists will grasp its secrets.”</u>
Mental Health	Missionários da Luz (Missionaries Of The Light) – page 18	<u>“As an organ of the ethereal body’s highest expression, it presides over the neural phenomena of the emotions”.</u>
Mental Health	Missionários da Luz (Missionaries Of The Light) – page 17	<u>“The pineal gland readjusts itself to the body’s organic order and reopens it wonderful world of sensations and impressions in the realm of the emotions.”</u>
Mental Health	Missionários da Luz (Missionaries Of The Light) – page 19	<u>“Secreting subtle psychic energies (...) In its capacity as controller of the world of the emotions (...)”</u>
Mental Health	Missionários da Luz (Missionaries Of The Light) – page 22	<u>“So, according to what we have stated, the function of the epiphysis in mental life is very important.”</u>
Mental Health	Missionários da Luz (Missionaries Of The Light) – page 20	<u>“Now do you understand that the functions of the epiphysis lie in the mental growth of human beings”</u>
Pineal gland and physical activity	Missionários da Luz (Missionaries Of The Light) – page 21	<u>“As a means of combating the potential dangers of the excessive accumulation of neural energies– as the electrical secretions of the epiphysis are called– they have advised the youths of all countries to practice rowing, ball games, jumping, pole vaulting, and running. In this way, the legitimate and normal organic qualities would be preserved for the functions of heredity.”</u>
Criticism of the theory that the organ exerts no function	Missionários da Luz (Missionaries Of The Light) – page 16	<u>“I had studied the function of the epiphysis during my modest work as a doctor on the earth. According to classic authors, its function was restricted to sexual control during infancy... Afterward, it decreased in strength, abated, and almost disappeared so that the genital glands could succeed it in taking over this field of energy”</u>
Criticism of the theory that the organ exerts no function	Missionários da Luz (Missionaries Of The Light) – page 17	<u>“It isn’t a dead organ as previously supposed,”</u>

could add to the importance of melatonin as a treatment option.

Conclusion of the section: The works analyzed suggest the pineal gland has great importance in the mental health of individuals, while also positing that this organ is “the gland of mental life”. Current evidence reveals a relationship between the pineal gland and mental health, including the role of melatonin receptor agonists for the treatment of depression. The role of the pineal gland in individuals’ mental health however is not yet fully elucidated.

B: Endocrine function

Historical background: The relationship between the pineal gland and endocrinology dates back more than a century. In 1898, Huebner was the first to describe this relationship, reporting a case of a boy with pinealoma and early puberty (addressed in more depth in the section: “reproductive function”) (Kappers *et al.* 1979). Reports by other scientists such as Marburg, Berblinger and Engel soon followed. However, it was in 1943 that Bargmann studied the pineal gland of mammals and

suggested the possible role of the organ in regulating hypothalamus function. According to historians, in the first half of the XX century, notions already existed of an antigonadotropic influence and cooperation among the pineal, hypothalamus and pituitary gland (Reiter & Fraschini 1969).

Vision held by Spiritism in the 1940s: On the endocrinologic function of the gland, André Luiz stated: “secreting subtle psychic energies, the pineal maintains control over the entire endocrine system”, “the epiphysis, akin to a small bluish sun, holds all the other bodies within its magnetic field, from the hypophysis to the region of the ovaries, like our life star” and also “The epiphysis, hypophysis, thyroid, parathyroids, thymus, supra-renals, pancreas and the genesic sacs were perfectly characterized against a living backdrop of perispiritual centers, which interact in harmony with one another”.

Current scientific evidence: The pineal gland is currently believed to play an active role in the integrative process of the neuroendocrine system (Cardinali *et al.* 1979). As demonstrated by Cardinali *et al.* (Cardinali

Tab. 3. Passages from books psychographed by Francisco Cândido Xavier mirroring current scientific findings.

Theme	Book title	Passage
Reproductive functions	Missionários da Luz (Missionaries Of The Light) – page 17	“ [the pineal gland] <u>The individual yields to the recapitulation of his or her sexuality</u> and examines the inventory of passions experienced in the past, which reappear under strong impulses.”
Reproductive functions	Missionários da Luz (Missionaries Of The Light) – page 18	the pineal gland – if I may put it this way – secretes the ‘psychic hormones’ or ‘power units’, which act positively on the generative energies. The chromosomes in the seminal sac cannot escape the pineal gland’s <u>absolute and determining influence.</u> ”
Reproductive functions	Missionários da Luz (Missionaries Of The Light) – page 19	In its capacity as controller of the world of the emotions, <u>its position in sexual experiences is basic and absolute</u>
Reproductive functions	Missionários da Luz (Missionaries Of The Light) – page 17	“During the period of childhood development – the readjustment phase for this important center of the preexistent perispiritual body– <u>the epiphysis seems to restrain the manifestations of sex</u> ”
Endocrine function	Missionários da Luz (Missionaries Of The Light) – page 163	“the coloration of the epiphysis, resembling a small bluish sun, keeps within <u>its magnetic field all the other bodies, from the hypophysis out to the region of the ovaries, like our life star</u> ”
Endocrine function	Missionários da Luz (Missionaries Of The Light) – page 18	“the pineal gland maintains control over the entire endocrine system (...) under its direction psychic energies are supplied to all the autonomous storage areas of the organs”
Endocrine function	No Mundo Maior (In the Greater World) – page 108	“I noted that the habitual light from the <u>endocrine centers dimmed, where only the epiphysis</u> continued to emit abnormal rays.”
Endocrine function	Ação e Reação (Action and Reaction) – pages 241 and 242	“The epiphysis, hypophysis, thyroid, parathyroids, thymus, supra-renals, pancreas and the genesic sacs were perfectly characterized against a living backdrop of perispiritual centers, which <u>interact in harmony with one another</u> ”, in highly subtle nerve branches, singularly adjusted, through the plexus, with each center emitting its own irradiations, together comprising one harmonic, which impels use to ecstatic contemplation.”
Description of hormone secreted by the gland (melatonin?)	Missionários da Luz (Missionaries Of The Light) – page 18	“The genital glands secrete the sex hormones, but the pineal gland – if I may put it this way, secretes the “psychic hormones” or “power units”, which act <u>positively on the generative energies.</u> ”

et al. 1979), the pineal gland exhibits characteristics of neuroendocrine transduction and integration, for example: (a) the existence of putative receptors for various hormones (estradiol, testosterone, 5 alpha-dihydrotestosterone, progesterone, prolactin); (b) the steroid metabolic pattern resembling other brain areas involved in gonadotrophic regulation, correlation of pineal responsiveness to hormones with activity of sympathetic nerves; (c) the modification by hormones of pineal beta-adrenergic mechanisms and; (d) the dissociation of hormone effects on the pineal gland in those mediated or modulated by changes in afferent neuronal activity and those relatively unaffected by denervation.

Similarly, the passage “*The epiphysis, hypophysis, thyroid, parathyroids, thymus, supra-renals, pancreas and the genic sacs were perfectly characterized against a living backdrop of perispiritual centers, which interact in harmony with one another*”, resembles the intimate relationship of the pineal gland to organs associated with the endocrine system. In fact, by regulating circadian rhythms, melatonin is directly involved in the photo-neuroendocrine system (Korf *et al.* 1998).

Melatonin interacts with other circadian periodic variables and thus indirectly controls or exerts influence on a wide variety of physiologic functions, such as the sleep/wake cycle, thermal regulation, feeding, and

sexual behavior and certain cardiovascular functions, and through its interaction with serotonin participates in the regulation of the secretion of ACTH, corticosteroids, β -endorphin, prolactin, renin, vasopressin, oxytocin, growth hormone, and luteinizing hormone (LH). (Touitou & Haus 2000).

There is evidence that Melatonin inhibits ACTH-induced production of cortisol in the adrenals (Campino *et al.* 2008), inhibiting the expression of the clock genes PER1 mRNA, BMAL1, StAR, the protein 3 β -HSD and ACTH-induced production of cortisol and progesterone in the adrenals (Campino *et al.* 2011). Melatonin also participates in the fine regulation of ACTH in corticotrophins, a mechanism related to the chronobiological action of the hormone from the pineal (Tsukamoto *et al.* 2013).

Melatonin is secreted at a rate ten times higher nocturnally than during the day and acts directly on the *Pars Tuberalis* of the adenohypophysis, inhibiting cAMP production through a Gi type g-protein signaling pathway coupled to the Melatonin Receptor (MT1). Thyroid stimulating hormone (TSH) is produced in the *Pars Tuberalis* and has the opposite action to melatonin, stimulating cAMP production through a Gs protein signalling pathway coupled to the TSH receptor (Dupré *et al.* 2011). Melatonin acting on the *Pars Tuberalis* medi-

Tab. 4. Passages from books psychographed by Francisco Cândido Xavier mirroring current scientific findings.

Theme	Book title	Passage
Connection with the spiritual world	Missionários da Luz (Missionaries Of The Light) – page 13	“In <u>any type of mediumistic practice, the pineal gland plays the most important role.</u> By means of its well-balanced energies, the human mind intensifies the power of the sending and receiving of rays peculiar to our realm”
Connection with the spiritual world	Missionários da Luz (Missionaries Of The Light) – page 18	“However, we are not examining problems of embryology. Let’s stick to the initial subject and analyze <u>the epiphysis as the gland of a person’s spiritual life</u> ”
Connection with the spiritual world	Missionários da Luz (Missionaries Of The Light) – page 13	“It is in <u>the epiphysis that human beings’ new sense lies</u> ; however, in most people the divine potential still sleeps in an embryonic state.”
Connection with the spiritual world	Missionários da Luz (Missionaries Of The Light) – page 163	“ From the <u>epiphysis</u> , situated between the cerebral hemispheres, to the procreating nuclei, the glands appear to form a beautiful luminous system, similar to tiny stars of life, congregating in a vertical direction, whose <u>gleaming antenna attracts light coming from the Higher realms.</u> ”
Connection with the spiritual world	Evolução em Dois Mundos (Evolution On Two Worlds) – page 58	“ <u>in spiritual form, the coronal center of the future perispirit, reflects in the pineal gland</u> ”
Connection with the spiritual world	Evolução em Dois Mundos (Evolution On Two Worlds) – page 58 and page 59	<u>The epiphysis starts to consolidate</u> , by energetic support of subtle sensations for the translation and selection of the various mental states, in mechanisms of reflection and thought, of meditation and discernment, presage <u>the operations of mediumship, conscious or unconscious, by which incarnate and discarnate Spirits consort with one another</u> , in the same band of vibrations, for the great creations of Science and Religion.”
Connection with the spiritual world	Mecanismos da Mediunidade (Mechanisms of Mediumship) – page 91	<u>the epiphysis of the hypnotized, a gland of utmost importance in all mediumistic processes</u> , given that it favors <u>the passivity of the receptive nuclei of the brain</u> , provoking at the same time, the attention or closed circuit in the magnetic field of the patient.

ates TSH gene expression and exerts a direct action on seasonal physiology (Barrett & Bolborea 2012). Both melatonin and cortisol have been identified as regulators of the hypothalamic-pituitary-thyroid axis (Maz-zoccoli *et al.* 2011).

Melatonin participates in immunoregulation by increasing production of the thymic peptides (Thymosin and Thymulin) (Batmanabane 2007). The fall in melatonin levels with ageing accompanies the age-related decline in the immune system, evidencing the immunomodulatory effect of melatonin (Espino *et al.* 2012).

Melatonin also promotes ultrastructural changes in parathyroid cells (Chen *et al.* 1991) and appears to influence bone metabolism (Ostrowska *et al.* 2003), representing a candidate modulator of osteoblasts with a possible therapeutic role (Cardinali *et al.* 2003).

Similarly, melatonin has been reported as a potential treatment for Metabolic Syndrome (Kozirog *et al.* 2011) given its action reducing insulin release directly within pancreatic β cells, increasing sensitivity to the action of insulin, and reducing intolerance to glucose and fructose (Korkmaz *et al.* 2009). Obesity, a component of Metabolic Syndrome, has been associated with the suppression of the endogenous production of melatonin and chronodisruption (Reiter *et al.* 2012).

In the case of Polycystic Ovary Syndrome (PCOS) (March *et al.* 2010), melatonin participates in the regulation of the hypothalamic-pituitary-gonadal axis (Shi *et al.* 2013). Melatonin receptor 1A gene polymorphism is also associated with the etiopathogeny of the disease (Li *et al.* 2011), perhaps explaining the elevated melatonin levels found in some studies (Luboshitzky *et al.* 2001; Luboshitzky *et al.* 2004). Melatonin has also been used in the treatment of PCOS (Saha *et al.* 2012) with controversial results.

Endocrinology is the study of hormones and hormonal signalling. Melatonin is considered a pleiotropic hormone given its versatility as a hormonal signal (Reiter 1995; Hardeland *et al.* 2011) and new assaying techniques are set to open up a vast new avenue of knowledge on the physiology of the pineal (Klein *et al.* 2010).

Conclusion of the section: The books analyzed, although not employing scientific language, appear to yield endocrinologic information about the pineal gland and its main hormone (melatonin) that closely mirrors the findings in the current scientific literature.

C: Pineal gland and the reproductive system

Historical background: The relationship of the pineal gland with human reproduction dates back to the mid-1900s when Huebner reported that a tumor of the human pineal gland altered pubertal development (Reiter *et al.* 2009). This led many scientists in the first half of the 20th century to experimentally examine the association of the pineal with the reproductive status

in a variety of species but with limited success in terms of demonstrating a functional relationship. The findings were not sufficiently compelling to convince most, if any, reproductive biologists that the pineal gland and the reproductive system were functionally linked (Reiter *et al.* 2009). Finally, the discovery of melatonin by Lerner in 1958 (Lerner *et al.* 1958) heralded a new field of research in reproductive physiology.

Vision held by Spiritism in the 1940s: With respect to reproductive function, the passages from the books yielded the following information:

“In its capacity as controller of the world of the emotions, its position in sexual experiences is basic and absolute”; “During the period of childhood development – the readjustment phase for this important center of the preexistent perispiritual body– the epiphysis seems to restrain the manifestations of sex” and, “The chromosomes in the seminal sac cannot escape the pineal gland’s absolute and determining influence”.

Current scientific evidence: In the 1940s, when the book under analysis was written, the information available on this correlation was extremely scant and highly conflicting. Nowadays, various different studies have linked melatonin production with fertility (Nir & Hirschmann 1979; Reiter *et al.* 2009). Pinealocytes also express receptors both for luteinizing hormone (LH) and for GHRH, hypophysiotropic regulator of LH (Itoh *et al.* 2006).

The role of melatonin also seems to be related to the mate selection due to its ability to enhance sexual and ornamental pigmentation (Bertrand *et al.* 2006), the reduction of morphophysiologicaly flawed traits being passed to the next generation, as studies have preliminarily shown its ability to protect the gametes from oxidative and nitrosative damage (Sarabia *et al.* 2009), and to an additional protection to the placenta, fetus, and mother from oxidative damage due to a variety of toxic oxidizing events associated with pregnancy (Nagai *et al.* 2008).

The passage “The chromosomes in the seminal sac cannot escape the pineal gland’s absolute and determining influence”, mirrors the current evidence showing that the seminal fluid contains melatonin (Bornman *et al.* 1989), and also how melatonin appears to be a protective factor in decreasing the radiation-induced chromosome damage as dimethyl sulfoxide at 1.0 M (Bornman *et al.* 1989).

Likewise, drawing parallels between the passage “During the period of childhood development (...), the epiphysis seems to restrain the manifestations of sex” and current knowledge reveals that deficiencies in melatonin may be related to sexual functioning in human males (Grugni *et al.* 1994) and there is evidence for a facilitatory role of melatonin in sexual behavior, through its mechanism involving the 5-HT_{2A} receptor (Grugni *et al.* 1994).

Conclusion of the section: The relationship between the pineal gland and human reproductive system is strong, being backed by solid contemporary evidence. As mentioned earlier in this section, this relationship was first suspected in the beginning of the XX century but rejected by scientists of the time due to studies with inconsistent results.

D: Pineal gland and physical activity:

Historical background: It is unclear exactly when the link between the pineal gland and physical exercise was first reported. However, the first studies showing that the exposure of rats to various types of stress (increasing catecholamines in the bloodstream) led to increased melatonin levels in plasma and in the pineal, date back to the late 1970s and early 1980s (Monteleone *et al.* 1990; Lynch *et al.* 1977). The first studies along these lines in humans were conducted in the 1980s (Monteleone *et al.* 1990).

Vision held by Spiritism in the 1940s: The books analyzed also contain a passage in which the “spirit” tells of a possible role of the pineal in physical activity: “As a means of combating the potential dangers of the excessive accumulation of neural energies— as the electrical secretions of the epiphysis are called— they have advised the youths of all countries to practice rowing, ball games, jumping, pole vaulting, and running”.

Current scientific evidence: According to a recent review, physical exercise acts as a *zeitgeber*. The impact of exercise on the rhythm of melatonin secretion was found to vary depending on the time of day, intensity of light and how closely the exercise coincided with the circadian production of melatonin (Escames *et al.* 2012).

However, the role of physical exercise in melatonin secretion remains controversial, with different studies showing increased (Skrinar *et al.* 1989), decreased (Monteleone *et al.* 1990) and unchanged production of the hormone (Elias *et al.* 1993). Notwithstanding the inconsistencies in the scientific evidence, there is a general consensus that nocturnal exercise, of moderate and high intensities, if performed routinely, can result in phase delays in melatonin onset (Escames *et al.* 2012; Van Reeth *et al.* 1994). Accumulating evidence also suggests that, in addition to its phase-shifting effects, exercise can also acutely alter melatonin levels (Buxton *et al.* 1997; Escames *et al.* 2012).

Moreover, studies investigating the role of melatonin in physical performance (Atkinson *et al.* 2005) have shown promising results and beneficial effects on the cardiovascular system, skeletal muscle, exercise-related metabolism and on muscle oxidative stress (Escames *et al.* 2012).

Conclusion of the section: Despite only one rather generic sentence from the book on the possible rela-

tionship between the pineal gland and physical exercise, it is noteworthy that this relationship was not embraced by the scientific literature in the 1940s. Current evidence holds that the exercise and melatonin effect appears to exert a favorable influence on several systems of the human body. Nevertheless, further studies are needed to clarify contradictory findings in this area.

E: Description of a hormone secreted by the gland

Historical background: As outlined previously, in the first half of the XX century, the notion that the pineal gland might be responsible for an endocrine function and for producing hormones had already been established (Kappers *et al.* 1979). It was only in 1958 however, that Lerner *et al.* (Lerner *et al.* 1958) isolated melatonin.

Vision held by Spiritism in the 1940s: According to the book “Missionaries of the Light”, the pineal gland “*secretes the psychic hormones or power units, which act positively on the generative energies*”. This passage suggests a role of a hormone produced by the pineal gland which may be alluding to the role of melatonin in the regulation of energy.

Current scientific evidence: Melatonin was isolated by Lerner in 1958 (Lerner *et al.* 1958) (13 years after the passage was written), and in recent years evidence has emerged confirming the role of the hormone in mitochondrial oxidative stress (Martinis *et al.* 2012), as a coadjuvant in hypothermic neuroprotection in neonates (Robertson *et al.* 2013), as well as in the physiology of brown adipose tissue (BAT) promoting hypertrophy and increasing its activation, having therapeutic potential for combating obesity (Tan *et al.* 2011).

Results of studies in rats (Hatzis *et al.* 2013) suggest the antioxidative role of melatonin appears to attenuate non-alcoholic fatty liver disease (NAFLD).

Melatonin may also play an epigenetic role in the prevention of perinatal oxidative stress, acting in fetal gene programming in high-risk pregnancies (Chen *et al.* 2013).

Conclusion of the section: The passage given above clearly describes the role of the pineal gland in the secretion of physical hormones, emphasizing the endocrine function of the gland. Speculation that the hormone alluded to was what later became known as melatonin, isolated 13 years after the book “Missionaries of the Light”, although plausible, should be viewed tentatively.

F: Pineal gland and the “connection with the spiritual world”

Historical background: Hindu philosophy and Vedic medicine, written some 5000 ago, describe the pineal – “the sixth chakra”, according to these traditions – as a window to the spiritual world, where mental power

resides, associating this gland with clairvoyance and meditation, professing that its activity is nocturnal (López-Muñoz *et al.* 2010b). However, the first detailed descriptions of the pineal are found in the works of Galen (131-200 AD), expounding on a theory that proposed the gland was an organ exercising valvular control. His underlying theoretical bases were founded on the pneumatic school of the Alexandria school (López-Muñoz *et al.* 2010a). Acting like a pump, the pineal gland was thought to distribute “*spiritus animalis*” around the body, Galen’s whole structure was called the “pneumatic-ventricular model” and was purely hydraulic in nature (López-Muñoz *et al.* 2010c).

The “pneumatic-ventricular model” provided the theoretical basis of René Descartes (1596–1650), a great philosopher renowned for pronouncing the pineal “the principal seat of the soul”. According to Descartes, the “*spiritus animalis*” were subtle fluids, like tiny, fast-moving particles which circulated through the interior of the cerebral ventricles and nerves – a kind of “quintessence” originated from blood fluid by rarefaction (Fishman 2008). Harmony between the mind and movements of the body, required perfect communication between the physical seat and the human soul, a role attributed to the gland (López-Muñoz *et al.* 2010b). The theory of Descartes began its demise with the principles of Claude-Nicolas Le Cat (1700–1768) who claimed the cerebral cortex, and not the pineal, was the seat of the soul (López-Muñoz *et al.* 2010c).

Vision held by Spiritism in the 1940s: André Luiz also defined the role of the pineal gland as the connector of the “spirit world”: “The tiny gland had become a radiating nucleus and its rays formed a lotus flower of sublime petals around it”.

This description by André Luiz was based on an observation he made of the pineal of a medium psychographing a message during a mediumistic session, showing the great flow of energies travelling along this path and identifying the structure as very important in communications from the spirit plane.

“You can see that every glandular center is an electrical power source. In any type of mediumistic practice, the pineal gland plays the most important role (...) “It is in the epiphysis that human beings’ new sense lies; however, in most people the divine potential still sleeps in an embryonic state”.

Current scientific evidence: In fact, the association between spirituality and the pineal gland has been consistently reported throughout the history of civilization. However, only in recent years has research confirmed an association between these variables.

Recently, five studies supported the long-standing speculation that the pineal plays an important role in the intrinsic awareness which might concern the spirit or soul. The first of these studies (6) found that the pineal gland was activated during religious medita-

tion, the second (7) found it was activated during Chinese original quiet sitting (a type of meditation with “intake of spiritual energy”), the third (8) showed that a kind of spiritual meditation elevated nighttime salivary melatonin levels, while the fourth (9) showed the gland was only activated during meditation involving a “spiritual connection” compared to observing breathing meditation.

Lastly, Messina *et al.* (Messina *et al.* 2010) investigated 50 metastatic lung cancer patients treated with chemotherapy and melatonin along with 100 patients in a control group treated with chemotherapy alone. The treatment associated with melatonin showed greater remission of tumors, and was further enhanced in patients whose psychological profile was based on their spiritual faith.

Conclusion of the section: The Spiritist works analysed point to a relationship between the pineal gland and spiritual connection. Current studies have shown some promising results in support of this hypothesis but remain preliminary, precluding the drawing of robust conclusions.

CONCLUSIONS

Analysis of the content of the information revealed the author has summarized the importance of the pineal gland under six main items, noting that it: (a) is responsible for governing the world of emotions; (b) maintains control over the entire endocrine-gonadal system; (c) commands subconscious powers under the direct determination of the will; (d) supplies all the autonomous storage areas of the organs with “psychic energy”; (e) is the gland of mental life; and (f) has primordial function in the mediumship phenomenon and spiritual connection.

However, it was noted that some key issues in the current scientific literature on the pineal gland are not reported in the books, such as the role of the gland in sleep and chronobiology.

The fact that a text written by an unlearned individual without academic training or involvement in the field of health, who resided in the hinterlands of Brazil during a time when access to articles was limited (the case of Mr. Francisco Cândido Xavier), furnishes highly complex concepts and information on the physiology of the pineal gland 60 years before any scientific confirmation, raises deeper questions as to the true source of this information.

The first hypothesis is that the author, drawing on books and articles available in the 1940s detailing the physiopathology of the pineal gland and published before the isolation of melatonin, created these theories himself, wording them in non-specific language thus allowing them to appear to be supported by subsequent advancements in science. A second hypothesis posits a mere coincidence of findings, whereby the author ran-

domly created several theories surrounding the pineal gland, many of which happened to be confirmed by scientific evidence. The third hypothesis centers on alleged communication with “spirits”, that have “brought forward” future findings related to the pineal gland.

The aim of investigation however, was not to draw hasty conclusions based on unsubstantiated evidence. The present article provides an analysis of the knowledge the scientific community can acquire from the history of humanity and from science itself. The process of formulating hypotheses and scientific theories can benefit by drawing on the cultural aspects of civilization, taking into account so-called non-traditional reports and theories.

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REFERENCES

- Atkinson G, Holder A, Robertson C, Gant N, Drust B, Reilly T, Waterhouse J (2005). Effects of melatonin on the thermoregulatory responses to intermittent exercise. *Journal of pineal research* **39**: 353–359.
- Barrett P, Bolborea M (2012). Molecular pathways involved in seasonal body weight and reproductive responses governed by melatonin. *Journal Of Pineal Research* **52**: 376–388.
- Batmanabane M (2007). Melatonin is responsible for the nocturnal increase observed in serum and thymus of alpha1-thymosin and thymulin concentrations: observations in rats and humans. *Journal Of Neuroimmunology* **183**: 239; author reply 240.
- Bertrand S, Faivre B, Sorci G (2006). Do carotenoid-based sexual traits signal the availability of non-pigmentary antioxidants? *Journal of Experimental Biology* **209**: 4414–4419.
- Bornman M, Oosthuizen J, Barnard H, Schulenburg G, Boomker D, Reif S (1989). Melatonin and Sperm Motility/Melatonin und Spermatozoenmotilität. *Andrologia* **21**: 483–485.
- Buxton OM, L'hermite-Balériaux M, Hirschfeld U, Van Cauter E (1997). Acute and delayed effects of exercise on human melatonin secretion. *Journal of biological rhythms* **12**: 568–574.
- Campino C, Valenzuela F, Arteaga E, Torres-Farfán C, Trucco C, Velasco A, Guzmán S, Serón-Ferré M (2008). [Melatonin reduces cortisol response to ACTH in humans]. *Revista Médica De Chile* **136**: 1390–1397.
- Campino C, Valenzuela FJ, Torres-Farfán C, Reynolds HE, Abarzua-Catalan L, Arteaga E, Trucco C, Guzmán S, et al. (2011). Melatonin exerts direct inhibitory actions on ACTH responses in the human adrenal gland. *Hormone And Metabolic Research = Hormon-Und Stoffwechselforschung = Hormones Et Métabolisme* **43**: 337–342.
- Cardinali DP, Ladizesky MG, Boggio V, Cutrera RA, Mautalen C (2003). Melatonin effects on bone: experimental facts and clinical perspectives. *Journal Of Pineal Research* **34**: 81–87.
- Cardinali Dp, Srinivasan V, Brzezinski A, Brown Gm (2012). Melatonin and its analogs in insomnia and depression. *Journal of pineal research* **52**: 365–375.
- Cardinali DP, Vacas MI, Lowenstein PR, Estévez E (1979). [Neurohumoral control of the pineal gland. A model for the study of neuroendocrine integrative processes]. *Acta Physiologica Latino Americana* **29**: 291–304.
- Chen H, Shoumura S, Emura S, Utsumi M, Yamahira T, Isono H (1991). Effects of melatonin on the ultrastructure of the golden hamster parathyroid gland. *Histology And Histopathology* **6**: 1–7.
- Chen Y-C, Sheen J-M, Tiao M-M, Tain Y-L, Huang L-T (2013). Roles of melatonin in fetal programming in compromised pregnancies. *International Journal Of Molecular Sciences* **14**: 5380–5401.
- Dupré SM, Dardente H, Birnie MJ, Loudon ASI, Lincoln GA, Hazlerigg DG (2011). Evidence for RGS4 modulation of melatonin and thyrotrophin signalling pathways in the pars tuberalis. *Journal Of Neuroendocrinology* **23**: 725–732.
- Elias A, Wilson A, Pandian M, Rojas F, Kayaleh R, Stone S, James N (1993). Melatonin and gonadotropin secretion after acute exercise in physically active males. *European journal of applied physiology and occupational physiology* **66**: 357–361.
- Escames G, Ozturk G, Baño-Otálora B, Pozo MJ, Madrid JA, Reiter RJ, Serrano E, Concepción M, et al. (2012). Exercise and melatonin in humans: reciprocal benefits. *Journal of pineal research* **52**: 1–11.
- Espino J, Pariente JA, Rodríguez AB (2012). Oxidative stress and immunosenescence: therapeutic effects of melatonin. *Oxidative Medicine And Cellular Longevity* **2012**: 670294–670294.
- Fishman RS (2008). The study of the wonderful: the first topographical mapping of vision in the brain. *Arch Ophthalmol* **126**: 1767–1773.
- Galano A, Tan DX, Reiter RJ (2011). Melatonin as a natural ally against oxidative stress: a physicochemical examination. *J Pineal Res* **51**: 1–16.
- Galano A, Tan DX, Reiter RJ (2013). On the free radical scavenging activities of melatonin's metabolites, AFMK and AMK. *J Pineal Res* **54**: 245–257.
- Grugni G, Carani C, Maestroni G, Guzzaloni G, Ardizzi A, Lissoni P, Granata A, Morabito F (1994). Melatonin levels in psychogenic impotence. *Hormone and metabolic research= Hormon-und Stoffwechselforschung= Hormones et métabolisme* **26**: 440–441.
- Guyton AC, Hall JE (2006). *Tratado de fisiologia médica*: Elsevier Brasil.
- Hardeland R, Cardinali DP, Srinivasan V, Spence DW, Brown GM, Pandi-Perumal SR (2011). Melatonin—a pleiotropic, orchestrating regulator molecule. *Prog Neurobiol* **93**: 350–384.
- Hatzis G, Ziakas P, Kavantzias N, Triantafyllou A, Sigalas P, Andreadou I, Ioannidis K, Chatzis S, et al. (2013). Melatonin attenuates high fat diet-induced fatty liver disease in rats. *World Journal Of Hepatology* **5**: 160–169.
- Itoh MT, Hosaka T, Takahashi N, Ishizuka B (2006). Expression of luteinizing hormone/chorionic gonadotropin receptor in the rat pineal gland. *Journal Of Pineal Research* **41**: 35–41.
- Jansen SFD, Duncan V, Morgan D, Malouf R (2011). Melatonin for the treatment of dementia. *Cochrane Database Syst Rev*: CD003802.
- Kappers Ja, Kappers J, Pévet P (1979). *Short history of pineal discovery and research*: Elsevier Amsterdam.
- Kitay JI, Altschule MD (1954). *The pineal gland. A review of the physiologic literature. The pineal gland A review of the physiologic literature.*
- Klein DC, Bailey MJ, Carter DA, Kim J-S, Shi Q, Ho AK, Chik CL, Gaildrat P, et al. (2010). Pineal function: impact of microarray analysis. *Molecular And Cellular Endocrinology* **314**: 170–183.
- Korf HW, Schomerus C, Stehle JH (1998). The pineal organ, its hormone melatonin, and the photoneuroendocrine system. *Advances In Anatomy, Embryology, And Cell Biology* **146**: 1–100.
- Korkmaz A, Topal T, Tan DX, Reiter RJ (2009). Role of melatonin in metabolic regulation. *Rev Endocr Metab Disord* **10**: 261–270.
- Kozirog M, Poliwczak AR, Duchnowicz P, Koter-Michalak M, Sikora J, Broncel M (2011). Melatonin treatment improves blood pressure, lipid profile, and parameters of oxidative stress in patients with metabolic syndrome. *J Pineal Res* **50**: 261–266.
- Lerner A, Case J, Takahashi Y, Lee T, Mori W (1958). Isolation of Melatonin, the pineal gland factor that lightens melanocytes. *Journal of the American Chemical Society* **80**: 2587–2587.
- Li C, Shi Y, You L, Wang L, Chen Z-J (2011). Melatonin receptor 1A gene polymorphism associated with polycystic ovary syndrome. *Gynecologic And Obstetric Investigation* **72**: 130–134.

- 35 López-Muñoz F, Alamo C, García-García P (2010a). La neurofisiología cartesiana: entre los spiritus animalis y el conarium. *Arch Neurocienc (Mex)* **15**: 179–193.
- 36 López-Muñoz F, Marín F, Álamo C (2010b). El devenir histórico de la glándula pineal: I. De válvula espiritual a sede del alma. *Revista de Neurología* **50**: 50–57.
- 37 López-Muñoz F, Marín F, Álamo C (2010c). El devenir histórico de la glándula pineal: II. De sede del alma a órgano neuroendocrino. *Rev Neurol* **50**: 117–125.
- 38 López-Muñoz F, Molina J, Rubio G, Alamo C (2011). An historical view of the pineal gland and mental disorders. *Journal of Clinical Neuroscience* **18**: 1028–1037.
- 39 Luboshitzky R, Herer P, Shen-Orr Z (2004). Urinary 6-sulfatoxymelatonin excretion in hyperandrogenic women: the effect of cyproterone acetate-ethinyl estradiol treatment. *Experimental And Clinical Endocrinology & Diabetes: Official Journal, German Society Of Endocrinology [And] German Diabetes Association* **112**: 102–107.
- 40 Luboshitzky R, Qupti G, Ishay A, Shen-Orr Z, Futerman B, Linn S (2001). Increased 6-sulfatoxymelatonin excretion in women with polycystic ovary syndrome. *Fertility And Sterility* **76**: 506–510.
- 41 Lucchetti G, Aguiar PRD, Braghetta CC, Vallada CP, Moreira-Almeida A, Vallada H (2012). Spiritist psychiatric hospitals in Brazil: integration of conventional psychiatric treatment and spiritual complementary therapy. *Culture, Medicine, and Psychiatry* **36**: 124–135.
- 42 Lucchetti G, Lucchetti ALG, Bassi RM, Nobre MRS (2011). Complementary spiritist therapy: systematic review of scientific evidence. *Evidence-Based Complementary and Alternative Medicine* **2011**: 1–18.
- 43 Lynch H, Ho M, Wurtman R (1977). The adrenal medulla may mediate the increase in pineal melatonin synthesis induced by stress, but not that caused by exposure to darkness. *Journal of neural transmission* **40**: 87–97.
- 44 Maldonado MD, Perez-San-Gregorio MA, Reiter RJ (2009a). The role of melatonin in the immuno-neuro-psychology of mental disorders. *Recent Pat CNS Drug Discov* **4**: 61–69.
- 45 Maldonado MD, Reiter RJ, Perez-San-Gregorio MA (2009b). Melatonin as a potential therapeutic agent in psychiatric illness. *Hum Psychopharmacol* **24**: 391–400.
- 46 March WA, Moore VM, Willson KJ, Phillips DIW, Norman RJ, Davies MJ (2010). The prevalence of polycystic ovary syndrome in a community sample assessed under contrasting diagnostic criteria. *Human Reproduction (Oxford, England)* **25**: 544–551.
- 47 Martinis P, Zago L, Maritati M, Battaglia V, Grancara S, Rizzoli V, Agostinelli E, Bragadin M, *et al.* (2012). Interactions of melatonin with mammalian mitochondria. Reducer of energy capacity and amplifier of permeability transition. *Amino acids* **42**: 1827–1837.
- 48 Mauriz JL, Collado PS, Veneroso C, Reiter RJ, González-Gallego J (2013). A review of the molecular aspects of melatonin's anti-inflammatory actions: recent insights and new perspectives. *Journal of pineal research* **54**: 1–14.
- 49 Mazzoccoli G, Carughi S, Sperandeo M, Paziienza V, Giuliani F, Tarquini R (2011). Neuro-endocrine correlations of hypothalamic-pituitary-thyroid axis in healthy humans. *Journal Of Biological Regulators And Homeostatic Agents* **25**: 249–257.
- 50 Messina G, Lissoni P, Marchiori P, Bartolacelli E, Brivio F, Magotti L (2010). Enhancement of the efficacy of cancer chemotherapy by the pineal hormone melatonin and its relation with the psychospiritual status of cancer patients. *Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences* **15**: 225–228.
- 51 Miles A, Philbrick DR (1988). Melatonin and psychiatry. *Biological psychiatry* **23**: 405–425.
- 52 Monteleone P, Maj M, Fusco M, Orazzo C, Kemali D (1990). Physical exercise at night blunts the nocturnal increase of plasma melatonin levels in healthy humans. *Life sciences* **47**: 1989–1995.
- 53 Moreira-Almeida A, De Almeida AAS, Neto FL (2005). History of 'Spiritist madness' in Brazil. *History of Psychiatry* **16**: 5–25.
- 54 Nagai R, Watanabe K, Wakatsuki A, Hamada F, Shinohara K, Hayashi Y, Imamura R, Fukaya T (2008). Melatonin preserves fetal growth in rats by protecting against ischemia/reperfusion-induced oxidative/nitrosative mitochondrial damage in the placenta. *Journal of pineal research* **45**: 271–276.
- 55 Nir I, Hirschmann N (1979). A possible role of the pineal gland in pregnancy and fertility. *Progress In Brain Research* **52**: 421–435.
- 56 Ostrowska Z, Kos-Kudla B, Marek B, Kajdaniuk D (2003). Influence of lighting conditions on daily rhythm of bone metabolism in rats and possible involvement of melatonin and other hormones in this process. *Endocrine Regulations* **37**: 163–174.
- 57 Raghavendra V, Kaur G, Kulkarni SK (2000). Anti-depressant action of melatonin in chronic forced swimming-induced behavioral despair in mice, role of peripheral benzodiazepine receptor modulation. *Eur Neuropsychopharmacol* **10**: 473–481.
- 58 Reiter RJ (1995). Functional pleiotropy of the neurohormone melatonin: antioxidant protection and neuroendocrine regulation. *Front Neuroendocrinol* **16**: 383–415.
- 59 Reiter RJ, Fraschini F (1969). Endocrine aspects of the mammalian pineal gland: a review. *Neuroendocrinology* **5**: 219–255.
- 60 Reiter RJ, Tan D-X, Korkmaz A, Ma S (2012). Obesity and metabolic syndrome: association with chronodisruption, sleep deprivation, and melatonin suppression. *Annals Of Medicine* **44**: 564–577.
- 61 Reiter RJ, Tan D-X, Manchester LC, Paredes SD, Mayo JC, Sainz RM (2009). Melatonin and reproduction revisited. *Biology of reproduction* **81**: 445–456.
- 62 Robertson NJ, Faulkner S, Fleiss B, Bainbridge A, Andorka C, Price D, Powell E, Lecky-Thompson L, *et al.* (2013). Melatonin augments hypothermic neuroprotection in a perinatal asphyxia model. *Brain: A Journal Of Neurology* **136**: 90–105.
- 63 Saha L, Kaur S, Saha PK (2012). Pharmacotherapy of polycystic ovary syndrome--an update. *Fundamental & clinical pharmacology* **26**: 54–62.
- 64 Sanchez-Barcelo EJ, Mediavilla MD, Tan DX, Reiter RJ (2010). Clinical uses of melatonin: evaluation of human trials. *Curr Med Chem* **17**: 2070–2095.
- 65 Sarabia L, Maurer I, Bustos-Obregón E (2009). Melatonin prevents damage elicited by the organophosphorous pesticide diazinon on mouse sperm DNA. *Ecotoxicology and Environmental Safety* **72**: 663–668.
- 66 Shi L, Li N, Bo L, Xu Z (2013). Melatonin and hypothalamic-pituitary-gonadal axis. *Current Medicinal Chemistry* **20**: 2017–2031.
- 67 Skrinar GS, Bullen BA, Reppert SM, Peachey SE, Turnbull BA, McArthur JW (1989). Melatonin response to exercise training in women. *Journal of pineal research* **7**: 185–194.
- 68 Tan DX, Manchester LC, Fuentes-Broto L, Paredes SD, Reiter RJ (2011). Significance and application of melatonin in the regulation of brown adipose tissue metabolism: relation to human obesity. *Obesity reviews: an official journal of the International Association for the Study of Obesity* **12**: 167–188.
- 69 Touitou Y, Haus E (2000). Alterations with aging of the endocrine and neuroendocrine circadian system in humans. *Chronobiology International* **17**: 369–390.
- 70 Tsukamoto N, Otsuka F, Ogura-Ochi K, Inagaki K, Nakamura E, Toma K, Terasaka T, Iwasaki Y, *et al.* (2013). Melatonin receptor activation suppresses adrenocorticotropin production via BMP-4 action by pituitary AtT20 cells. *Molecular And Cellular Endocrinology*.
- 71 Van Reeth O, Sturis J, Byrne Mm, Blackman JD, L'hermite-Balériaux M, Leproult R, Oliner C, Refetoff S, *et al.* (1994). Nocturnal exercise phase delays circadian rhythms of melatonin and thyrotropin secretion in normal men. *American Journal of Physiology-Endocrinology And Metabolism* **266**: E964–E974.
- 72 Verster G (2009). Melatonin and its agonists, circadian rhythms and psychiatry. *African journal of psychiatry* **12**: 42–46.
- 73 Webb SM, Puig-Domingo M (1995a). Role of melatonin in health and disease. *Clinical endocrinology* **42**: 221–234.
- 74 Webb SM, Puig-Domingo M (1995b). Role of melatonin in health and disease. *Clin Endocrinol (Oxf)* **42**: 221–234.
- 75 Wu Y-H, Ursinus J, Zhou J-N, Scheer FA, Ai-Min B, Jockers R, Van Heerikhuizen J, Swaab DF (2013). Alterations of melatonin receptors MT1 and MT2 in the hypothalamic suprachiasmatic nucleus during depression. *Journal of affective disorders* **148**: 357–367.
- 76 Xavier F (2009/1945). Missionaries of the light. *Brasilia: International Spiritist Council*.
- 77 Xavier FC (1945). *Missionários da Luz*. Rio de Janeiro: FEB.