ISSN: 2230-9926

Available online at http://www.journalijdr.com

IJDR

International Journal of Development Research
Vol. 07, Issue, 09, pp.15625-15631, September, 2017

ORIGINAL RESEARCH ARTICLE OPEN ACCESS

ASSOCIATION BETWEEN INSOMNIA AND CHRONIC NONCOMMUNICABLE DISEASES: CURRENT FINDINGS AND FUTURE DIRECTIONS

***,[1]Lígia Aurélio Bezerra Maranhão Mendonça, [1]Natali Camposano Calças, [2]João Pedro Teixeira Basmage, [2]Larissa Sawaris Neto and [2]José Carlos Souza**

[1]Programa de Pós-Graduação em Biotecnologia, Universidade Católica Dom Bosco, Avenida Tamandaré, 6.000 - Jardim Seminário, 79117-900, Campo Grande, Mato Grosso do Sul, Brazil
[2]Curso de Medicina da Universidade Estadual de Mato Grosso do Sul, R. Ernesto de Fiori, 51 - Conj. Jose Abrão, Campo Grande, Mato Grosso do Sul, Brazil

ARTICLE INFO

Article History:
Received 20th June, 2017
Received in revised form
17th July, 2017
Accepted 24th August, 2017
Published online 30th September, 2017

Keywords:
Hypertension, Diabetes Mellitus, Sleep, Sleep Wake Disorders, Metabolism.

ABSTRACT

Insomnia is a sleep disorder that consistently interferes with the quantity and quality of sleep. It is a condition responsible for the development of neuro-endocrine metabolic changes connected to an increased risk of developing noncommunicable chronic diseases. Thus, changes in the neuro-endocrine metabolic axis due to insomnia lead to an increase or decrease in the synthesis and/or secretion of hormones, which is directly associated with important changes in glucose, lipid and protein metabolism, resulting in a physiological and metabolic condition as an alternative to the resumption of homeostasis. This condition, when chronic, allows the development of metabolic diseases such as cardiovascular diseases, diabetes mellitus type 2, systemic arterial hypertension, hypercholesterolemia, among others which have become endemic in modern society.

Corresponding author

Citation: Lígia Aurélio Bezerra Maranhão Mendonça, Natali Camposano Calças et al. 2017. "Association between Insomnia and Chronic Noncommunicable Diseases: Current findings and future directions", *International Journal of Development Research*, 7, (09), 15625-15631.

INTRODUCTION

The relationship between sleep and neuro-endocrine system is bidirectional. Both are closely interlinked. The synthesis and hormonal secretion are directly influenced by quality, conditions and duration of sleep. Therefore, all conditions that interfere with homeostasis, such as disorders, specifically insomnia, result in important changes which can advance to the development diseases, especially metabolic diseases (Morgan; Tsai, 2015; Viot-Blanc, 2015; Tan et al., 2016; Adamsson; Laike; Morita, 2017). Therefore, it is possible to verify a subtle and delicate relation between pathologic processes associated to sleep, insomnia and metabolic neuro-endocrine status. This relation needs constant attention to prevent any type of disorder, since insomnia, diabetes mellitus 2 (DM 2), hypercholesterolemia (HC), systemic arterial hypertension (SAH) and cardiovascular diseases (CD) are considered important agents contributing to the inharmonious and costly process of public and private health in the country. The aim this study is to provide a unifying framework and provide information for future studies ultimately leading to improved understanding efforts by providing a more complete knowledge about a relevant sleep disorder, i.e., insomnia, and its relation with important neuro-endocrine metabolic changes including the increased risk of developing noncommunicable chronic diseases (NCD).

Insomnia: Difficulty to Sleep

According to the Diagnostic and Statistical Manual, Fifth Edition (DSM-V), insomnia is considered a condition in which there are difficulties to fall asleep. Other diagnosis symptoms include waking up in the middle of the night, difficulty to

resume sleep, or waking up very early in the morning. Insomnia is therefore commonly characterized by difficulties in initiating or maintaining sleep at least 3 times a week for a minimum of 90 days. It is also a psychiatric disorder. Insomnia is a disease and requires specific treatment (Jansson-Fröjmark; Norell-Clarke, 2016), and is considered a major public health problem (Morin; Jarrin, 2013). According to the ICD-10, for a definitive diagnosis of insomnia the main complaint must be difficulty of falling asleep, staying asleep or poor sleep quality. The main symptoms and the period abovementioned must also be taken into account. These factors must be present because the quantity and the quality of sleep may directly interfere with social life and occupational functions (Iacoponi, 1999), such as high rates of absenteeism at work and a decreased work performance (Wilson et al., 2010). Furthermore, insomnia may result in the development of important metabolic conditions such as NCD. Such conditions result in a loss of homeostasis (Wilson et al., 2010). The risk of developing such conditions is relevant, since the epidemiological panorama is worrisome. Chronic insomnia is highly prevalent and affects approximately 30 % of the general population. Epidemiological surges are associated with several risk factors, including advanced age, the female gender and medical and psychiatric comorbidities (Wilson et al., 2010). The treatment for insomnia can be managed by psychological therapy, pharmacological therapy or a combination of both. Options for psychological therapy include, for example, cognitive-behavioral therapy (CBT-I), which is the first-choice treatment comprising of individual face-to-face sessions over the course of 6-8 weeks (Boullin; Ellwood; Ellis, 2016). It consists of a combination of cognitive

therapy, behavioral interventions (such as sleep restriction and stimulus control), educational interventions and other approaches such as multicomponent behavioral therapy or brief behavioral therapy (BBT) for insomnia (Qaseem et al., 2016), in addition to other interventions such as sleep hygiene, biofeedback and deep breathing exercises (Souza; Carvalho, 2015). Regarding the pharmacological therapy for insomnia, doctors in the United States use benzodiazepines, a non-benzodiazepine hypnotic. More recently, doctors also use suvorexant, an orexin receptor antagonist; ramelteon, a melatonin receptor agonist; doxepin, an antidepressant; off-label drugs such as other antidepressants, antihistamines and antipsychotics and melatonin (Qaseem et al., 2016). However, the commercialization of melatonin is not allowed in Brazil because safety criteria and its efficacy have not yet been evaluated (Anvisa, 2017). The pharmacological treatment in Brazil, similar to that mentioned above, includes the following category of hypnotics: benzodiazepines and new non-benzodiazepines, called zopiclone, zolpidem and zaleplon. All act on the macromolecule of the GABA inhibitory receptor complex (gamma-aminobutyric acid) (Souza; Camargo, 2016). Depending on the cause of insomnia, other medications may be used, such as antidepressants, anxiolytics, antipsychotics, mood stabilizers, analgesics, muscle relaxers, among others (Souza; Carvalho, 2015).

Circadian Rhythm: Mechanisms and its Importance for Organic Metabolism

The circadian rhythm is defined by oscillations of biological processes associated with an internal timer (Fu; Lee, 2003). The correct functioning of this system is essential for the life of the human organism at a systemic and cellular level, covering different areas such as the sleep-wake cycle, endocrine functions (stress, growth, division and reproduction), thermoregulation, arterial pressure in systemic circulation, immune response and digestive system, associated with metabolism (Turek; van Cauter, 1994, Zee; Attarian; Videnovic, 2013). This system is hierarchized into a central system (suprachiasmatic nucleus) and peripheral clocks (all organs and individual cells in the body) that have a synchronized or independent relation according to physiological situations (Eckel; Corsi, 2013). The central system consists of three parts: entrance path (retinohypothalamic tract, intergeniculate leaflet and raphe nuclei), central pacemaker (suprachiasmatic nucleus), and exit pathways (different areas of the cortex, pituitary and cranial nerves) (Chan et al., 2012). The rhythm is generated endogenously. Therefore, under conditions in which there are no influences from the outside world (constant conditions), the circadian system will continue to generate daily rhythms. Stimuli to the entrance ways are environmental signals such as external light. Their importance lies in the influence they exert on the association between the generated internal rhythm (periodicity) and the rhythm of the environment (day or night) (Pittendrigh; DAAN, 1976). Endogenous generation of rhythm in men occurs by a negative feedback mechanism within pacemaker cells throughout the brain and the body. Such feedback system contains proteins produced by known "clock" genes inhibiting their own transcription and leading to daily oscillations. Clock genes are divided into positive (Bmal1 and Clock) and negative (PER1, PER2, PER3, CRY1 and CRY2). The positive group is responsible for activating the trigger signals of the system and the transcription of the negative group that inhibited the rhythm (Hastings; Herzog, 2004).

At the central level, an important connection of the system is made with the hypothalamic-pituitary-adrenal (HPA) axis through synapses performed by the HPA between the suprachiasmatic nucleus and the ventricular nucleus, which contains neurons responsible for the production and release of hormones, among them corticotropin-releasing hormone (CRH), responsible for the activation of the pituitary- adrenal axis (Yeh, 2015). At the peripheral level, the bidirectional relation between the molecular circadian rhythm and its metabolism is highlighted. Studies point to a synthesis of nucleotides and hepatic ribosomes resulting in circadian rhythms associated with an evidence of NAD (Nicotinamide adenine dinucleotide) oscillation, which controls rhythmic mitochondrial oxidation (Nakahata et al., 2008; Nakahata et al., 2009).

The relationship is called ―bidirectional‖ because the clock may also be influenced by the metabolism. New research points to the influence of NAD in opposition to Clock genes and changes in the PER2 and BMAL1 genes. Glucose may also affect the circadian rhythm because of its contribution in controlling the PER2 gene activity (Kohsaka; BASS, 2007). The relation glucose-circadian rhythm is evidenced by the inference according to which people with sleep disorders are more likely to develop diabetes in the long term and patients already with diabetes experience difficulty in controlling the disease (VOIGT et al., 2014). One of the most important factors for maintaining a regulated circadian cycle is related to a hygienic and restorative sleep. People who sleep poorly or have insomnia tend to present growth problems, scarring, depressed immunity and stress (VOIGT et al., 2014). This population tends to compromise its chronotype (morning, afternoon or night).

Melatonin: Regulation of Sleep and Circadian Rhythm

Melatonin (N-acetyl-5-methoxytryptamine) is a neuro-hormone produced by the pineal gland by stimulating the sympathetic noradrenergic through postganglionic innervation originating from the superior cervical ganglion in the presence of tryptophan. This hormone derives from serotonin (5-hidroxitriptamina), resulting from reactions of acetylation. It may also be produced by other regions of the organism, such as the gastrointestinal tract (GIT), bone marrow, several leukocytes, membranous cochlea and presumably skin and the central nervous system (Zitouni; Pevet; Masson-Pevet, 1996). The production of the hormone is controlled by the suprachiasmatic nucleus (SCN), which presents melatonin receptors, influencing the pineal gland. Such receptors decrease after birth, remain stable for approximately 1 month and increase again at puberty (Zitouni; Pevet; Masson-Pevet, 1996). It is important to emphasize that this hormone decreases with the advancing age and in the presence of diseases (Hardeland, 2012). Among classical receptors, tehere are MT1 (MTRN1a) and MT2 (MTRN1b), both belonging to the family of G-protein-coupled receptors. They are located in different areas of the brain (Hardeland et al., 2011), which justifies the action of these neuro-hormones (Ekmekcioglu, 2006). Another important class of receptors of this hormone is MT3, whose structure resembles that of the enzyme quinone reductase and the nucleate receptors RECT/ROR. An important fact related with the liberation and secretion of this hormone is its regulation by the circadian timing system. The daily production of melatonin obeys a precisely rhythmic circadian production synchronized to the cycle of environmental illumination (day and night), with a nocturnal peak production. This property makes the melatonin an important hormone in the process of circadian synchronization of the 7 organism, in particular, the sleep-wake cycle and energy metabolism (Poyares et al., 2005; Hardeland et al., 2011; Cipolla-Neto, 2014). Thus, this hormone acts of the background of regulation and induction of the sleep. However, this function is controversial even after years of study (Gandhi et al., 2015). Given the importance of this hormone, it is possible to observe its connection with the organic metabolism, especially in relation to the regulation of energy metabolism. This is why individuals with decreasing levels of melatonin may have resistance to insulin, intolerance to glucose, insulin secretion disorders, dyslipidemia, obesity and energy balance disorders. An important metabolic instability is observed in the absence or with decreasing melatonin levels, leading to metabolic disorders and mutually intensifying rhythmic circadian disorders, which may increase the risk metabolic diseases.

Insomnia *versus* Hormonal-Metabolic Imbalance: Noncommunicable Chronic Diseases (NCD)

As it is an important sleep disorder, insomnia causes hormonal neuro- metabolic changes, greatly impacting human health. Therefore, the general recommendation of a good night's sleep equivalent to 7/8 hours is essential, allowing the increase in the organism's capacity to withstand hormonal changes that may trigger the development of metabolic diseases such as NCD (Rogers et al., 2016). Thus, diseases such as DM 2, SAH, HC and cardiovascular disease stand out (Sabanayagam; Shankar, 2012; Rogers et al., 2016). Multifactorial conditions are considered a public health problem of great magnitude (Brasil, 2017) and are responsible for innumerable cases of physic and mental incapacities.

Hypothalamic-Hypophysis-Adrenal Axis: Corticotrophin (CRH) – Adrenocorticotrophic (ACTH) – Cortisol - DM2 and SAH

The hypothalamic-hypophysis-adrenal axis (HHA) is an important regulatory neuroendocrine mechanism of the organic metabolism. It acts by synthetizing and secreting hormones responsible for performing modulatory functions. The HHA is stimulated by CRH and sensitized by the hypothalamus, an agent responsible for controlling the release of hypophysis secretions. It stimulates the synthesis and secretion of ACTH by the adeno-hypophysis. Subsequently, ACTH, when in the bloodstream, moves to the adrenal cortex, allowing the stimulation of the gland and the consequent release of glucocorticoids such as cortisol, into the fasciculate zone. Both are regulated by the potential of negative feedback by glucocorticoids (Vale et al., 2012). Such hormones are relevant for metabolic maintenance and the balance of the circadian rhythm, since the production of ACTH, and consequently cortisol, is higher in the morning and lower in the afternoon and evening, increasing again during sleep. Besides that, other factors interfere consistently with the concentrations of such hormonal modalities due to the activation of hypothalamic centers. Such factors include stress, high environment temperature, fever, sleep conditions, hypoglycemia, inflammation, fasting, pain, trauma and fear, factors that promotes the increase and the release of CRH/ACTH, which consequently increase the adrenocortical activity, especially the fasciculate zone (Adamsson; LAIKE; Morita, 2017). Cortisol synthesis depends on the levels of CRH and ACTH, derived from the activity of the adreno-cortical axis in the fasciculate zone. This hormone presents a singular metabolic function in carbohydrates related to the synthesis of glycogen due to the inhibition of the use of glucose by cells and the stimulation to glycogen storage. In relation to proteins, cortisol acts by stimulating the catabolism protein, which leads to a consistent increase in urinary nitrogen. Cortisol also raise the levels of serum amino acids, and cause their subsequent degradation. This results in an increase in plasmatic urea. As for lipids, cortisol acts by performing lipolysis, which allows a high action of lipase, activating hormones such as glucagon, adrenaline and GH. Thus, there is oxidation of fatty acids and, therefore, an increase in acetyl-CoA (Vale et al., 2012). The functions and influences of cortisol on the human organism are diverse and complex. It also acts on the immune system, the bone system and the gastrointestinal tract by secreting hydrochloric acid, pepsin and pancreatic trypsin and decreasing mucus secretion, a condition that allows the development of gastroduodenal ulcers (Vale et al., 2012). When considering the impacts of cortisol on the organic metabolism, its action on sleep conditions stands out. Tamura; Kruger (2016) emphasize that it is a relevant hormone for the circadian rhythm balance. The release of this hormone is directly related to environmental conditions, especially luminosity, emotional states (stress) and sleep disorders such as insomnia (Adamsson; Laike; Morita, 2017), which is related to damage to the glucose metabolism and insulin function. There is an increase 9 in insulin resistance, glucose tolerance and insulin sensibility, factors observed in several population studies relating such conditions to a consistent increase of DM 2 risk (Bopparaju; SURANI, 2010; Morgan; Tsai, 2015; Viot-Blanc, 2015; Abell et al.,

2016). Metabolically, increased glucose levels lead to its increased use by organs, specially the brain. Due the cerebral demand, however, high cortisol concentrations inhibit the uptake of tissue glucose and causes a persistent increase of blood glucose, which may cause DM 2 (Costa; Mousovich-Neto, 2016). This arises from important changes in cellular glucose transporters such as GLUT4. It is emphasized that GLUT4 has its activity substantiated from insulin. However, high levels of cortisol lead to insulin resistance. Therefore, this hormone is diabetogenic. Such changes are justified by the activation and potentiation of hepatic gluconeogenic routes, that is, the synthesis of glucose by atypical routes due to the degradation of amino acids, lipids, lactate and glycerol, which causes a persistent increase in blood glucose in such way that explains the proteolytic characteristic of cortisol (van Raalte; Ouwens; Diamant, 2009; Bopparaju; Surani, 2010). Furthermore, such routes can be activated in the presence of cortisol by hormones such as catecholamines and glucagon, the latter a cortisol analogue. This enables intensifying the degradation of atypical substrates (Van Raalte; Ouwens; Diamant, 2009; Bopparaju; Surani, 2010). This condition was evidenced decades ago by Kawakami; Takatsuka; Shimizu, (2004), cited by Viot-Blanc (2015), in a study that analyzed a population with difficulties in initiating and maintaining sleep for a period of eight years. The authors verified an increase in the relatively high incidence of DM 2. Similar conditions were observed by Meisinger; Heier; Loewel (2005), cited by the same author, in a study that followed 8.269 individuals of both sexes for seven years and six months. These findings were emphasized by Bhattacharya; Sen; Suri, (2013) and Viot-Blanc (2015), who also highlighted the effects of insomnia on glycidic metabolism. This was also evidenced in children and adolescents, according to Kaczor; Skalski (2016). The authors further claimed that this disease has increased in recent decades and has taken alarming proportions, becoming a serious and challenging public health problem. When considering the metabolic functions of cortisol, it is verified, for example, that high levels of this hormone during insomnia cause other metabolic diseases such as coronary diseases and SAH (Vale et al., 2012; Sofi et al., 2014; Abell et al., 2016; Garbarino et al., 2016).

The mechanism that causes SAH has not been well elucidated. However, it is known that such relationship exists and that hypotheses refer to an increased sympathetic activity, a low endogenous production of melatonin, the stimulation of the renin-angiotensin-aldosterone axis (RAA), pro- inflammatory responses, the activity of the HHA axis, decrease of leptin, increase in ghrelin and a low sensitivity to insulin. Such factors cause the other systemic changes such as renal insufficiency, endothelial dysfunction, changed circadian cycle, obesity and increased ACTH and cortisol (MENG et al., 2013). Therefore, sleep disorders deserve attention, as they result in important stress conditions that lead to a systemic change, as discussed here. In addition, studies have shown that the effects of cortisol on blood pressure levels occur by activation of ERAA because it leads to the water retention, inhibition of nitric oxide production (NO), increased sensitivity to catecholamines and other vasoconstrictors, including Endothelin-1(ET-1) (SINGH; KOTWAL; MENON, 2011).

Thyrotropin - Thyroid Stimulant (TSH) Hormone in NCD

Thyroid-stimulating hormone (TSH) is secreted by the hypophysis by hypothalamic stimulation by the thyrotropin-releasing hormone (TRH). Its binding mechanism arises from the bonding to the G protein, which results in an increase in intracellular cAMP, with a consequent release of TSH (Hershman, 1974). Its secretion is circadian and usually occurs between 10 p.m. and 4 p.m. It is influenced by other hormones such as dopamine, somatostatin, leptin and cortisol (Langroudi et al., 2010). One of the important functions of the TSH is to stimulate the production and the release of thyroxine (T4), with the subsequent release of triiodothyronine (T3), responsible for the negative feedback of HRT by the G-TSH protein binding and at its receptors in follicular thyroid cells (Schroeder; Privalsky, 2014). Thyroid hormones associated with the sympathetic nervous system regulates metabolic processes in a complementary manner (Arbeck et al., 2015). It is able to change the basal metabolic rate by increasing ATP production and generating ions (Na+ and K+) in the metabolic cycles involving lipids, glucose, catabolism and protein anabolism, for example (Hafner et al., 1988).

Regulation is maintained by the decoupling mechanism of the mitochondrial oxidative phosphorylation by the TSH associated with the decrease in reducing molecules. In the skeletal muscle, for example, TSH increases the efflux of mitochondrial ions to stimulate a greater oxidation in order to maintain the synthesis of ATP due to the impairment of the proton-matrix force (Harper; Seifert, 2008). Thus, numerous examples of TSH binding to organic metabolic processes are verified. Among the metabolic relationships related to TSH, its association with sleep disorders such as insomnia is evident, since its production peak occurs during night hours. Besides NCD, in which inadequate levels of hormone contribute to the development of SAH (Abdul et al., 2001) and increased adiposity (Cheng; Chiang; Chen, 2015), there are increased levels of total cholesterol, low-density lipoprotein cholesterol and triglycerides, suggesting its interference with lipid homeostasis (Tagami et al., 2010; Pasqualetti; TOGNINI; Polini, 2013; Boggio et al., 2014). Because it is a very influential hormone in the organic metabolism, TSH, when changed, also directly affects insulin levels, resulting in increased resistance to insulin and high serum glucose levels. This is justified by its increased intestinal absorption, as well as by an increased hepatic production (Brenta et al., 2009). Such changes are high risk factors for the development of DM 2 (Wang, 2013).

Damage to the Hormonal Route of GH (Growth Hormone) and NCD

The GH is the most abundant hormone secreted by the adenohypophysis. Its synthesis by the pituitary gland is associated with the normal gene (GH-N or GH-1) according to the excitatory and inhibitory influence of hypothalamic peptides, growth hormone-releasing hormone (GHRH) and growth hormone-inhibiting hormone (GHIH) (Barake et al., 2014). The stimuli for its release are influenced by several neurotransmitters such as acetylcholine, noradrenaline, serotonin and dopamine and peripheral hormones such as glucocorticoids and insulin. Its secretion is circadian, with several moments of elevations in levels. The peak occurs during the onset of sleep (85% of daily production) (Murray; HIGHAM; Clayton, 2014). Much of the GH in the circulation is linked to binding proteins such as growth hormone protein (GHBP). Its mechanism of action is linked in to two ways: indirectly by the regulation of growth factor synthesis and directly by binding to specific

membrane receptors using the intracellular signaling cascade (via janus tyrosine kinase 2, JAK 2, and signal transducer and transcription activator, STAT) (Martinelli; Custódio; AGUAR-Oliveira, 2008). The performance of the GH in the human metabolism affects all macronutrients. In relation to carbohydrates, the GH has an opposite effect to that of insulin, increasing the level of circulating glucose by decreasing glucose oxidation and tissue uptake (Ghanaat; Tayek, 2005). As for lipids, the GH increases lipolysis and oxidation of fatty acids in the adipose tissue, skeletal and cardiac musculature, besides the activation of the glycogenolysis hepatic pathway (Oliveria et al., 2011, Silva et al., 2014).

In protein metabolism, the GH is responsible for increasing its synthesis and reducing its degradation. The increased protein synthesis results from an increased release of insulin-growing factor (IGF-1), resulting in an increased muscle hypertrophy when associated with physical activity, increased strength, VO2max, and lean body weight (Casagrande; Czepielewski, 2007). Because it is a hormone mostly produced during sleep, all functions related to it can be affected in patients with insomnia. Nocturnal physical exercises in this case are the most responsible for this disorder. It is not appropriate that such activities be performed close to bedtime due to their relation with an increase in body temperature. For the body to fall asleep, the temperature must be decreased. Changes in blood levels of GH are capable of triggering chronic diseases such as SAH. Arterial disease has been shown to be present by different mechanisms of action and the influence of GH, such as sodium and water regulation, changes in the renin-angiotensin-aldosterone system, changes in atrial natriuretic peptide action and peripheral vascular resistance disorders (Isgaard et al., 2015, Mavinkurve; O'gorman, 2015). The GH acts in conjunction with insulin and other hormone axes. It is important in normal metabolism (CORNFORD, 2011). A reduced GH secretion contributes to a shift towards visceral adiposity, while total insulin growth factor I (IGF- I) levels remain relatively unchanged due to an increased hepatic GH sensitivity. Insulin plays a key role in these changes, also acting on the inhibition of insulin-like growth factor-binding protein 1 (IGFBP-1), representing a high risk factor for the development of DM 2 in the long term.

Conclusion and Suggestions for further studies

The interaction between neural, metabolic and endocrine aspects is relevant to ensure that all functions and mechanisms occur in the homeostatic mode. The organic homeostasis and the body balance are directly influenced by environmental, emotional and genetic factors, what may lead to a high risk of developing metabolic diseases such NCD. One of the main environmental aspects relevant to the development of NCDs is sleep disorders, above all insomnia. It is known that there is a production of hormones during sleep. However, sleep disorders, such as insomnia, cause important changes in the sleep standard, which leads the metabolic maladjustment. In spite of the scientific advance that has already been made regarding insomnia and its relation with the development of important metabolic changes until the occurrence of NCDs, many factors still need to be explained regarding this complex mechanism of neuro-endocrine regulation, emphasizing the increased risk of development of NCDs. These are increasing conditions in recent years. It is emphasized, therefore, that a suitable sleep duration seems to be relevant to the maintenance of a balance in the neuro-endocrine metabolic axis.

Conflicts of interests

The authors declare no conflicts of interests.

Authors' contributions

LABMM: Drafting and conducting the review, writing; primary responsibility for final content.
NCC: conducting the review and writing.
JPTB: Writing.
LSN: Writing.
JCS: Conducting the review; primary responsibility for the final content. 14

REFERENCES

Abdu, T.A. et al. 2001. Endothelial dysfunction in endocrine disease. Trends Endocrinol Metab. 12, p. 257-265.

Abell, J.G. et al. 2016) Recurrent short sleep, chronic insomnia symptoms and salivary cortisol: A 10-year follow-up in the Whitehall II study. Psychoneuroendocrinology 68, p. 91–99.

Adamsson, M., Laike, T. and Morita, T. 2017. Annual variation in daily light exposure and circadian change of melatonin and cortisol concentrations at a northern latitude with large seasonal differences in photoperiod length. Journal of Physiological Anthropology p. 36.

Anvisa (Agência Nacional de Vigilância Sanitária). Melatonina. 2017. Available in: <http://portal.anvisa.gov.br/informacoes-tecnicas13//asset_publisher/FXrpx9qY7FbU/content/melatonina/219201/pop_up?_101_INSTANCE_FXrpx9qY7FbU_viewMode=print&_101_INSTANCE_FXrpx9qY7FbU_languageId=en_US>. Access in: 30 january 2017.

Arbeck, B. et al. 2015. No stress after 24-hour on-call shifts? Journal of Occupational Health 57, p. 438-447.

Barake, M., Klibanski, A. and Tritos, N.A. 2014. Effects of recombinant human growth hormone therapy on bone mineral density in adults with growth hormone deficiency: a meta-analysis. The Journal of Clinical Endocrinology and Metabolism 99, p. 852–860.

Bhattacharya, D., Sen, MK. and Suri, JC. 2013. Epidemiology of insomnia: A review of the Global and Indian scenario. Indian J Sleep Med. 8, p. 100-110.

Boggio, A. et al. 2014. Is thyroid-stimulating hormone within the normal reference range a risk factor for atherosclerosis in women? Intern Emerg Med. 9, p. 51-57.

Bopparaju, S., and Surani, S. 2010. Sleep and Diabetes. International Journal of Endocrinology 1, p. 1-9.

Boullin, P., Ellwood, C. and Ellis, J. 2016. Group vs. Individual Treatment for Acute Insomnia: A Pilot Study Evaluating a ―One-Shot‖ Treatment Strategy. Brain Sciences 7, p. 1-10.

Brasil. Ministério da Saúde. Vigilância de Doenças Crônicas Não Transmissíveis. 2017. Available in: <http://portalsaude.saude.gov.br/index.php/o-ministerio/principal/secretarias/svs/doencas-cronicas-nao-transmissiveis>. Access in: 12 February 2017.

Brenta, G. et al. 2009. Thyroid Acute thyroid hormone withdrawal in athyreotic patients results in a state of insulin resistance. Thyroid. 19, p. 665-9.

Casagrande, A. and Czepielewski, M.A. 2007. Ensaios para a medida de hormônio do crescimento (GH) e IGF-I: aspectos metodológicos e suas implicações no diagnóstico e seguimento da acromegalia. Arq Bras Endocrinol Metab. 51, p. 511-519.

Chan, M.C. et al. 2012. Circadian rhythms: from basic mechanisms to the intensive care unit. Crit Care Med. 40, p. 246–253.

Cheng, H., Chiang, C. and Chen, C. 2015. The Novelty of the 2015 Guidelines of the Taiwan Society of Cardiology and the Taiwan Hypertension Society for the Management of Hypertension. Pulse 3, p. 29-34.

Cipolla-Neto, J. et al. 2014. Melatonin, energy metabolism, and obesity: a review. J Pineal Res. 56, p. 371–381.

Cornford, A.S., Barkan, A.L. and Horowitz, J.F. 2011. Rapid suppression of growth hormone concentration by overeating: Potential mediation by hyperinsulinemia. J Clin Endocrinol Metab. 96, p. 824–830.

Costa, C.V.M. and Mousovich-Neto, F. 2016. Chronic Stress: Glucocorticoids and Metabolic Disturbances. Journal of Clinical and Molecular Endocrinology 1, p. 34.

Eckel, K.M., Corsi, P.S. 2013. Metabolism and the Circadian Clock Converge. Physiological Reviews 93, p. 107-135.

Ekmekcioglu, C. 2006. Melatonin receptors in humans: biological role and clinical relevance. Biomedicine and Pharmacotherapy 60, p. 97-108.

Fu, L. and Lee, CC. 2003. The circadian clock: pacemaker and tumor suppressor. Nature Reviews Cancer 3, p. 350–361.

Gandhi, A.V. et al. 2015. Melatonin is required for the circadian regulation of sleep. Neuron 85, p. 1193-1199.

Garbarino, S. et al. 2016. Corrigendum to "Screening, Diagnosis, and Management of Obstructive Sleep Apnea in Dangerous-Goods Truck Drivers: To Be Aware or Not?" Sleep Med 39, p. 1211-1218.

Ghanaat, F. and Tayek, JA. 2005. Growth hormone administration increases glucose production by preventing the expected decrease in glycogenolys is seen with fasting in healthy volunteers. Metab Clin Exp. 54, p. 604- 609.

Hafner, R.P. et al. 1988. Altered relationship between proton motive force and respiration rate in non-phosphorylating liver mitochondria isolated from rats of different thyroid hormone status. *Eur J Biochem.* 178, p. 511–518.

Hardeland, R. 2012. Melatonin in Aging and Disease — Multiple Consequences of Reduced Secretion, Options and Limits of Treatment. Aging and Disease 3, p. 194-225.

Harper, M.E., and Seifert, E.L. 2008. Thyroid hormone effects on mitochondrial energetics. Thyroid. 18, p. 145–156.

Hastings, M.H. and Herzog, E.D. 2004. Clock Genes, Oscillators, and Cellular Networks in the Suprachiasmatic Nuclei. *J Biol Rhythms* 19, p. 400–413.

Hershman, J.M. 1974. Clinical application of thyrotropin-releasing hormone. *N Engl J Med*. 290, p. 886–890.

Iacoponi, E. 1999. Classificação de Transtornos Mentais e de Comportamento da CID-10 - Diretrizes Diagnósticas e de Tratamento para Transtornos Mentais em Cuidados Primários. *Rev Bras Psiquiatr.* 21, p. 132.

Isgaard, J. et al. 2015. GH and the cardiovascular system: an update on a topic at heart. Endocrine. 48, p. 25-35.

Jansson-Fröjmark, M. and Norell-Clarke, A. 2016. Cognitive Behavioral Therapy for Insomnia in Psychiatric Disorders. Current Sleep Medicine Reports 2, p. 233-240.

Kaczor, M. and Skalski, M. 2016. Prevalence and consequences of insomnia in pediatric population. Psychiatr Pol. 50, p. 555-569.

Kohsaka, A. and Bass, J. 2007. A sense of time: how molecular clocks organize metabolism. *Trends Endocrinol Metab.* 18, p. 4-11.

Langroudi, M.G. et al. 2010. Regulation of thyrotropin-releasing hormone-expressing neurons in paraventricular nucleus of the hypothalamus by signals of adiposity. Mol Endocrinol. 24, p. 2366–2381.

Martinelli, C.E., Custódio, R.J. and Aguiar-Oliveira, M.H. 2008. Fisiologia do eixo GH-Sistema IGF. Revista brasileira de endocrinologia e metabólica 52.

Mavinkurve, M. and O'gorman, C.S. 2015. Cardiometabolic and vascular risks in young and adolescent girls with Turner syndrome. BBA Clinical 3, p. 304-309.

Meng, L., Zheng, Y. and Hui, R. 2013. The relationship of sleep duration and insomnia to risk of hypertension incidence: a meta-analysis of prospective cohort studies. Hypertension Research 36, p. 985–995.

Morgan, D. and Tsai, S.C. 2016. Sleep and the Endocrine System. Sleep Med Clin. 11, p. 115–126.

Morin, C.M. and Jarrin, D.C. 2013. Epidemiology of Insomnia. Sleep Medicine Clinics 8, p. 281-297.

Murray, P.G., Higham, C.E. and Clayton, P.E. 2014. 60 Years of Neuroendocrinology: Celebrating the brain's other output-input system and the monograph that defined neuroendocrinology. *J Endocrinol.* 226, E3-6.

Nakahata, Y. et al. 2008. The NAD+-dependent deacetylase SIRT1 modulates CLOCK-mediated chromatin remodeling and circadian control. Cell 134, p.329–340.

Nakahata, Y. et al. 2009. Circadian control of the NAD+ salvage pathway by CLOCK- SIRT1. Science May 1, p.654-7.

Oliveira, C.R.P. et al. 2011. Papel emergente do eixo GH/IGF-I no controle cardiometabólico. Arq Bras Cardiol. 97, p. 434-439.

Pasqualetti, G. et al. 2013. Is subclinical hypothyroidism a cardiovascular risk factor in the elderly? J Clin Endocrinol Metab. 98, p. 2256-2266.

Pittendrigh, C.S. and Daan, S. 1976. Functional Analysis of Circadian Pacemakers in Nocturnal Rodents IV: Entrainment: Pacemaker as Clock. *J Comp Physiol.* 106, p. 291– 331.

Poyares, D. et al. 2005. Hipnoindutores e insônia. Revista Brasileira de Psiquiatria 27,p. 2-7.

Qaseem, A. et al. 2016. Management of Chronic Insomnia Disorder in Adults: A Clinical Practice Guideline from the American College of Physicians. Annals of Internal Medicine 165, p. 125-133.

Rogers, P.J., Ferriday, D. and Jebb, S.A. 2016. Connecting biology with psychology to makesense of appetite control. Nutrition Bulletin 41, p. 344-352.

Sabanayagam, C. and Shankar, A. 2012. Sleep duration and hypercholesterolemia: Results from the National Health Interview Survey 2008. Sleep Med. 13, p. 145-50.

Schroeder, AC., and Privalsky, M. 2014. Thyroid Hormones, T3 and T4, in the Brain. Frontiers in Endocrinology 5, p. 40.

Silva, A.J. et al. 2014. Estudo do comportamento cortisol, GH e insulina após uma sessão de exercício resistido agudo. Revista Brasileira de Medicina do Esporte 20, p. 21-25.

Singh, Y., Kotwal, N. and Menon, A.S. 2011. Endocrine hypertension - Cushing's syndrome. Indian Journal of endocrinology and metabolism 15, p. 313-316.

Sofi, F. et al. 2014. Insomnia and risk of cardiovascular disease: a meta-analysis. European Journal of Preventive Cardiology 21, p. 57.

Souza, J.C. and Camargo, D.A. 2016. Psicofarmacologia e equipe multidisciplinar. 4 ed. Campo Grande: UCDB (Universidade Católica Dom Bosco).

Souza, J.C. and Carvalho, A.B. 2015. Sono e qualidade de vida. 2 ed. São Paulo: Segmento Farma.

Tagami, T. et al. 2010. Lipid profiles in the un-treated patients with Hashimoto thyroiditis and the effects of thyroxin treatment on subclinical hypothyroidism with Hashimotothyroiditis. Endocr J. 57, p. 253-258.

Tamura, C.A. and Kruger, E.L. 2016. Estudo piloto em câmara climática: efeito da luz natural em aspectos de saúde e bem-estar não relacionados à visão. Ambiente Construido 16, p. 149-168.

Tan, X. et al. 2016. Effect of Six-Month Diet Intervention on Sleep among Overweight and Obese Men with Chronic Insomnia Symptoms: A Randomized Controlled Trial. Nutrients 8, p. 751.

Turek, F.W. and Van Cauter, E. 1994. Rhythms in Reproduction. In: The Physiolog of Reproduction (Ed. KNOBIL E., and NEILL JD), p. 487–540, Raven.

Vale, R. et al. 2017. Cortisol and Physical Exercise. Available in: https://www.researchgate.net/publication/228160384_Cortisol_and_physical_exercise. Access in: 30 June 2017.

Van Raalte, D.H., Ouwens, D.M. and Diamant, M. 2009. Novel insights into glucocorticoid-mediated diabetogenic effects: towards expansion of therapeutic options? *Eur J Clin Invest.* 39, p. 81-93.

Viot-Blanc, V. 2015. Durée de sommeil et métabolisme. Revue des Maladies Respiratoires 32, p. 1047—1058.

Voigt, R.M. et al. 2014. Circadian Disorganization Alters Intestinal Microbiota. Plos One 9, e97500.

Wang, C. 2013. The Relationship between Type 2 Diabetes Mellitus and Related Thyroid Diseases. Journal of Diabetes Research 2013, p. 390534.

Wilson, S.J. et al. 2010. British Association for Psychopharmacology consensus statement on evidence-based treatment of insomnia, parasomnias and circadian rhythm disorders. Journal of Psychopharmacology 24, p. 1577-1601.

Yeh, C.M. 2015. The Basal NPO *crh* Fluctuation is Sustained Under Compromised Glucocorticoid Signaling in Diurnal *Zebrafish*. Frontiers in Neuroscience 9, p. 1-8.

Zee, P.C., Attarian, H. and Videnovic, A. Circadian Rhythm Abnormalities. Continuum: Lifelong Learning in Neurology, Ovid Technologies. Wolters Kluwer Health 19, 132- 147, 2013.

Zitouni, M., Pevet, P. and Masson-Pevet, M. 1996. Brain and pituitary melatonin receptors in male rat during post-natal and pubertal development and the effect of pinealectomy and testosterone manipulation. *J Neuroendocrinol* 8, p. 571-577.

****