CERTIFICACIÓ

'Certifico que aquest és el meu treball I que no ha estat presentat prèviament a cap altra institució educacional. Reconec que els drets que se'n desprenen pertanyen a la Fundació Escola d'Osteopatia de Barcelona'

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Osteopathy in Insomnia

A review of the literature of; diagnosis and treatment of insomnia, the processes involved in the sleep mechanism and the intervention of CV4 as a treatment option

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ABSTRACT

This paper reviews the literature of insomnia diagnosis and treatment, sleep mechanisms and their alteration in insomnia and the intervention of CV4 as a treatment option.

Insomnia is a common complaint amongst the general population and is on the increase. It has a tendency to chronicity and leads to impaired life quality. It contributes to elevated costs in terms of health care, accidents and absenteeism. Recent literature supports the evidence linking insomnia to more serious pathologies such as depression, obesity and heart failure.

Diagnosis has been hindered by a lack of universally standardized diagnostic tools and a high incidence of self treatment of those with insomnia. The former is being addressed with the implementation of universally accepted sleep questionnaires and regulation in its definition.

Treatment for insomnia is far from satisfactory; being effective only in the short term, or causing side-effects, or necessitating costly training and implementation and are largely unsupported by evidence of effectivity. Currently, pharmalogical treatment is recommended in conjunction with Cognitive Behavioural Therapy (CBT). Self-prescription is common in people suffering from insomnia and includes non-prescription (OTC) supplements, mind-body relaxation techniques and alcohol. The lack of effective, and possibly, damaging treatment for insomnia is what brings about this proposal for an alternative approach to the treatment of insomnia; namely Osteopathy and within this; the compression of the fourth ventricle (CV4).

Sleep involves homeostatically controlled biobehavioural mechanisms and circadian rhythms. Insomnia sees a breakdown in these systems. The intervention of CV4 proposes to address these alterations and instill a return to a norm.

There is little available literature on the intervention of osteopathy and CV4 as a treatment option in insomnia and is currently not included in other reviews of insomnia management. However, the literature reviewed shows autonomic response to CV4 treatment and a pilot study shows it to improve sleep latency.

The paper concludes that there is a scientifically valid basis supporting the use of CV4 and that it warrants further clinical trials. Further research is imperative as to the viability of the CV4, particularly as it is so significant for national productivity and for the safety of individuals. Given the public interest in sleep it is recommended that osteopaths are proactive in publicizing what they can to do help.

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ABBREVIATIONS USED

nBZD	non-Benzodiazepines
BZD	Benzodiazepines
CBT	Cognitive Behavioural Treatment
OTC	Over the Counter
CV4	Compression of the 4th Ventricle
HPA	Hypothalamus - Pituitary- Adrenal
TOL	Total Osteopathic Lesion
DSM-IV	Diagnostic and Statistical Manual IV
ISD-10	International Sleep Disorders
CAM	Complementary and Alternative Medicine
CHF	Congestive Heart Failure
HBP	High Blood Pressure
VLPO	Ventrolateral Preoptic Nucleus
TMN	Tuberomammillary Nucleus
LC	Locus Coeruleus
GAS	General Adaptive Syndrome
DRN	Dorsal Raphe Nuclei
REM	Rapid Eye Movement
NREM	Non rapid eye movement
ACTH	Adrenocorticotropic Hormone
CRI	Cranial Rhythm Impulse
PAG	Periaqueductal Gray Tissue
CNS	Central Nervous System
GABA	Gamma-aminobutryric Acid
MSNA	Muscle Sympathetic Nerve Activity
SHT	Spinohypothalmic tract

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1. INTRODUCTION

1.1 INTRODUCTION TO THE STUDY

INSOMNIA is usually defined as "difficulty falling or staying asleep or a sensation of unrefreshing sleep."[(1)]."Almost half of all people in the US report sleep-related problems. Disordered sleep can cause emotional disturbance, memory difficulty, poor motor skills, decreased work efficiency, and increased risk of traffic accidents. It can even contribute to cardiovascular disorders and mortality."[(1)] It is also a drain on resources with between $92.5 and $107.5 billion a year spent[(35)]both in health care and absenteeism.

However, treatment for it is far from satisfactory[(2)]; a common form of treatment is pharmacological, majorly of the group non-benzodiazepines(nBZD); effective in the short term, but less effective in the long term, and causing unwanted effects in sleep architecture.[(5,p44)] Other treatments are; Cognitive Behavioural Therapy (CBT),non-prescription (OTC) supplements (i.e. melatonin) and mind-body relaxation techniques. The lack of effective, and possibly, damaging treatment for insomnia is what brings about this proposal for an alternative approach to the treatment of insomnia; namely Osteopathy and within this; the compression of the fourth ventricle (CV4).

Sleep is a biobehavioural mechanism involving homeostatic mechanisms of the hypothalamus-pituiatary-adrenal (HPA) axis, the central nervous system (CNS) and circadian rhythms. Imbalances of these are adjustments are seen in insomnia. [(5, 55)] Osteopathic treatment aims to restore normal function of systems by removing the barriers to the body's ability to optimize its function. [(3 p1225)] It is proposed that "manipulation may intervene in homeostasis and affect mechanisms of auto-curation inherent in the body." and further that "manual techniques applied to the body affect the body's physiology". [(32)]

As stated in the Foundations for Osteopathic Medicine [(3 p242)]; "The therapeutic goal in insomnia should be to decrease the overall level of physiologic and emotional arousal, and not just to improve the nighttime sleep." Furthermore, that for a treatment to be successful "an understanding of the biophyscosocial factors that led to that state" is required. [(3 p243)]

This study proposes to show how CV4 treatment and osteopathy can be a valid and effective option in the treatment of insomnia. This will be done through a review of the literature of; sleep and the physiological mechanisms involved, the definition of insomnia, its pathology and current treatment, and the proposed functioning of cranial osteopathy. Insomnia is also reviewed in the broader context of systems breakdown and implicit consequences of this. It serves as a preface to and rationale for engaging in further primary research and investigative osteopathic studies.

1.2 SOURCES

Material was primarily sourced through Medline, JAOA and Science Direct using key words; *insomnia, sleep disorders, cranial osteopathy and CV4*. Material accessed was restricted to more recent sources; as ongoing research on insomnia is constantly bringing new information as to its underlying pathology, and also its very definition.

Pertinent to this paper is the definition of insomnia, its diagnosis, as well as its treatment. Comments from the latest research group for the Diagnostic and Statistical Manual V (DSMV) [(4)] are included, including proposed changes.

Basic text books of osteopathic medicine and sleep manuals were consulted.

This paper has drawn from all areas of the aetiology of insomnia: socioeconomic, psychosocial, anatomical, and physiological, in order to highlight the multitude of systems involved and give a complete picture of the pathology. This lack of cohesion, lack of overlapping in the literature and fields of investigation, and the wide spectrum of treatments available for the treatment are all perhaps indicative of, or perhaps the contributing factors to, its "undertreatment and mistreatment" [(2)]. We have a situation where only one axis of the pathology is being addressed at one time, having been classified and sub classified into the disciplines of endocrinology, neurology, psychiatry, etc. Here is an opportunity to draw together all these perspectives and analyze the pathology of insomnia under an osteopathic model and see where its intervention may be of use.

When sourcing data through Medline and others sources using the above mentioned words; what became immediately apparent was the dichotomy between the paucity of data found on insomnia and osteopathy and the claim of one of the most recently published books on sleep and sleep related problems which states that "sleep in relation to the functions of the nervous system is one of the topics of most interest to the general public [5, p1].

Furthermore, what became even more apparent was the lack of inclusion of Osteopathy as treatment option. In 4 recent exhaustive studies [7,2,9,16] which reviewed the literature on insomnia and its treatment all fail to consider Osteopathy as a treatment option. This paper intends to fill this deficit reviewing the evidence available.

1.3 RELEVANCE OF THE STUDY

To understand the relevance of the treatment proposed, we need to understand the basis of Osteopathic principles and how the major sciences are incorporated within. AJ Cathie [41] stated that osteopathic principles are "the scientific application of basic sciences in the study and care of man."

Insomnia, as we shall see, involves a breakdown of biobehavioural mechanisms involving; neurological, endocrine, physiological and behavioural systems. It seems relevant therefore to apply a treatment coming from the osteopathic armamentarium. Osteopathy and specifically the CV4 treatment address these alterations through manual adjustment and effect a change in these systems or stimulate the body's inherent capacity to self curation. The treatment studied, the CV4, is believed to work by affecting fluid dynamics and effecting a change toward normal functioning of the body. [23]

Insomnia is worthy of study as it is hugely prevalent among the general population, [1, 2, 7, 9] and is on the increase [49, 50]. It is largely under diagnosed and when diagnosed, inadequately treated. [7, 9, 11] It is a drain on state resources both in hospital care and absenteeism. [11, 2] Recent literature links it to more serious pathologies such as obesity, heart failure, depression and HPA. [5, 16, 43] It is an area which is recognized as being

under-researched both in the public domain as in medical fields. Finally, as mentioned above, there is a paucity of informed literature concerning osteopathy as a treatment option for insomnia.

The review of sleep and its regulation has been included as a necessary component to understand the workings of the treatment proposed.

2 INSOMNIA

2.1 DEFINITION OF INSOMNIA

The diagnostic criteria used are from the DSM –IV[21] and International Sleep Disorders-10 (ICD-10) [22] with additional comments from the most recent Sleep Wake Disorders Work Group Project.[4] Their comments indicate a move towards a multisystem approach in diagnosis; among other things the work group suggest integrating categorical and dimensional measures.

Diagnostic Criteria for 307.42 Primary Insomnia [21]

A. The predominant complaint is difficulty initiating or maintaining sleep, or nonrestorative sleep, for at least one month
B. The sleep disturbance (or associated daytime fatigue) causes clinically significant distress or impairment in social, occupational or other important areas of functioning
C. The sleep disturbance does not occur exclusively during the course of Narcolepsy, Breathing-Related Sleep Disorder, Circadian Rhythm Sleep Disorder, or a Parasomnia.
D. The disorder does not occur exclusively during the course of another mental disorder (e.g. Major Depressive Order, Generalized Anxiety Disorder, a delirium.)
E. The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

Other sub groups of insomnia have been left aside. (see DSMIV) [21] However this is not to say that the treatment proposed in this paper would not be relevant or effective for these pathologies. They are not included because these subgroups maybe related/co morbid with other pathologies, and it would be difficult to extrapolate the affects of these on the insomnia from that of the CV4 treatment.

A development in the diagnostic process has been the renaming of secondary insomnia to comorbid insomnia. This came about because the causal link between the associated condition and insomnia is not always clear “or whether insomnia is the

primary or secondary condition in such a relationship". [13, 2] A complex relationship exists and " in some cases, insomnia and other sleep disorders may exacerbate or even be part of the cause of the comorbid condition". [13]

The work group acknowledges that little scientific progress has been made since DSM-IV but state that scientifically valid and clinically useful measures of impairment have been identified which "convey accurately the severity, impairment, and distress occasioned by disturbed sleep and wakefulness". These physiological responses are what are measured in polysomnographic sleep monitoring, but are, as yet, not included in the clinical diagnostic criteria. The work group however insists that "the science of sleep disorders makes the revisiting of this issue mandatory."[4]

The use of physiological parameters could be useful in differential diagnosis. One could discriminate those with insomnia from those who are suffering from stress, sleep deprivation, or other disorders. A controlled study undertaken by AN Vgontzas et al 2001 [6] indicates a clear relationship between cortisol levels and chronic insomniacs. They note that "the pathophysiology of chronic insomnia is most likely different from that of sleep loss" and that of perceived stress.

While the inclusion of more parameters is welcomed, particularly the recognition of an alteration to a homeostatic system, there is always the danger that if the parameters are reduced to quantifiable amounts they will then become standardized leading to normal and abnormal measurements. Sleep is not a static entity and healthy variables exist among and between the different age groups. [2, 9]

Researching the literature shows contradictions in definitions of insomnia. It is this lack of cohesion which may be leading to poor diagnosis and misconceived ideas of what insomnia is by patients and physicians alike. In the highly respected manual of medicine Merck [1] we find the following statement: "Insomnia … (are) not disorders themselves but are symptoms of various sleeprelated disorders". Yet in ICD-II and DSMIV, concurrently, we have many groups and sub groups of insomnia; *with primary insomnia standing alone as a pathology in its own right.*

2.2 PREDISPOSING, PRECIPITATING AND PERPTUATING FACTORS OF INSOMNIA AND DEREGULATION OF SYSTEMS

Over 75% of patients with insomnia associate its onset with a stressful life event [13] There is evidence that insomniacs have a tendency to internalize emotions in the face of stress events [13]. "This results in a combination of emotional arousal and physiological activation "and "leads to a vicious circle that perpetuates insomnia" [13] In the late 80's a model was proposed by Speilman [9], describing the predisposing, precipitating and perpetuating factors.

- Predisposing factors included a genetic influence on genes controlling circadian rhythms. There are neurobiological factors which include; increased body temperature, higher secretion levels of cortisol, adrenaline and ACTH. These individuals also have higher response levels to stress.[9]
- Precipitating factors involve any or all of the following; changes in sleep wake schedule, depression, anxiety, medications, other sleep disorders, and medical conditions. In addition, positive or negative family, work-related, and health events are common insomnia precipitants.
- Finally, perpetuating factors involve cognitive and behavioural mechanisms; bad sleep hygiene, day time naps, worrying about the consequences, use of alcohol or other stimulants.[9]

The consequences of the chronic deregulation of the stress system have been long recognized since the introduction of Hans Sayle`s model in the Stress of Life. [25] Briefly this model describes three stages:

A healthy physiological response to an external stressor results in physiological changes in the body. Once the stressor is eliminated the body returns to its original state; this being a function of the HPA axis.[51,55,32]

A second stage occurs in the face of continued stress, known as the general adaption syndrome (GAS).The body adapts and functions well within this adaptation. This stage is reversible. Dysfunction will occur when this persistence passes its point of usefulness. [18] It is at this stage that we propose the intervention of the CV4

treatment in an attempt to break the cycle or unhealthy adaptation. The very mechanisms which can be life saving in a danger situation can become noxious to the body in the long term as chronic stimulation of the sympathetic system will lead to suppression of immune function and defence systems. [17, 54]

This brings us to a third final stage "fatigue" whereby the adaptations and compensations fail, leading to a breakdown of systems and ultimately death.

This model explains well the dysfunction of insomnia and its chronic progression; leading to, as evidenced [2, 5], breakdown of systems and further pathology. [6]

2.3 PATHOPHYSIOLOGY OF INSOMNIA

Chronic insomnia shows increased physiological action; seen in increased body temperature, heart rate, whole metabolic rate, increased blood pressure, heart rate and cardiac output, skeletal blood flow, vasoconstriction in the kidneys, splanchnic and skin vasculature. High levels of norepinephrine, cortisol and serotonin are found. [6, 51]

The normal functioning of the sleep process has been disrupted and its course is chronic [63]. One study showed that of those who reported severe insomnia to still have moderate or severe insomnia 2 years later. [11, 62]

Both limbs of the stress system are activated leading to a significant deregulation. [13]

This activity of the stress systems relates positively to the degree of objective sleep disturbance. [13] Good restful sleep would be associated with low cortisol plasma level and low cytokine levels. [13]

2.4 PSYCHOSOCIAL ASPECTS OF INSOMNIA

Those with insomnia have a diminished quality of life [64, 9, 12]. One of the diagnostic features is a disruption of social or labour relationships. Prevalence is higher in those widowed, unemployed or of low socioeconomic status. [11] It is often the case that the patient has endured years of complaint before seeking treatment, even while the burden is shown to be equal to that of many psychiatric disorders. [12]

2.5 PREVALANCE OF INSOMNIA

"Insomnia is, by far, the most commonly encountered sleep disorder in medical practise". [6, 11] Yet despite the high prevalence, only 5% of persons with chronic insomnia visit their physician specifically to discuss their insomnia. Only 26% discuss their insomnia during a visit made for another problem. [9, 2]

Prevalence has always varied in the existing literature. The World Health Organization study, America Sleep Poll 2005 and many more put incidence at between 10% to 40% of the population.[2,6,7 ,9,11,12]This variance is due to difficulties in diagnosis due to non-standardized protocol[64] .The introduction of the use of standardized international sleep questionnaires has addressed this problem and facilitated diagnosis, leading to more reliable figures [64]. As did the introduction of a defined working definition of the pathology (see DSMIV [21] and ISDII [22]). The better defined a pathology the more effective the treatment [64]

Furthermore, "the majority of individuals who have trouble sleeping attempt to treat the problem independently using over-the-counter medications or alcohol [11, 13] hence do not appear in the statistics.

2.6 COST OF INSOMNIA

Cost to the state comes in health care, absenteeism and accidents; as shown by the following statistics. Health care expenditure is approximately 60% higher among patients with insomnia and was shown to be $13.96 billion in the US in 1995 [11], in direct costs (2 million of this going towards sleep promoting agents); another report states $100 billion. [35] There is double the number of hospitalizations in insomnia sufferers. [9,16] Falling asleep while driving is responsible for at least 100,000 crashes, 40,000 injuries, and 1550 deaths per year.[26] And reports show that insomniacs are 2.5 to 4.5 times more likely to have an accident." [11] Domestic accidents are also a concern as a secondary effect of hypnotics taken by the elderly.

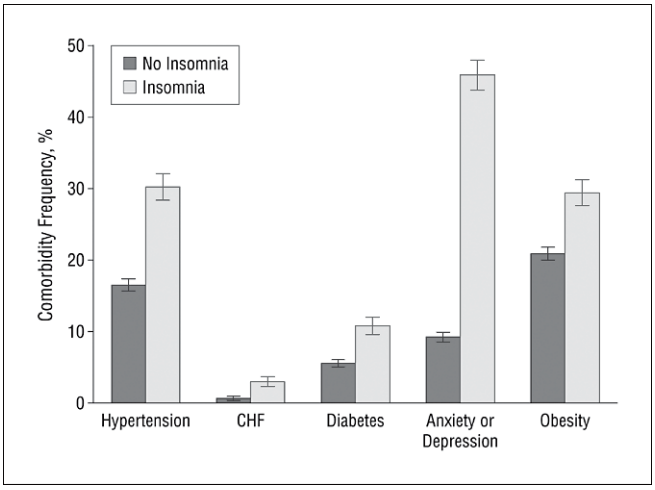
[12]Another source of cost is in absenteeism which is ten times greater. [9] Lost productivity as a result per year amounting to nearly $50 billion. [50] Cost in terms of functional impairment appears as great as that due to many other psychiatric and general medical disorders [12].

2.7 EVIDENCE LINKS INSOMNIA TO OTHER PATHOLOGIES

There is also growing evidence that shows alterations of sleep patterns contributing to the development of disease and psychiatric disorders [11, 6, 48] and that significant alteration leads to mortality. [3] It is suggested in Life Extension [14] that insomnia promotes "a constant state of low grade inflammation that may accelerate many diseases of aging".

It has a strong positive correlation to the following conditions; Depression, Hypertension, Congestive Heart failure (CHF), Diabetes and Obesity. [13, 10, 9, 3]

These correlations are illustrated in the figure below [9]:



Insomnia or trouble sleeping and comorbidity status. Results are expressed as prevalence rates with 99% confidence interval bars. [9]

Subsequently, those people who do not view insomnia as a disease, and rather as an innocuous problem and who self medicate (see 2.2.5) are those who are not

diagnosed or misdiagnosed, [11] are putting themselves at a risk of all the consequences of sleep time loss; cognitive dysfunction, accidents, absenteeism at work as well as the more serious problems and pathologies linked with chronic insomnia; obesity, HPA, depression and heart failure. [15]

This raises an important question as to whether insomnia is a "marker" for potential future pathologies and whether an early effective treatment of insomnia would decrease the risk of possible future pathologies. A part of the diagnostic process is to determine whether the insomnia presenting is due to pathology or is causing pathology. It is now generally accepted that when pathology and insomnia present together, treatment of the insomnia will positively affect the other pathology.[2] This is an area which warrants further research both to better understand the pathology of insomnia and to justify treatment of insomnia in a preventative role.

2.8 CLINICAL PRESENTATION OF INSOMNIA

Insomnia leads to a lack of sleep and the clinical symptoms presented by the patient are the results of this. We have a chronic activation or deregulation of the stress system. [13] This is associated with poor mental and physical health; decreased feelings of well being, mood alteration, a decrease in energy, concentration and attention, and a decrease in quality of life. [11, 12, 21] These increases with the severity of the insomnia [11]

Signs and symptoms include an increase in the prevalence of the following [64, 12, 11, 16]:

- psychosomatic type illnesses showing non specific physical symptoms; non specific pain ,muscle , neck and back pain, tiredness and weakness,
- poor daily functioning, poor concentration, depression and anxiety
- allergy, colitis, asthma, elevated blood pressure, migraine headaches, ulcers, headache, diarrhoea, constipation, stomach discomfort, palpitations shortness of breath.

Insomnia affects men and women, the latter group showing higher incidence. [9] The elderly are the group who most suffer from insomnia. [2, 5, 7] However figures released this year show a disconcerting change in this trend. The use of sleep aids has tripled among young adults (from 1998-2006) and also the average length of use is up by almost 40% (from 64 days to 93 days). [49, 50] This trend relegates the long held idea that sleep disruption in the elderly was a natural consequence of the aging process and gives credence to the idea that it is a consequence of chronic systems breakdown. (See 2.5)

2.9 DIAGNOSIS

The criteria mentioned earlier must be met. (See 2.1) One of the most effective methods of analysis is through clinical interviews. [64] This involves questioning on all aspects of the patients life; medication, ambient factors, background, differential diagnosis from other pathologies, details of the sleep problem, onset latency, awakenings etc. This interview is important as there is often a variance between the subjective reporting of a sleep disorder and objective measurements. [64, 2] The heterogeneity of the problem necessitates that diagnosis should not be based on a global evaluation but a detailed miniscule evaluation. [64].

The introduction of standardized, easy to use sleep questionnaires has aided diagnosis. [64] However diagnosis is still hindered by a common misunderstanding as to what insomnia is and a tendency to relegate it to "obsessions" of otherwise healthy individuals [10]. In general, both patients and physicians find the treatment challenging, unsatisfactory, and frustrating [2,6] Although it is often assumed to be secondary to another pathology it has been shown that half of insomnia diagnoses were not related to a primary psychiatric disorder. [12]

All this is compounded by a lack of training in medical schools on sleep pathology in such areas as its health impact or quality of life. [9] Healthcare workers recognize their knowledge only as "fair" and also lack awareness of sleep protocols and benefits and dangers of treatments on offer. [9] Clinical reality shows that "less than 50% of physicians ask patients about their sleep patterns because of a perceived lack of effective treatments and easy-to-use diagnostic tools". [16] "Only a small

percentage of those who experience insomnia symptoms receive adequate evaluation and treatment" [16] and we are talking about a total of 1,6 million in the US alone.[16], and 50-70 million with sleep disorders[50]. Insomnia is undertreated by heath care providers, despite its serious consequences" [11, 6]

2.10 CURRENT TREATMENT OPTIONS

New evidence concerning the aetiology [51-55], definition [4] and treatment of insomnia [16] is bringing about a change on treatment perspective. It is now indicated that any treatment of insomnia should be involved with a sleep hygiene programme. [2] The use of hypnotics is more effective when combined with CBT programmes. [44]Stress management measures are routinely recommended as part of treatment, [13] and osteopathic manipulative treatment has been recommended as part of this. [29]

There is amplitude of treatment options available; hypnotics, antidepressants, melatonin, relaxation techniques, alcohol, and many OTC products including herbal preparations. Of these, research shows that "alcohol and OTC aids are more widely used by troubled sleepers than prescription medications" [11]

What follows are brief resumes of some of the treatment options, more details can be found in the literature cited in the bibliography [9, 16, 46]:

2.10.1 HYPNOTICS

These are a group of pharmacos that induce sleep. The group non-Benzodiazepines (nBZD) and BZD work via GABAa receptors and inhibit arousal pathways, thus enhancing sleep. [9] They are also believed to initiate thermoregulatory controls in the body. Their properties and actions involve; anti-anxiety, sedation, hypnotic, muscle relaxant and anticonvulsant. [5,p43]

The groups have varying properties, functioning with short term or long term action and are prescribed appropriately to the patient's symptoms depending whether they have problems with sleep latency or night time awakenings. [5,p43]

The ideal hypnotic would have "quick onset, sustained action throughout the night, not alter normal sleep architecture nor have residual effects the next day". [5,p43] The most promising shows to be antagonists to the orexina receptors: Orexinas are neuropeptides produced in the lateral and posterior parts of the hypothalamus. So far they have been proven to have few side effects and do not affect sleep architecture. [5, p48)

The drawbacks in long term use of hypnotics are loss of effectiveness, tolerance, and changes in sleep architecture. They are associated with significant risk of accident and injury, have side effects, and at times are no more effective than placebos. [16, 11, 12)

It is generally agreed that they are effective in short term acute insomnia but that they are less adequate in long term chronic insomnia [9, 16].Furthermore, clinical trials for most hypnotics last an average of ten days [44]. Unfortunately, currently, the highest incidence of insomnia sufferers is the elderly, who have chronic insomnia. [9, 11)

2.10.2 ANTIDEPRESSANTS

Some drugs used in depression have been shown to be useful in the treatment of insomnia, for example trazodona, mirtazapina which have sedatory effects. [5)

Insomnia and depression are intimately related. It is thought that chronic hypercortisol secretions and chronic unrelieved stress (as seen in insomnia) will lead to depression.[11] The drugs are believed to suppress a hyper stimulated HPA axis and favour regulation of insomnia. [6]

2.10.3 COGNITIVE BEHAVIOURAL THERAPY (CBT)

The CBT approach and stress management techniques go a long way to addressing the factors of perpetuating insomnia; poor sleep habits, inadequate sleep hygiene, hyper arousal, irregular schedules and handling external conflict [8, 13] and cognitive processes which contribute to maintenance of insomnia [16]

The optimal dosing has been stated as 4 biweekly individual treatments. [2]

In spoken testimonies patients who received CBT treatment over a period of 8 weeks recognized a subjective feeling of well- being and improved sleep patterns. [63] It has

been shown to improve SWS in trials. [2] The course and sequence of treatment is important. [16]

While CBT is most effective for primary insomnia, it can also be effective for comorbid insomnia as adjunctive therapy. It has shown to be effective in patients with chronic insomnia, and is an effective intervention in late life insomnia ([63] A Norwegian study that found CBT was better at treating long-term insomnia than the sleep medication zopiclone. [28]

A limitation of CBT is the time and training required for the specialists. [12] One manner of offsetting the expense involved in CBT are programmes available on-line; and preliminary evidence has shown the benefits of written material. [2, 43]

2.10.4 MELATONIN

Melatonin is a popular non prescription remedy for many insomnia sufferers and is thought to improve sleep latency. [7] It has the advantage over some pharmacological intervention in that it has no side effects and does not affect sleep architecture. A drawback is that Melatonin has a very short time life, and would therefore only be effective in insomniac patients with sleep onset problems. A synthetic form of Melatonin has been produced (Ramelton) which has a longer life and would therefore be more effective in awake after sleep onset problems. [7, 9]

Supporting evidence from controlled trials is conflictive as to its effectiveness. [5 p43, 16] However it is recommended as an alternative to pharmacological intervention, "in patients who have an increased fall risk and in patients with a history of substance abuse." [2]

2.10.5 OVER THE COUNTER (OTC)

A large study [7] came to the conclusion that despite lack of efficacy data OTC sleep aids are growing in popularity. This indicates "the propensity for patients to self medicate and the level of patient satisfaction with the performance of these agents". [16] OTC and alcohol use are more prevalent than the use of prescription medicine in the treatment of insomnia. [16]

The abundance of OTC remedies used and on offer is perhaps indicative of the fact people do not consider insomnia to be of sufficient worth to go to a doctor (or perhaps do not believe in the drugs offered). The huge variety of treatment on offer may also indicate a lack of true understanding of what insomnia is.

A negative aspect of these sleep aids is that their " widespread availability, perceived safety, and low cost " leads to " encouraging experimentation and potentially delaying medical treatment and effective treatment." [16] Thus exposing people to the risks mentioned earlier. (See 2.7)

3 SLEEP

3.1 WHY WE SLEEP?

Sleep is a biobehavioural mechanism[3 p1203] understood to be necessary for our physical and mental well being, a necessary "anti-stress" mechanism that allows us to maintain a homeostasis or equilibrium, and a mechanism which is necessary for our survival, the actual workings in the organism are little understood. [5 p4, 13, 20] This indicating, perhaps, why treatment outcome is relatively poor. "The more we know about these mechanisms the better we are able to treat sleep dysfunctions" [13]

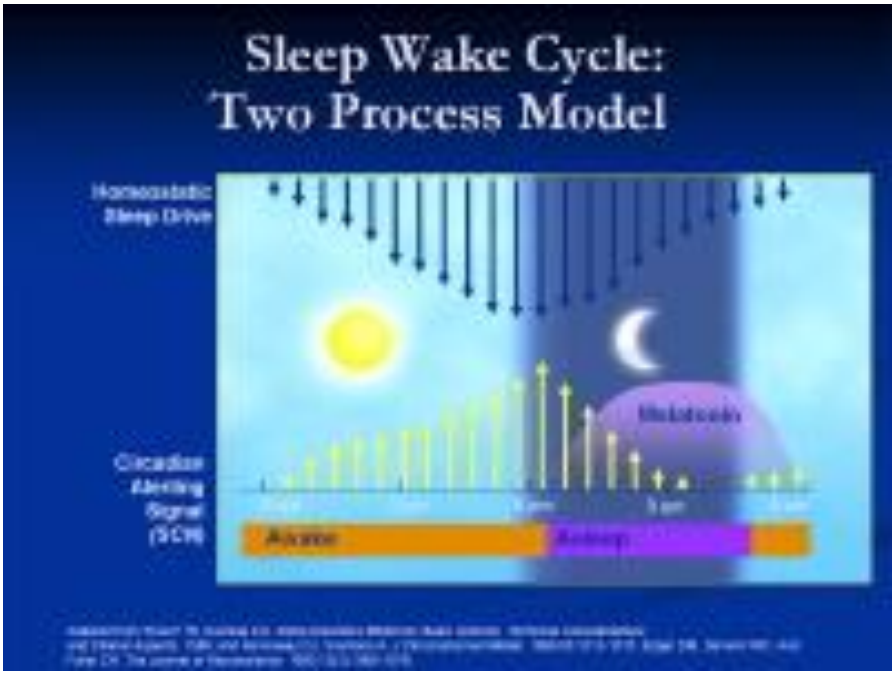
As well as regulating our homeostatic mechanisms and stress systems it has been proposed that sleep, particularly deep sleep (SWS) may have a reparative function and improve immune system function. [5] SWS has an inhibitory influence on the stress system". [6] In contrast, sleep deprivation represents a stress to the body and subsequently activates the stress systems and leads to poor immune function. [13] When taken to an extreme, sleep deprivation gives rise to hypothalamic alterations, aggression, weight gain, and finally, death..." [5 p13] Put simply, without sleep we die.

3.2 WHAT IS SLEEP?

What is sleep, we spend a third of our lives doing it? Sleep is concisely defined as "a physiological active state involving various encephalic structures, forming a neural network, with complex inhibitory and excitatory mechanisms, with a cyclic regulation, and over which can be modulated by will, establishing determined attitudes and behaviours". [5, p16] Insomnia shows a disruption of all these systems and states. [13, 51-55]

In the late 80`s Saper proposed a "flip-flop" model as to describe the sleep process. [9] In this model there are two sets of mutually inhibiting components. One side is arousing and the other sleep provoking. Each side inhibits the other though positive inhibition. This model allows for rapid state transitions between the two kinds of

sleep: Rapid Eye Movement (REM) sleep and Non Rapid Eye Movement (NREM) sleep. [9]. See chart below for details [9]:



Sleep-wake cycle.

These two states of sleep are each marked by characteristic physiologic changes.[9] These changes in EEG (electroencephalographic activity), EOG (electrooculargraphic activity)and EMG (electromyographic activity) are measured in the polysomnography. NREM sleep, also called slow wave sleep (SWS) and is perceived as high quality or restorative sleep.[6] Velayos states that the two stages regulating REM and non-REM sleep are independent but interrelated rhythmically. They are also independent of the sleep-wake-sleep cycle itself [6] which is governed by circadian rhythms.

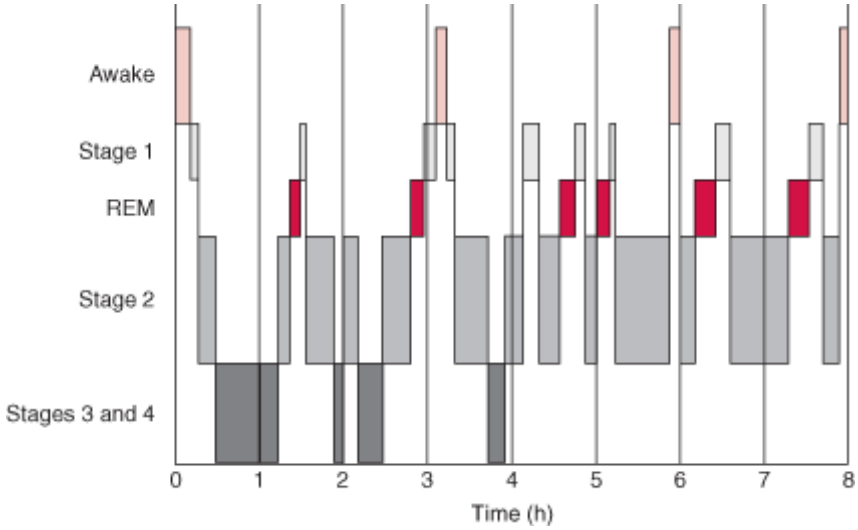
The cycle shows natural healthy variables; although all stages are necessary. The accepted average is between 6 and 8 hours.[9] Variants in groups show children and adolescents sleeping more and young adults sleeping more than older people.[13,1] In the elderly there is seen to be a decrease in NREM sleep , particularly stages 3 and 4.[5]

There is a diurnal cycle of approximately 25h[9] ; and natural sleep wake patterns follow this cycle; hence the need for external cues to maintain this cycle. For example light plays an important role. [9]

The central nervous system cells are as active in wakefulness stages as they are in sleep phases. [5 p19]

These stages and percentages of the stages are shown graphically below [21]:

TYPICAL SLEEP PATTERN IN YOUNG ADULTS



Rapid eye movement (REM) sleep occurs cyclically throughout the night every 90–120 min Sleep time is spent as follows:

- Stage 1: 2–5%
- Stage 2: 45–55%
- Stage 3: 3–8%
- Stage 4: 10–15%

3.3 *WHAT IS INVOLVED IN SLEEP REGULATION?*

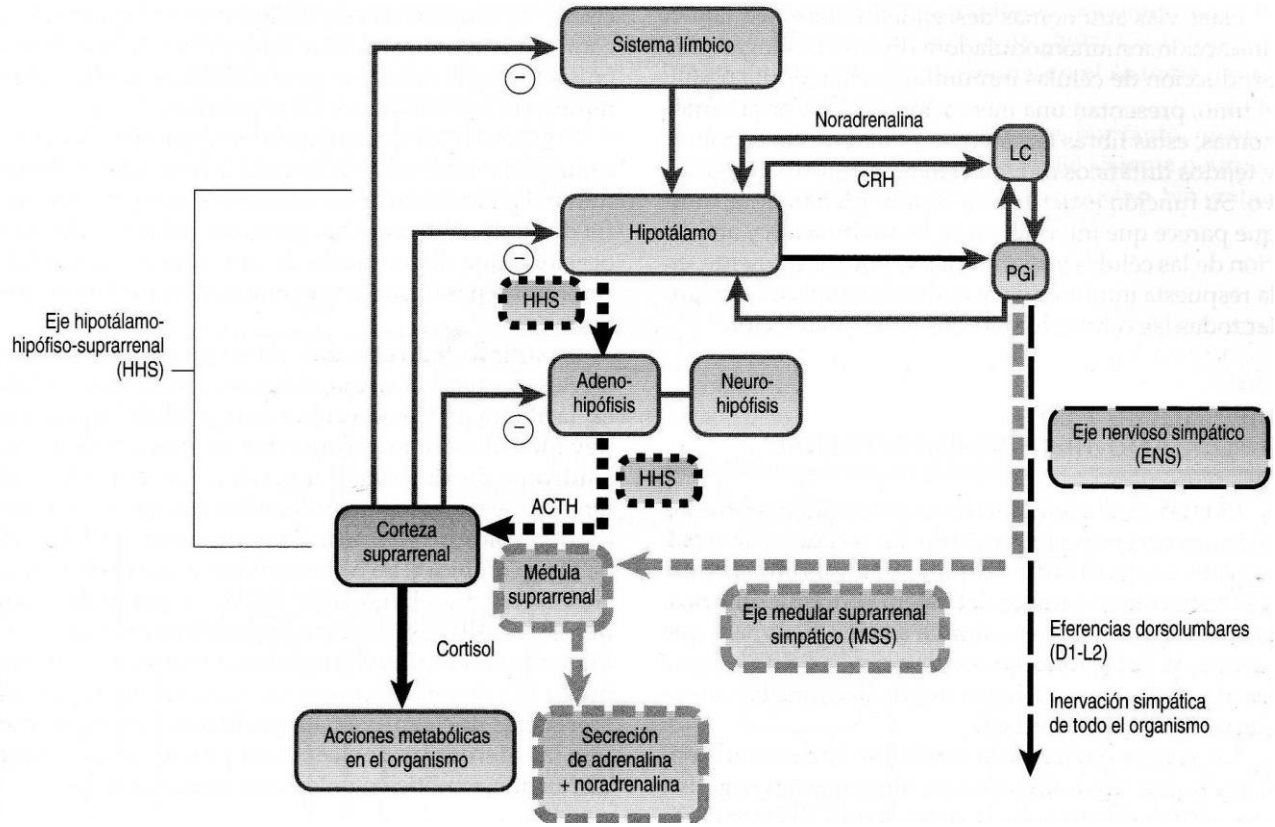
Homeostatic responses and circadian rhythms are the two processes that regulate sleep and wakefulness. [9] Alterations from these healthy patterns are then maintained by inappropriate feedback mechanisms, and in the long term disruptive sleep patterns are maintained by inappropriate learned behaviour patterns.[9] Which would explain the necessity of combined treatments in insomnia; one addressing chemical changes and the other addressing cognitive functioning.

The areas which control sleep wake mechanisms are found in the confluence of major physiological centres; limbic, neurological, endocrine and immune. These networks are each intimately involved with more than one system and function, working independently as well as together.

While we are dealing with systems and various structures a "centre of sleep" has been nominated. It is thought to be in the anteromedial area of the thalamus. Experiments have shown that stimulus of this area produces sleep states [5]. "The supraquiasmatic nucleus establishes the sleep wake cycle and is *influenced bidirectionally* by all its connections [5, p13]

This complexity of function gives rise to the confusion of data surrounding sleep. For example the role of cortisol is seemingly contradictory. Cortisol plasma secretion is known to increase in stress system responses and leads to increased arousal in subjects. [13] When this secretion is chronic, as seen in insomnia patients, it leads to a constant state of low grade inflammation and becomes a barrier to sleep. [14] However, research has shown that pulsatile nightly cortisol administration in fact *increases SWS* sleep time in subjects. [19]

The following diagram [31, p127] illustrates the interrelatedness of the systems involved in sleep and can be referred to when reading the following sub sections.



Schemtatic Representation showing interrelatedness of systems involved in sleep regulation

Representación esquemática del eje hipotálamo-hipófiso-suprarrenal, el eje nervioso simpatico (ENS) y el eje suprarrenal simpático (ESS). ACTH, corticotropina; CRH, corticoliberina; LC, locus coereleus; PGi, núcleo paragigantocelular

3.3.1 HOMOSTATIC REGULATION: HPA AXIS

The hypothalamus-pituitary-adrenal (HPA) axis forms a major part of the neuroendocrine system that controls reactions to stress. Hyperarousal of the HPA axis as seen in insomnia is from alteration of the post lateral ganglion. [20]

Stimulus of the HPA axis is not only from external stressors, (e.g. danger and trauma) it may also be stimulated by memories in the amygdale and hippocampus (centre of emotions) and nocioceptive input via the spinohypothalamic tract. [18]

The hypothalamus receives a stress signal and releases corticotrophin releasing hormone (CRH). This is produced and released from parvocellular neurons of the paraventricular nucleus (PVN). [18,p453] CRH goes to the anterior pituitary gland which in turn produces adrenocorticotrophic hormone (ACTH). ACTH is released into the blood stream and goes to the adrenal glands where it stimulates production of Cortisol (and other steroids).

The negative feedback loop continues through two axis; one on the hypothalamus and limbic system. This has a long term action and takes hours or minutes to work. The other is through the anterior pituitary where it directly inhibits CRH secretion. It is fast acting but of short duration. [18]

Cortisol exerts its effects on the receptors in the hypothalamus decreasing production of CRH and effectively braking the cycle and the stress response and returning to the original homeostasis. However if there is a continual firing the receptors become sensitized and lose their ability to function; in this way the stress response continues chronically. This state of high sympathetic activation and increased levels of cortisol has a two fold effect; in the short term it leads to a constant state of vigilance and alertness; and inability to sleep. In the long term it will inhibit the immune system leading to reduced immune function. . [18]

Cortisol also has important consequences on the thyroid, as it can inhibit TSH secretion. This has an adverse effect on the immune system as proper thyroid production function is necessary for the immunocyte proliferation. An altered immune system will subsequently cause further alterations as "lymphocytes are miniature producers of endocrine substances" secreting "TSH in addition to progesterone, CRH and ACTH. [18 p115] This may explain why poor immune function is seen in insomnia. Thyroid hormone has a sympathetic mimetic effect. This leads to excessive adrenergic tone and may lead to organic vasoconstriction. This vasoconstriction in the long term may lead to congestion and stasis and its consequent effects. [18]

CRH controls some behaviours and influences sleep wake patterns; it decreases SWS and increases stage 1 and 2. Older age persons are more sensitive to its effects. It is excitatory in the locus correleus (LC), hippocampus, cerebral cortex and some portions of the hypothalamus. (13)

ACTH is associated with general CNS activation consisting of a decreased sleep period time and sleep efficiency and an increase of sleep latency. (13)

These three hormones CRH, ACTH and Cortisol basically are excitatory on the CNS and are associated with decreased sleep time and sleep efficiency and increased sleep latency. (6, 13)

3.3.2 CIRCADIAN RHYTHMNS: AMYGDALE

Circadian rhythms are important both in coordinating internal metabolic processes and coordinating with the environment and form part of the sleep mechanism. (5)

The amygdale is the interface between the external light environment and the suprachiasmatic nuclei (SNC) located in the hypothalamus; this is the primary circadian "clock". (5 p27) The amygdale produces Melatonin which is liberated into the blood stream. Highest production is at night and production is inhibited by light. It is thought to favour sleep onset by triggering a drop in body temperature through a complex interaction with the HPA axis and by stimulation or suppression of certain corollary hormones and regulate the circadian sleep-wake cycle. It is also produced in other tissues involved in the circadian rhythm cycle: retina, GI tract, skin, lymphocytes. (5 p27)

Melatonin is also believed to potentiate the effects of the neurotransmitter most associated with sleep and relaxation, gamma-aminobutryric acid (GABA), through direct interaction with GABA receptors. (14)

Serotonin[a] is a precursor of Melatonin. It is released in response to increases in pressure, glucose or acid. It is produced in the dorsal raphe nuclei. It stimulates both

[a] It is synthesized from Tryptophan, an essential amino acid. This raises the question of dietary importance in circadian rhythms

intrinsic and extrinsic sensory neurons [20]. It is a neuromodulator and is found in the cerebrospinal fluid (CSF) where they modulate or influence activity of the brain.

It is possible to measure this rhythm and its alterations through measuring melatonin secretion in saliva and core body temperature [60, 61] (see 3.3.4)

3.3.3 CENTRAL NERVOUS SYSTEM (CNS): LOCUS COERULEUS (LC)

The locus coeruleus (LC) is located on the superior floor of the 4th ventricle. It produces norepinephrine and influences all parts of the body. It is also in direct communication with the hypothalamus activating the stress response through the HPA axis and CRH production through secretion of norepinephrine. This is a two way positive feedback mechanism, where the hypothalamus sends CRH to the LC. If these two components are in dysfunction or chronically stimulated the stress response will not down regulate. In a maladaptive state it may lead to of states of hyper vigilance and arousal. Spontaneous discharge rates are in the LC are highest during arousal and lowest during sleep. The LC may be "chronically stimulated by the amygdale and by chronic nocioceptive input from the visceral and somatic systems". [17]

Norepinephrine: is produced in stress situations in the adrenal medulla and forms part of the flight fight response. It regulates the central and peripheral nervous system. It is found in the nerves of the sympathetic nervous system innervating visceral organs, hormone secreting cells, heart muscle, immune system and the lymphatic system. It is involved in the waking response; correlating positively for stage 1 sleep and wake time after sleep onset and negatively with percentage SWS. [13]

Other neurotransmitters of the central nervous system are **gamma-aminobutryric acid (GABA)** which promotes sleep states and inhibits wakefulness [9, 20] and

Acetylcholine in the basal forebrain projects diffusely to cortical areas and the TMN to promote wakefulness. [9]

3.3.4 TEMPERATURE CONTROL

It has been proposed that there is a tenuous relationship between sleep onset and reduction of body temperature. [5 p24] For example, people with vasospastic syndrome are unable to initiate sleep. [2] It is one of the most commonly used variables in measuring physiological change and is considered a marker and reference point of other biological rhythms [5 p24] ; such as the circadian rhythm as mentioned above.

3.3.5 COMMUNICATION

The means of communication between cells and in the above mentioned physiological centres is through the cytokines, neurotransmitters and hormones mentioned. These are all chemicals and neurotransmission at synapses and action potentials are all changes in movement of small ions across cell membranes. They all need the correct chemical environment for optimal functioning. [17]

RA Holding [20] proposes that neurotransmitters could be the key to modifications made in body adaptation. They have a key role in the internal environment.

The main disturbances in the regulatory systems are due to a disruption in intracellular communication; whether this be due to changes in pH, stasis or hypersensitisation (facilitation) and this will have a knock on effect in all other systems; all things being interrelated. In the case of insomnia, the homeostasis of sleep wake mechanisms has been deregulated and the patient is in a state of unnecessary and excessive vigilance. They show heightened secretions of cortisol plasma levels and serotonin. [6]

4. AN OSTEOPATHIC PERSPECTIVE OF INSOMNIA

Osteopathy "defines the status of the whole human organism, a unit mechanism, in relation to its fluid environment, as well as the external surroundings." [23]
If we see the body as a self regulating set of systems, working in homeostatic balance then "ill health" in this case insomnia, is seen an alteration of these systems. As all systems are interrelated, imbalances or incorrect functioning in one will lead to compensatory measure in all other systems; endocrine, nervous system, immune and limbic.[32 p82] These changes or impaired systems or systems function will manifest as a somatic component; seen as tissue change, rigidity, compression, and congestion ; all palpable to the well trained hand. [18] The chemical and physical integrity of the tissues of the body are of prime importance in the osteopathic approach to disease."[23 p26]

The physiologist Irvin Korr first demonstrated a neurophysiological component in an osteopathic lesion (somatic dysfunction) [33]. His model of hypersensitisation was proposed on his work on spinal vertebrae. Magoun [23] then proposed applying the physiology of the spinal lesion to the cranial lesion, where the treatment will "restore some degree of normalcy to the primary respiratory mechanism in all of its ramifications throughout the body". He continues "In as much as this central nervous system plays a dominant part in the defence and repair of the entire body, treatment directed to the facilitated somatic component can improve the structure and hence the chemistry of the whole organism".[23,p94] This is the basis for the proposed CV4 treatment.

Under the Korr model, the HPA axis and CNS are responding to nocioceptive stimuli; they will become sensitized to repeated stimuli and become "facilitated"; where the normal threshold has been lowered and a response is triggered by minimal almost imperceptible stimuli.

The nocioceptive stimuli are from all areas:

- Limbic and Cognitive; learned patterned behaviours is one of the maintaining factors in chronic insomnia (hence the use of sleep hygiene training and CBT in its treatment)[64]
- Physical/mechanical: chronic tense muscles lead to nerve irritation; particularly of the vagus in the sub occipital area. This may lead to altered parasympathetic function.[31]
- Chemical: altered chemical environment, altered levels of secretion cortisol, serotonin, cytokines etc. [13]

4.1 DIAGNOSIS

Diagnosis in an osteopathic setting is also through clinical interview. All screening, as a matter of course, involves questions concerning sleep; quality and quantity, with additional questioning in the case of any anomaly.

Additionally, the Cranial Rhythmic Impulse (CRI) is measured which can give an indication of the health of the individual. A healthy CRI oscillates between 8-12 cycles per minute. Deviations from the rhythm or pattern in quality and degree indicate a pathological process [23].

The cycle is measured through cranial palpation. Magoun advises that the movement we are palpating is unlike that of other joints in the body. Instead we are looking for a resiliency "a combination of slight yielding or suppleness in the articulation plus the flexibility of live and pliant bone". [18 p565]

Restricted movement[b] and altered cranial rhythm will be detected in the palpation of the cranium. Tissue change, brought about by a change in the chemical environment

[b] : The following excerpt is included as it illustrates the underlying difficulty in being able to acknowledge movement in bone:

"Bones from preserved cadavers yield misleading values, especially in regards to plastic deformation, but also in elasticity, hardness and compressive and tensile properties." We are talking about physics; while everyone recognizes that if you lie on your arm /hand it "goes to sleep" ; something explained by lack of irrigation to that part of the extremity, others may find it less reconcilable that you can affect fluids dynamics , or affect compression of bone articulation; more than likely this is so , as a common perception of bone is that it is hard." However , "living bone is approximately 60% water. Its properties are closer to other connective tissues than cadaveric study would have one believe. The limited mobility allowed by sutures makes the plasticity of bone a relatively important source of motion for the cranium. The thin flat bones of the cranium are well suited to plastic deformity. Structures of the cranial sutures allowsvarious types of motion between contiguous bones." (23)

of the LCR and related structures will be perceived in muscle tissue. [23] Alterations are indicated by the presence of congestion, rigidity and asymmetric, weak or absent cranial rhythm. All movement or lack of movement is influenced by and continuous with sacral articular mobility and fluid fluctuation patterns. [21]

4.2 ANATOMY AND COMMUNICATION OF THE 4th VENTRICLE

The structures and tissues involved in the sleep mechanism are all intimately connected. [5] There is a continuity of all membranes throughout the body. The reciprocal tension membranes are intimately connected to the whole of the vertebral column via the foramen magnum. The pituitary is found under the hypothalamus and covered by the diaphragma sellae.[5] This arrangement means that during the phases of Primary Respiratory Movement (PRM or CRI) the shape of the pituitary will change. Likewise a lack of movement or altered movement will accordingly affect portal circulation. [5]

Irrigation comes from the terminal branches of the external and internal carotid arteries providing the blood supply to the dura.

Innervation comes from all three branches of the trigeminal nerve, sympathetic nerves from the carotid plexus, the superior cervical ganglion, and C1 and C2 sensory nerves. Impingement on any of these structures will affect function [5,p2].

Venous drainage is through the sinuses; they have no elasticity, nor can rely on muscle contraction as found in other parts of the body hence circulation is dependent on motion.

The blood circulating is carrying all the hormones from pituitary outflow.[5] and lymphocytes through lymphatic fluid.

Another fluid environment of utmost importance is that of cerebrospinal fluid (CSF). This carries secretions from the posterior lobe to its destination.

Cerebrospinal fluid acts as a support and a buffer to the CNS and is vital to its metabolism; bringing elements of nutrition and eliminating waste products. "The

sessile (those attached to the substrate) cells of the central nervous system depend on a constant mix of their fluid surroundings to maintain concentration gradients adequate for nutrition and waste disposal. It is a healthy fluctuation of the CSF that helps maintain these gradients. (18 p549)

CSF is found in the ventricles, the subachranoid space and the central canal of the cord. It is in constant rhythmic movement and renovated approximately 3 times a day by the choroid plexuses of the four ventricles. Movement is dictated by dialysis, secretion villous absorption and perineural dispersion. (36)

It flows from the first and second lateral ventricle through the foramina of Monroe into the third ventricle through the cerebral aqueduct to the 4th ventricle and finally leaves here through the foramen of Magendie and foramina of Luschka to the subacranoid space of the cord. It drains via the Pacchioninan bodies into the venous sinuses and also to the fibres of the fascia into the lymphatic system. (23, 36)

Hence we can see any alteration of its fluid composition will be taken to each and every cell of the body.

It is a closed hydrodynamic system. This basic pressure, with variants of 5-15mm, is fundamental to the physiology and pathology of the central nervous system. (23) This fluctuation has a potency acting as a hydraulic mechanism and an electrical potential. (34 p97) The pressure is dependent also on the venous system as this is where it vents; congestion here will affect pressure. Alteration in the chemical composition of CSF will be reflected in alteration of nervous function and subsequent dysfunction. (34)

4.3 TREATMENT USING COMPRESSION OF THE 4TH VENTRICLE (CV4)

The treatment proposed for treatment of insomnia is known as the compression of the fourth ventricle (CV4), as first proposed by WJ Sutherland. (36) The 4th ventricle is the centre of the higher physiological centres. (24) Its role is as "a primary physiological control centre of respiration that controls secondary respiratory

activities."[23] It is believed the cicumventricular organs in the walls of the third and fourth ventricles are sensory apparatus designed to monitor the Cerebral Spinal Fluid (CSF) for the operation of various feedback mechanisms of the Central Nervous System (CNS), which include the regulation of temperature, electrolyte balance, hypothalamic-pituitary function, and cardiovascular and respiratory function. [18]

The objective of the treatment is to essentially increase intracranial hydraulic pressure and consequent dispersal of fluid. [36] The intensified fluid exchange is thought to affect all fluids in the body.[18,p575]

The 4th ventricle is sided laterally by the peduncles, superiorly by the cerebellum and on the floor the pons. During the treatment, as Magoun [23] explains, the tentorium cerebella which is attached to the internal surface of the occipital squama, is drawn more closely to the cerebellum, whose hemispheres are thereby brought down over the roof of the 4th ventricle, while the middle cerebellar pedunculos are pulled up to elevate the floor; thus augmenting the squeeze both ways. Chaitow [34 p100] suggests that the changes provoked in the body are via periaqueductal gray (PAG) tissue, which surrounds the fourth ventricle. This tissue is lined with neuroreceptors (opoid and cannabinoid receptor) and he suggests it responds to the hydraulic pressure by activating these neuroreceptors by releasing endorphins and endocannabinoids.[c]

4.4 DESCRIPTION OF COMPRESSION OF THE 4TH VENTRICLE (CV4)

The therapist sits at the head of the supine patient, and taking the occiput in her hands places her thenar eminences on the occipital squama, below the superior nuchalline. Fingers are overlapped or interlaced. Care is taken not to block the occipitomastoid sutures and compress the associated bones and meninges. The movement is followed into extension, flexion is resisted, and this is followed through various cycles where CRI is monitored until a still point is reached where it is maintained. There will be a noticeable softening in the occipital, warmth, possible perspiration and changes in breathing pattern and relaxation of the whole body.

c these differ from neurotransmitters as they are not stored in vesicles but are synthesized on demand) Rodriguez de Fonseca *et al.*, 2004, Wikipedia).

Follow the new cycle checking the amplitude and symmetry of the movement. The technique lasts approximately 7-8 minutes. [18, 36, 37,)]

There do not seem to be any contraindications however most texts recommend that before embarking on a CV4 treatment to check that all lesions in this area are resolved. Likewise on completion it is advisable to check all areas are free and "breathing" well [(23)]

4.5 SPECIFIC OBJECTIVES OF CV4 AND EVIDENCE OF FUNCTION

The mechanics of CV4 are to cause an alteration of fluid fluctuation via the compression of fluid in the fourth ventricle and affect the functioning of the physiological centres found there. [(36)] The objectives are to:

Counteract stress-producing factors by normalizing function of the cerebrum, thalamus, hypothalamus and pituitary body.

Vgontzas et al [(6)] found "the 24h ACTH and cortisol secretions were significantly higher in insomniacs; compared with normal controls" bringing them to the conclusion that "insomnia is associated with an overall increase of ACTH and cortisol secretion" and "activation of the HPA axis". Their findings are "consistent with a disorder of central nervous system hyperarousal rather than one of sleep loss, which is usually associated with no change or decrease in cortisol secretion or a circadian disturbance." [(6)]

AN Vgontzas et al [(6)] found deep sleep has an inhibitory effect on the stress system; the HPA axis being a major component. They hypothesize that "there would be a positive correlation between the severity of insomnia and the degree of HPA axis activation."It would follow then that dampening down the CNS and HPA axis would lead to decreased output, and benefit sleep patterns.

The CV4 is stated to affect diaphragmatic activity and autonomic control of respiration, and "seems to relax the sympathetic nervous system tonus to a significant degree…" "..autonomic functional improvement is *always expected* as a result of still

point induction" [34]. It relaxes all connective tissues of the body enhancing tissue and fluid motion and "restores flexibility of autonomic response " [34] Recent investigation [56-59] has affirmed these statements; using studies of CV4 treatments and measuring sympathetic response. They have statistically valid evidence showing the effect of CV4 treatment on cutaneous blood flow, autonomic balance during paced breathing, these physiologically induced changes are measured by transcutaneous laser Doppler flowmeteters. This research was originally shown as posters (2006) and this and other material summarizing the research done on CV4 will be published later this year (2010). [42]

Cutler et al 2005 [40] set out to discover the effects of cranial manipulation on muscle sympathetic nerve activity (MSNA) as potential mechanism for altered sleep latency. They also wanted to "statistically determine if cranial manipulation is associated with altered sleep latency". [40]. They conclude that "cranial manipulation, specifically the CV4 technique, *can* later sleep latency and directly measured MSNA in healthy humans". [40]

Normalize nerve function of all cranial and spinal nerves as well as the autonomic nervous system. Nerves are especially sensitive to changed chemical environment. [23]Alteration in the chemical composition of LCR will be reflected in alteration of nervous function and subsequent dysfunction. [37] Nerves are also subject to irritation. This may be via "impeded blood supply, pressure of venous congestion, or lymphatic stasis and oedema, disturbed fluctuation of the cerebrospinal fluid, dural tension or traction ..." [23]. Restoring movement will eliminate stasis, pressure and oedema and hence improve chemical composition.

Eliminate circulatory stasis by normalizing arterial, venous and lymphatic channels. Drainage of the venous channels is vulnerable to impingement on the foramen; this causes stasis and affects 9th, 10th and 11th cranial nerves. The brain is very sensitive to changes in composition and pressure, hence it is imperative for healthy function to have good blood flow.[39 p76] Vascular resistance is much more important than arterial pressure as 95% of venous blood leaves the two jugular foramen. Any congestion and stasis will lead to raised intracranial pressure and it

subsequent effects. [23] Cranial lesions are some of the causes of this resistance, and will manifest as tensions in the duramadre and oedema.

Magoun [23] comments that this compression will also be affecting blood pressure, as the mechanisms that raise or drop blood pressure are found in the 4th ventricle. Aponeurotic action and contracted suboccipital tissue are equally responsible for the instauration and persistence of elevated blood pressure. [23] Furthermore, "aponeurotic tensions can affect hypothalamic function; which is controlling hydric balance in the body, temperature control, blood pressure, sleep wake mechanism." (39).

To normalize cerebrospinal fluid fluctuation: this may be affected by misalignment of the cranial bones. "Healing is facilitated by a stimulation of CSF flow" (3 p999) and will restore a "balance in the autonomics, the neuroendocrines or the psychosomatic realm..." (23 p115)

To release membranous tension: releasing from any strains caused by misalignment of cranial bones. [23] "…adjusting sutures and foramina affects the function of cranial nerves and vessels, as well as the function of muscles that originate or insert on cranial bones". (34 p99)

To correct cranial articular lesions: all soft tissues have a degree of excursion. Any alterations will lead to restricted motion which in turn invariably leads to lesion. Untoward stress or pressure on membranes, or tissue over time will lead to changes in pressure, fluid flow and tissue composition. (5 p2) and the subsequent alterations of homeostasis.

As mentioned earlier these lesions would be attended to before applying CV4 in order to increase the effectivity of the aforesaid treatment.

To modify gross structural patterns: working on the fluid components of the neurological, endocrine and vascular system and all these effects will be carried out to cells throughout the body in all fluid mediums , whether it be CSF, lymph or blood.

5. COMMENT

5.1 BENEFITS OF OSTEOPATHIC INTERVENTION

Osteopathic intervention seems well suited to the heterogeneous nature of insomnia. The therapy can be tailored to match the symptoms of each individual, bearing in mind that the symptoms may change in intensity over time and from one night to the next. (11)

Osteopathy treatment avoids some of the barriers encountered in other approaches to insomnia. For example difficult access [2] to facilities that can adequately diagnose [7] and treat insomnia. However, in an osteopathic session, it is standard practise to question the patient on their sleep habits and satisfaction with this, enquiries are also made into perceived quality of life, stress, labour and social status. In the case of anomalies encountered the use of sleep questionnaires would consolidate diagnosis or the patient is referred to a specialist where deemed necessary. This is based on the understanding that a successful treatment requires an understanding of the biopsyscosocial factors that have led to this state. [2] The individual in seen in his whole state.

How the individual interacts with his external environment can determine the long-term health status of the individual [3 p242] , an important factor in pathology and one which the osteopathic approach addresses. These issues are addressed by giving advice on stressors and sleep hygiene management and by giving and monitoring stress-related responses towards positive coping behaviours and strategies. [3 p243]

Sleep hygiene would be an integral part of the treatment process. This is concurrent with standard medical practise which calls for behavioural and sleep hygiene measures from the onset. Osteopathic treatment recommends the intervention of "specific behavioural strategies to counteract the learned aspects of insomnia" in any insomnia over 3 weeks [3 p242]

This detailed clinical interview is complimented with a physical exploration. This allows for screening of any underlying physical pathologies which may lead to insomnia and aids the differential diagnosis process. The synthesis of the information obtained from the evaluation by history, observation and physical examination enhances the clinical information obtained by traditional methods.[18,p573)]

The importance of a diagnosis taking into consideration all aspects of the pathology cannot be stressed enough. Currently diagnosis of insomnia is inadequate because there is poor integration between the fisiopatology and the behavioural symptoms. As we saw earlier this is being addressed by the latest work study group for DSMIV [(4)] and will possibly be incorporated into the next DSM. They "plan to incorporate links in the text and show how DSM-IV and ISDII map onto each other" using categorical, polysomnography and dimensional measuring to aid a more comprehensive diagnosis of the person and disease with a scientific basis…" [(4)]. ISD10 is considered to have a more multidimensional approach. [(4)]

C Ruiz [(64,)] insists on the need for there to be a global questionnaire which addresses all parameters of the illness; its aetiology, maintaining factors and affectation in other areas of life of the individual. The AIS (Athens Insomnia Scale) is recommended as a first step in screening. [(10)]

Incorporation of these as part of the screening process in patients with sleep complaints is recommended in osteopathic treatments.

The implementation of sleep questionnaires is also recommended as a tool to use in dialogue with other specialists. They are quick and easy to administer and would facilitate dialogue between physicians, psychiatrists and osteopaths. They would also facilitate the process of differential diagnosis for any underlying psychiatric disorders, and help as a common reference point in the case of referrals.

They have the added benefit of being cost effective and could be used in initial diagnose without recourse to the use of polysomnographs. Polysomnographs are expensive, and while they are indicated for other sleep related diagnosis they are not particularly indicated in the diagnosis of primary insomnia. [(8)] Actigraphy is a cheaper, reliable and effective tool [(62)]

As an alternative treatment option CV4 avoids "some patients' reluctance to take hypnotic medication because of fears of side effects, dependence, or the stigma associated with 'sleeping pills'."[2.] Osteopathic intervention is non invasive and certainly has none of the side effects associated with hypnotics, risk of falls or accidents, nor does it have any stigma attached to it. In fact many patients who are anxious or depressed (both consequences of insomnia) "report great comfort and tensional relief from basic osteopathic manipulative techniques..." [3 p248]

Acute insomnia has been shown to be effectively treated by hypnotics, but there are, however, no studies which support evidence of effectiveness of hypnotics in the long term. [2, 16, 44] Furthermore, some authors have concluded that behavioural therapy is as effective in the short term as pharmacotherapy [38]. It is common in clinical practise for patients to present their symptoms only after many years of suffering, in these cases the use of hypnotics is a poor solution.

Lack of effectivity of hypnotics in the long term suggests that there may be differences in the underlying physiological causes of acute and chronic insomnia; as are the underlying differences in the physiology of stress, sleep deprivation, depression etc. It seems that further unbalancing brings in further compensatory measures; an endless tract of infinite variables. It would therefore be impossible to create a range of medicine able to address these infinite variables. It would necessitate clinical studies to determine the physiological differences, if they exist, in chronic and acute insomnia.

Also the long term use of hypnotics is shown to alter the natural sleep-wake cycle. [5, p44]. In this instance it is unrealistic to expect to see relief of symptoms. In the osteopathic approach we are treating the cause and not only the symptoms [6] and aiding the body to readjust to a healthy homeostatic balance. Disrupted sleep is merely symptomatic of the underlying cause.

5.2 NEED FOR MORE RESEARCH

"Although insomnia is, by far, the most commonly encountered sleep disorder in medical practice, our knowledge in regard to its neurobiology and medical significance is limited" [6] and also contradictory [5,6,1,41] Hence, the more investigation undertaken the better our understanding and subsequently more effective treatments.

The investigative studies quoted in this paper support the model proposed: where insomnia is seen a consequence CNS and HPA axis arousal; showing the corresponding physiological arousal. CV4 intervention has been shown to reduce sleep latency in healthy adults [40] and empirical studies show clinically significant sympathetic response to CV4, irrespective of age or breathing [57].

There is not enough data currently available to make any conclusive statements about its viability. However, having said this the research on autonomic response during CV4 treatment is enormously promising and has opened the opens doors for substantiated future clinical trials; having demonstrated measurable physiological parameters, and thus eliminating the barrier to unquantifiable scientific research in CV4 treatment of insomnia.

- Effective diagnosis can be made using sleep questionnaires and sleep scales. Physiological arousal or activity can be measured though polysomnography and through laser Doppler flowmeter.
- Circadian rhythms and their disruption can be measured through core body temperature measurements, and melatonin levels through saliva analysis.
- Cortisol levels and sympathetic muscle activity can also be measured.[40,6]

This is an opportunity for the science of osteopathy to make its presence felt and to be at the vanguard of further scientific investigation. To carry out clinical trials to prove the efficacy of CV4 treatment.

This coupled with recent studies in memory loss, depression and other psychiatric illnesses relating to insomnia make this study imperative. [5 p4]. One of the implications being that these investigations into sleep mechanisms and treatment will aid our understanding of these related pathologies. [5]

It is not only research that is needed; poor diagnosis, lack of information and misinformation both in medical and public spheres highlight a major need for public and private investment in educational programs directed at physicians, health care providers, and the public." [2,] "Currently its position in literature as a pathology in its own right is compromised both by the lay person and the physician." [6]

5.3 MODELS OF INVESTIGATION

We see in the previous section the need for substantial research which should include "developing research tools and conducting longitudinal studies of randomized clinical trials. "This will highlight questions about the duration and manner of pharmacological treatment and the optimum number and duration of cognitive-behavioural therapy sessions for insomnia" [2]. However, it is important and relevant to stress the danger of a reductionist approach to the diagnosis and treatment of insomnia [27]. The promotion of non medical alternatives; sleep hygiene, relaxation, psychotherapy and behavioural is urged [2] both in research and in treatment.

The validity of the evidence of science based models may be questionable. A great deal of scientific evidence for insomnia is based on sleep laboratory testing. This is an artificially created situation; which in itself maybe disrupting sleep patterns. [64, 7].

Integration of basic science with data from studies of cognitive function improves our understanding of the health maintenance process.[3] The more integrated the multi systems approach in diagnosis is the higher the chances of a better integrated treatment approach and therefore a successful outcome.

Reinoso- Suarez[5 p2], a specialist in neurobiology affirms this by saying "as he has done over 50 years- that any simple explanation, however attractive, of the functional

activity of the central nervous system is false, or at least, incomplete" he concludes by saying it is obvous that further investigative studies be multidisciplinary.

C Ruiz, a specialist in cognitive therapy [64] also concurs with this, as she recognizes the discrepancies observed in the behavioural, subjective and physiological measures of sleep, and says these measures can be used as complementary tools, but that we should be wary of taking only one angle of the pathology and treating it, as we may be ignoring the maintaining factors of the insomnia, and the treatment proposed may not be effective.

The implicit message is that the various current approaches are failing as they are treating a multisystem disease by treating only one axis (e.g. administration of pharmacological drugs), when what is needed is a multi-system approach. It must never be forgotten that delineations within medicine are artefacts of intellectual creativity and that these are merely paradigms and invented "borders" to aid comprehension and that the reality of the health of an individual is the interaction of these systems. Treating only one aspect of pathology is erroneous because it is not taking into account the heterogeneity of the disease.

A multidimensional approach is implicit in osteopathic medicine and research, and multidimensional treatment is generally more effective than single intervention alone". [3] As evidenced in the current practise of pharmalogical treatment in conjunction with CBT. This approach is the basis of osteopathic medicine and is supported by the new medical research model psiconeuroimmunology (PNI) which recognizes the integration and interinfluenciability and bidirectional relationship of the systems of neurology, immunology and the limbic system.

5.4 OSTEOPATHIC MODELS AND EXPLANATION OF SUBSEQUENT PATHOLOGIES

It is accepted that sleep patterns in the elderly will change (as they do from babies to children) and this leads to an assumption that sleep disruption or insomnia in the

elderly is a natural part of the aging process, but this very premise needs questioning itself, as Pearson et al [7] conclude there are irrefutably many elderly people who have no problems whatsoever sleeping.

"Osteopathy is ideally suited by its philosophy and clincal experience to look at the effects of early disruptions of body unity on the deterioation of old age." [3 p1227] under an osteopathic model deterioration of normal function is a central concept [3 p1127], and insomnia is seen as the somatic manifestation of a breakdown in systems functioning.

And if, as recent literature is showing, insomnia is a marker of a more serious pathology these pathologies would be manifestations of further systems breakdown. These causal links and bidirectional influences are controversial and under study, [16] however, it is recognized that addressing and treating the symptoms of insomnia may favourably benefit symptoms of (other) disorders. [3]

Treating the insomnia before we reach "stage three" of the H Seyle model (ver 2.2) would make osteopathy a valuable tool in preventative medicine. Early treatment would be beneficial to the patient as the statistics show; nearly half (41%) of mood disorder patients suffered insomnia symptoms prior to the disorder and furthermore in 52.6% of cases insomnia symptoms preceded a mood order relapse [11] As Roth suggests there is "an opportunity for disease and relapse prevention" [11]. This would represent a huge cost saving to the medical institutions and be of great benefit to public health and work productivity. It would be more cost effective to treat the somatic dysfunction [3 p1227]; the start of body breakdown, before waiting until the final breakdown of clinical disease has occurred; as seen by CHF, depression, obesity and HBP.

6. CONCLUSION

The trend is toward more people with insomnia and across more age groups. These are alarming facts given the causal connections between insomnia and more serious pathologies. There is a disparity between the seriousness of the pathology and public understanding. It calls for expenditure in public education, health care workers and research.

A hindrance to successful diagnosis was lack of common agreement as to what insomnia is. This has been remedied by the introduction of universally standardized questionnaires. They address all aspects of insomnia, they are easily distributed and they can be used in all spheres of mental health and primary care medicine (including that of osteopathy). Their incorporation would generate a homogeny of diagnosis within all fields of medicine. Enabling interchange of information among the various disciplines and enhancing effectivity in treatment.

The inclusion of these questionnaires, the tendency towards the incorporation of scientific evidence from polysomnographs as well as the existence of multidisciplinary approach to treatment indicate a move towards a more multidisciplinary approach in the understanding, diagnosis and treatment of insomnia.

Sleep is a major bio behavioural mechanism and alterations lead to a patient with an altered HPA axis, a compromised immune response and poor cognitive functioning. All systems and relationships are affected; social, labour, physiological, neural, vascular, endocrine, and all need to be attended in the first instance of diagnosis. Osteopathic diagnosis and treatment attend all these parameters. It has the added benefit of having no side effects, is cost effective, and does not have the stigma attached to some other treatments. In this review there is insufficient clinical evidence to come to any substantial conclusion as to the validity of effectivity of the CV4 treatment. However, the research carried out by Cutler (40) has shown a

reduction in sleep latency using CV4. Furthermore, the studies carried out on cranial manipulation affecting sympathetic response are statistically viable. [56-59] They provide a much needed scientifically valid platform for further investigation.

Given the public interest in sleep it is recommended that osteopaths are proactive in publicizing what they can to do help. Further research is imperative as to the viability of the CV4, particularly as it is so significant for national productivity and for the safety of individuals.

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