

**U. PORTO**



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**THE EFFECTS OF “HEIDELBERG SCALP  
ACUPUNCTURE” ON OBSTRUCTIVE SLEEP APNEA.  
-A PRELIMINAR STUDY-**

Maria João Rodrigues Ferreira Rocha dos Santos

Dissertação de mestrado em Medicina Tradicional Chinesa

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Dissertação de Candidatura ao grau de Mestre  
em Medicina Tradicional Chinesa submetida  
ao Instituto de Ciências Biomédicas de Abel Salazar  
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**DEDICATION:**

*To my parents ...*

*To Ana Maria Grande,  
For the "philosopher stone",  
For the scientific enchantment.*



*We are the scientific civilization ...  
Knowledge is our destiny "*

Jacob Bronowski

*"In the history of human thinking,  
the most fruitful thoughts occur, in general,  
when two streams totally distinct meet together ..."*

Werner Heisenberg





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## Resumo:

**Introdução:** O Síndrome da Apneia Obstrutiva do Sono (SAOS) é uma doença respiratória muito comum. Recentemente o SAOS tem sido associado com o síndrome metabólico, morbidades cardiovasculares e cerebrovasculares, entre outras condições. A Pressão Contínua Positiva nas vias respiratórias (CPAP) permanece como tratamento *gold-standard* no tratamento do SAOS. No entanto, vários estudos indicam uma grande variabilidade na adesão ao CPAP, exigindo abordagens de tratamento mais eficientes. Estudos anteriores fornecem dados limitados que sugerem efeitos positivos imediatos e mediatos da acupunctura no SAOS, suportando a tese de que a acupunctura pode ser útil neste síndrome. Neste estudo apresentam-se dez casos clínicos de SAOS tratados por acupunctura craniana de Heidelberg (ACH).

**Objectivos:** Avaliar o efeito agudo da ACH no SAOS, analisando mensurações objectivas do estudo de sono, realizado através de poligrafia cardio-respiratória e verificando a percepção de qualidade de sono através da realização de um questionário matinal.

**Método:** Indivíduos com SAOS e *naïve* para acupunctura serão seleccionados a partir de um Departamento de Pneumologia. Por questões éticas, o estudo é dividido em duas fases:

- **Fase 1** (estudo preliminar): Dez pacientes serão tratados com ACH, com micro-agulhas permanentes, durante 24 horas. As medições incluem poligrafia cardio-respiratória (PG) antes e depois da acupunctura e a realização de um questionário matinal na manhã seguinte à segunda poligrafia.
- **Fase 2:** Após uma medição basal de PG, 40 pacientes serão randomizados em 2 grupos: a) grupo com micro-agulhas permanentes de ACH durante 10 dias e b) um grupo controlo sujeito a acupunctura falsa. Uma segunda medição de PG irá avaliar o efeito

## Resultados:

Fase 1: 8 em 10 pacientes tratados com ACH responderam à terapia, o que é demonstrado por uma melhoria 51.4% (p value = 0,069) no índice de Apneia-Hiponea; 51.3% (p value = 0,089) nos eventos respiratórios; 14,8% (p value = 0,226) na dessaturação de oxigénio e de 28.8% (p value = 0,88) no tempo relativo de ronco. Em termos de percepção de qualidade de sono, nenhum paciente relatou que a qualidade de sono tenha piorado. Sete dos dez pacientes classificaram a qualidade de sono como igual e 3 como de melhor qualidade que no dia-a-dia.

Fase 2: com base nestes resultados preliminares e em estudos prévios, é expectável uma melhoria do índice de apneia-hipopneia, da percepção da qualidade do sono e da qualidade de vida.

**Discussão:** Apesar de não terem significância estatística, os dados da fase 1 sugerem uma melhoria nos parâmetros da poligrafia e na qualidade de percepção do sono, a favor da fase 2 do estudo. O sistema somatotópico facial correlaciona-se com as principais projecções anatómicas dos pontos do couro cabeludo o que possivelmente explicará os efeitos positivos nas vias aéreas. Estas relações hipotéticas podem ser suportadas pela teoria fractal aplicada à fisiologia e ontogenia humana.

**Conclusão:** Se se comprovar a sua eficácia, a ACH poderá ser uma terapia complementar no tratamento da SAOS. Os seus mecanismos de acção poderão estar relacionados com aspectos de neurofisiologia, embriologia e ontogenia. Investigação adicional é necessária para avaliar o feito de longo termo da ACH no SAOS.

**Palavras-chave:** Síndrome de apneia obstrutiva do sono; índice de apneia Hipopneia ; acupunctura craniana; acupunctura; Medicina Tradicional Chinesa.

## Abstract

**Introduction:** Obstructive sleep apnea (OSA) is a very common respiratory disease. Recently OSA has been associated with metabolic syndrome, cardiovascular and cerebrovascular morbidity, among other conditions. Continuous positive airway pressure (CPAP) remains the “gold-standard” treatment in the management of OSA. However, several studies indicate a great variability in compliance to CPAP demanding more efficient treatment approaches. Previous studies provide limited data that suggests immediate and mediate positive effects of acupuncture in OSA, supporting the thesis that acupuncture may be useful for this syndrome. We report 10 clinical cases of OSA treated by “Heidelberg Scalp Acupuncture” (HSA).

**Objective:** To evaluate the acute effect of HSA in OSA, analyzing objective measurements of a sleep study, conducted by cardiorespiratory polygraphy and checking the perception of quality of sleep, through the realization of a morning questionnaire.

**Methods:** Individuals with OSA (AHI > 5) and naïve for acupuncture will be sampled from the Pulmonology Department. For ethical reasons, the study is divided in two phases.

- **Phase 1** (preliminary study): Ten patients were treated once with HSA, applying permanent micro-needles for 24 hours. Measurements include cardio-respiratory polygraphy (PG) prior and after acupuncture.
- **Phase 2:** After a baseline measurement of PG, 40 patients will be randomized into two groups: a) a group with permanent HSA needles for ten days and b) a control group subject to sham acupuncture. A second PG assessment will evaluate the effect.

**Results:** Phase 1: 8 out of 10 patients treated with HSA responded to therapy, as demonstrated by a improvement of: 51.4% (p value = 0.069) in the Apnea-Hypopnea index; 51.3% (p value = 0.089) in respiratory events, 14.8% (p value = 0.226) in the desaturation of oxygen and 28.8% (p value = .88) in snoring relative time. In terms of perception of the quality of sleep, none of the patients reported that sleep quality has worsened. Seven of the ten patients have classified sleep quality as the same and 3 classified the quality of sleep as better than in everyday life.

Phase 2: based on these preliminary results and previous studies, it is expected an improvement of the Apnea-Hypopnea Index, perception of sleep and quality of life.

**Discussion:** Although without statistically significance, phase 1 data suggests an improvement in PG parameters and sleep quality perception, in favor of phase 2 of the study. The facial somatotopic system of HSA apparently correlates with the major anatomical projections of the scalp points possibly explaining the positive effects on the

airways. These postulated relationships would be supported by the “fractal theory” applied to human physiology and ontogeny.

**Conclusion:** If proven to be effective HSA may be a complementary therapy for the treatment of OSA. Its mechanisms of action may be related to neurophysiological, embryological and ontogenetic aspects. Additional research is needed to evaluate long-term effects of HSA on OSA.

**Keywords:** Obstructive Sleep Apnea; Apnea Hypopnea index; Scalp acupuncture; Acupuncture; Traditional Chinese Medicine.

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## LIST OF ABBREVIATIONS:

OSA – Obstructive Sleep Apnea	SAOS – Síndrome da Apneia Obstrutiva do Sono
CV – Cardiovascular	AC – Acupuntura Craniana
NHS – National Health System	HTN – Hypertension
TCM – Tradicional Chinese Medicine	ACH – Acupuntura Craniana de Heidelberg
AHI – Apnea-Hipopnea Index	HTA – Hipertensão Arterial
HSA – Heidelberg Sleep Apnea	PGC – Poligrafia cardiorespiratoria
SJHC – São João Hospital Center	EAV – Escala Analogia Visual
EPS – Epworth Scale	TA – Tensão Arterial
SDQ – Sleep Diagnosis Questionnaire	MAPA – Monitorização Ambulatória da Pressão Arterial
TCS – Treatment Credibility Scale	TM – Tradicional Medicine
MQ – Morning Questionnaire	BC – Before Christ
VAS – Visual Analogical Scale	WHO – World Health Organization
PG – Polygraphy	CNS – Central Nervous System
ABPM – Ambulatory Blood Pressure Monitoring	5-HT- Serotonine
BP – Blood Pressure	GH – Growth Hormone
PSG – Polysomnography	TSH – Thyroid Stimulating Hormone
CVD – Cardiovascular Diseases	SA – Scalp Acupuncture
UA – Upper Airways	SA-OSA – Scalp Acupuncture for OSA treatment
PAP- Positive Airways Pressure	DNA – Deoxyribonucleic Acid
CPAP – Continuous Positive Airways Pressure	GD – Guiding Criteria
BiPAP – Bilevel Positive Airway pressure	HM – Heidelberg Model
APAP – Automatic Positive Airway Pressure	ALT – Algor Laedens Theory
NCC – Neural Crest Cells	SaO <sub>2</sub> – Oxygen Saturation
CNCC – Cranial Neural Crest Cells	NO – Nitric Oxide
CN – Cranial Nerves	SVE – Special Visceral Efferent
AH – Apnea - Hipopnea	GVA – General Visceral Afferent
AH/h – Apnea – Hipopnea per hour	GSA – General Somatic Afferent
	HBP – High Blood Pressure

## CHAPTER 1:



## **1. Introduction:**

It is generally accepted that conventional medicine (allopathic) and current health systems have contributed decisively to advances in health.

Conventional medicine, in recent decades, has evolved exponentially, result of technological development; of the bio-engineering, biotechnology and pharmaceutical sciences development that has led to a deeper understanding of the human "machine".

All scientific and technical progress has brought to science and to medicine, an increase of scientific challenge and an incessant search for answers. Today's society, as a result of its new insights and developments, is facing new realities, new challenges and therefore new paradigms too.

The conventional model ("western") biomedical, contemplate the human being as the sum of several mechanisms whose knowledge depends on the fractional understanding of matter and living organisms.

Globalization and cultural miscegenation have made emerge a new model of health care, so-called "integrative medicine", whose concept assumes that the living organism contains an intrinsic functional capacity that modulates all physiological activities and physico-chemical properties that can be optimized from a therapeutic standpoint (1, 2).

Advocating such an integrative approach as a medical background, this research fundamental goal is to study the validity of a *new model of scalp acupuncture*, hereafter designated **Heidelberg Scalp Acupuncture (HSA)**, as applied on the treatment of Obstructive Sleep Apnea (OSA) and whether special somatotopic correlations can be established.

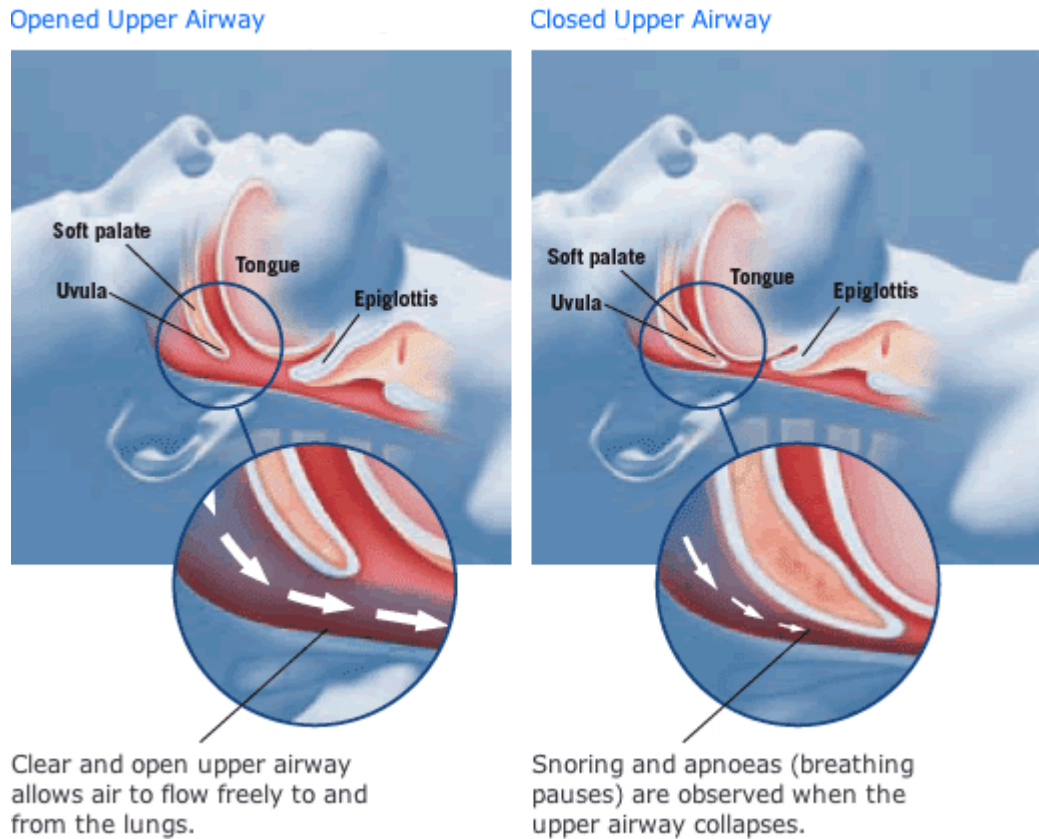
## **2. Obstructive Sleep Apnea Syndrome**

### **2.1 Definition:**

Syndrome Obstructive Sleep Apnea (OSA) is a disorder of breathing patterns during sleep which is characterized by repeated cessations of airflow and or reductions in airflow (apnea and or hyponea) caused by complete or partial obstruction of upper airways by partial or complete collapse of the oropharyngeal pathway by relaxation of the muscles of the pharynx during sleep (Fig.1) (3-6). By convention, apnea is defined as cessation of airflow for more than 10 seconds and hypopnea is defined as the reduction of air flow resulting in frequent awakenings during sleep or oxygen desaturation (33).

The repetitive cycle of apnea and hypopnea begins with the reduction of the airflow by obstruction that produces hypoxia and hypercapnia, requiring stimulation of the

autonomic nervous system to restore patency of the airway by increasing muscular tonus of the oropharynx thus reopening the obstructed airway (7, 8). This stimulation causes arousals and sleep fragmentation. After the restored of ventilation, the patient goes back to sleep, repeating this cycle several times per night (9).



**Figure 1: OSA anatomical changes. Source: <http://sleepapnoea.respironics.eu>**

The nocturnal oscillations of breathing in patients with OSA can induce intermittent hypoxia and CO<sub>2</sub> retention during sleep, leading to a decrease of oxygen saturation (SatO<sub>2</sub>), interrupting the normal hemodynamic and autonomic responses, resulting in increased heart rate and blood pressure. Overnight hypoxia leads to activation of neuronal, humoral, inflammatory and thrombotic mechanisms, implicated in the pathogenesis of various diseases including cardiovascular diseases. (3, 7, 10)

The clinical manifestations are characterized by a set of concurrent symptoms that lead the clinician to suspect the disease. Excessive somnolence during the day, fatigue, reports of snoring and breathing pauses during sleep, cognitive disturbances, impaired memory and attention, decreased manual dexterity and visual and motor skills, changes in verbal fluency, obesity, are the most prevalent signs. (11, 12)



## **2.2. Epidemiology:**

Since the 90s, several studies indicate that OSA is more prevalent than previously thought and is often under-diagnosed (28, 29). This disease can affect any age group, but its prevalence is higher on middle-aged adults reaching 2 to 4%. It is estimated that OSA prevalence will increase by 30% in 2016 in association with concurrent increase of risk factors such as intake of alcohol and obesity (7, 16, 17).

Considering only data from polysomnography, its prevalence reaches 24% in men and 9% in women. OSA can occur at any age, reaching a peak incidence between 40 and 50 years of age. Particularly in hypertension (HTN), studies show a prevalence of OSA in 35% to 50% of hypertensive patients, reaching 70% in cases of refractory hypertension. Moreover, some 40% of hypertensive patients may have undiagnosed OSA. The prevalence of OSA in coronary patients is 30%; in patients with atrial fibrillation OSA is present at around 50% and in heart failure it may vary from 12% to 53% in published studies. In obese individuals, the prevalence of OSA reaches 40%, while 70% have increased weight or obesity (7).

### **2.2.1. Risk Factors:**

OSA is a complex and chronic condition that can be initiated and develop in the presence of multiple risk factors such as obesity, age, gender, genetic factors, craniofacial abnormalities, excess weight, smoking, alcohol consumption, upper airway anatomy, nasal congestion and hormonal changes during menopause, family and behavioral factors (6, 28). Several risk factors have been identified in the development of OSA but the most outstanding risk factor is obesity (6).

#### **2.2.1.1. Obesity:**

Obesity, especially when the deposition of adipose tissue is found in the upper part of the body, increases the risk for OSA between 10 and 14 times, with greater effects in middle-aged men (28).

The measure most often used to define the overweight and obesity is given by calculating the Body Mass Index (BMI), obtained by dividing the weight in kilograms and height in squared meters ( $\text{kg}/\text{m}^2$ ). (28)

Weight changes have also been associated with the progression or regression of OSA. In subjects with no OSA or with mild OSA ( $\text{AHI} < 15$ ), a 10% weight gain increases the probability of developing moderate or worse OSA ( $\text{AHI} \geq 15$ ). Extreme obesity defined

as a BMI  $\geq 40$  kg/m<sup>2</sup>. can lead to severe OSA and in some cases can lead to daytime and nocturnal hypoventilation, a condition known as obesity hypoventilation syndrome. The prevalence this syndrome has been estimated to be 25% in patients with OSA who are extremely obese. (6) The BMI measures the total body mass, but does not inform about the location of excess adipose tissue, it is necessary to use other anthropometric measurements to verify that the excess weight caused deposition of adipose in the upper body, thus it is necessary to measure the external circumference of the neck. which, when raised, is an indicator of excess deposition adipose tissue in the lateral pharyngeal areas and consequent narrowing of the upper airways. (28)

#### **2.2.1.2. Age**

The prevalence of OSA increases with age because overweight and obesity are more common in adulthood. Additionally, certain changes, intrinsic to the process of biological aging, begin to manifest itself more markedly, such as a higher rigidity of the thoracic cage and a lower muscle tone.

A high prevalence of OSA in the elderly may result from several factors including collapsibility an increased result of anatomical aging changes of pharynx. Loss of teeth also produces anatomical changes which can alter the dimensions and function of the upper airway (28).

#### **2.2.1.3. Gender:**

OSA is more common in males than in females, with a ratio of 2:1, probably due to higher risk factors in men. Menopause is a risk factor for sleep apnea, but the existence of OSA in childhood, adolescence and older age means that there is no simple positive correlation of OSA with age (16).

The increased incidence of OSA in women after menopause suggests that female sex hormones play a protective role or male sex hormones contribute to the genesis of the disease. These effects may result from hormonal influences on ventilation control over the mechanical behavior of the upper airway or in patterns of body fat distribution (28).

##### **2.2.1.3.1. Menopause**

In contrast to men, women with similar degree of obesity have less collapsible upper airway. This pathophysiologic difference in the upper airway anatomy could explain the overall lower prevalence of OSA in premenopausal women. The increased prevalence

of OSA in menopausal women draws again attention to hormonal differences in the pathogenesis of OSA. However, hormone replacement therapy has not been shown to be an effective treatment of OSA in post-menopausal women; therefore, other factors play a role and the optimal treatment for OSA in postmenopausal women remains continuous positive airway pressure (CPAP) therapy (6).

#### **2.2.1.4. Ethnicity**

There are ethnic differences in the prevalence and severity of OSA. There is some recent data suggesting that certain races or ethnic groups have a higher risk for the disease. The Afro-americans have higher levels of apnea than elderly Caucasians. These racial differences appear to result from anatomical risk factors that in african-americans are more pronounced such as soft tissue augmentation on the airways, rather than from the dimensional characteristics of the airways (6).

The prevalence of OSA in Chinese population-based studies was similar to that of the white population; despite a lower BMI (only 5% of men had a BMI greater than 30 kg/m<sup>2</sup>). A similar prevalence of OSA in these two populations can be attributed to cephalometric differences of White and Asian patients, such as an inferiorly positioned hyoid bone, an extended soft palate width and reduced upper airway soft palate (6).

#### **2.2.1.5. Craniofacial factors**

Craniofacial morphology may predispose for OSA by affecting bones and soft tissues, causing a reduction in the dimensions of the upper airway. Several structural anomalies have been described in patients with OSA, namely: reduction of anterior-posterior dimension of the skull base and reduction of the dimensions of the airspaces posterior and superior, inferior displacement of the hyoid, elongation of the soft palate, adenoid hypertrophy and / or tonsils, increased vertical facial dimension, retrognathia, micrognathia and class II malocclusion (28).

#### **2.2.1.6. Alcohol Intake:**

Alcohol intake at bedtime can have adverse effects on nocturnal breathing and even in the duration of apneic/hypopneic episodes. There is an association between alcohol intake and snoring, as alcohol relaxes the muscle and therefore increases the probability of pharyngeal collapse (28).

### **2.2.1.7. Smoking**

There is a positive association between cigarette smoking and OSA. Several mechanisms explain why smoking affects OSA, such as instability during sleep and mucosal inflammation of the airways. The association with OSA is relatively weak, but smoking may interact with and add to the cardiovascular risk (16, 28).

### **2.2.2. Consequences of OSA**

Untreated OSA can contribute to the development or progression of other disorders. If not diagnosed and properly treated, OSA can cause multiple complications, whose effects may project negatively at personal, family and social level, contributing to a drastic reduction in quality of life and also to an increased general rate of morbidity and mortality associated with cardiovascular and cerebrovascular complications (16, 28).

#### **2.2.2.1. OSA and Cardiovascular diseases:**

OSA may have hemodynamic consequences such as pulmonary and systemic hypertension, cardiac arrhythmias, ischemic heart disease, congestive heart failure and Cheyne-Stokes breathing in patients with congestive heart failure (28).

Obstructive apneas may lead to severe intermittent hypoxemia and CO<sub>2</sub> retention during sleep, disrupting the normal structured autonomic and hemodynamic responses to sleep. Apneas can occur repetitively during the night, increasing sympathetic activity to peripheral blood vessels and consequent vasoconstriction. This level of hemodynamic stress occurs at a time of severe hypoxemia, hypercapnia, and adrenergic activation. The nocturnal apneas initiate pathophysiological mechanisms which may act to promote cardiac and vascular disease (Fig. 2) (3).

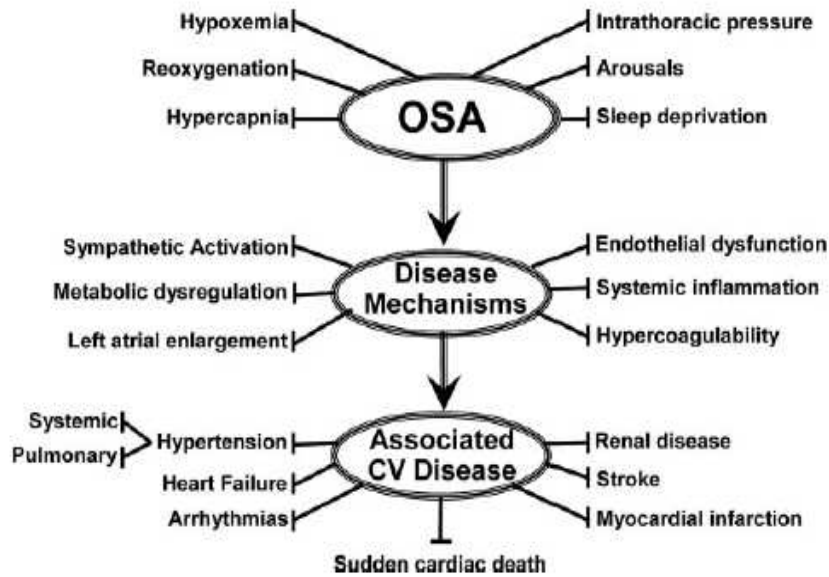


Figure 2. Source: Sommers, 2008 - Pathophysiological components of OSA; related to cardiovascular disease mechanisms (3)

#### 2.2.2.1.1 OSA and Hypertension:

Several reports have shown that the prevalence of HTN is greater in patients with OSA. The association between OSA and hypertension was seen in men and women, older and younger ages, all ethnic groups, and among normal-weight and overweight individuals. (4)

The episodes of apnea / hypopnea during sleep induce transient increases in blood pressure that can reach 30 mmHg or more in mean arterial pressure. During apnea there is an increased sympathetic activity which leads to an increase in blood pressure. There is a reduction in sympathetic activity by administering CPAP thus can contribute to a reduction in blood pressure. (28) OSA has been proposed as an independent risk factor for the development of essential hypertension because it can precede and predict the onset of hypertension (3).

#### 2.2.2.1.2. Other cardiovascular complications

Over 30% of patients with ischemic heart disease suffer from OSA. An AHI greater than 11 is a risk factor for heart failure, independent of other risk factors. Cardiac arrhythmias are frequently observed in patients with obstructive sleep apnea, especially during apnea bradycardia, followed by tachycardia reawakening when the apnea ends, and the change in heart rate caused by vagal stimulation. Other changes in heart rate can occur, but more rarely, such as ventricular tachycardia (3, 28).

#### **2.2.2.2. Cerebrovascular complications**

Among subjects with stroke, the incidence of sleep-disordered breathing may be greater than 50%. Obstructive sleep apnea is a risk but also a consequence of stroke. (106).

Taking into account that OSA causes HTN, and that this is a major causative factor in stroke, it is easy to understand the contribution of HTN to develop stroke in patients with OSA. Some data provide evidence that men with increasing AHI levels experience an increased risk of stroke. Increased risk may be through a number of pathogenic factors influenced by intermittent hypoxemia and sympathetic stimulation that influence the cerebral vasoregulation, atherogenesis, and atrial fibrillation. Among them are: the reduction of cerebral blood flow, the hypercoagulability blood, increased platelet aggregation, endothelial dysfunction, increased intracranial pressure and a change of cerebral auto-regulation triggered by changes in blood gases that have been described in patients with OSA (30, 106).

#### **2.2.2.3. Psychosocial consequences**

Excessive daytime drowsiness is characteristic of OSA with adverse effects on neurocognitive function, memory, and performance of diverse tasks. In relation to neurocognitive function impaired, patients with OSA have an increased risk for motor vehicle accidents. OSA causes impairment in performance and is associated with an increased risk of traffic accidents compared with the general population of drivers. Sleep apnea, with its repeated episodes of nocturnal hypoxemia and sleep fragmentation, will increase fatigue and sleepiness, which in turn increase lack of alertness while driving. As a result, there are increased collision rates in OSA sufferers. During the night can occur several manifestations such as nocturia, agitation associated with multiple awakenings and sometimes accompanied by intense diaphoresis. Sexual impotence develops in association with snoring. All these symptoms can contribute to a significant increase in the frequency of divorce. Still relatively frequent are morning headaches, decreased libido, impotence and psychological and cognitive changes. All this manifestations lead to negative consequences in lives of patients with OSA (28, 31, 32).

### 2.3. Diagnosis:

The diagnostic criteria established for OSA are based on clinical symptoms and signs during sleep evaluation including a physical examination and oriented sleep history, and findings identified by sleep testing.

During a routine consultation some questions should be done to access to a history of snoring, daytime sleepiness and an assessment of Body Mass Index, retrognathia, or hypertension.

A comprehensive sleep history in a patient should include an evaluation for snoring, witness apneas, breathless and or asphyxia episodes, excessive somnolence, Epworth Sleepiness Scale (EPS) evaluation, total time of sleep, nocturia, fatigue in the morning, morning headache, sleep insomnia or fragmentation, decreased concentration and memory.

The **diagnosis of OSA** requires the occurrence of 2 or more of the following symptoms: difficulty in breathing during sleep, fatigue during the day, difficulty in concentrating, reports of non-restorative sleep and frequent awakenings at night. The apnea-hypopnea index (AHI), demonstrated by polysomnography or cardiorespiratory polygraphy, must be greater than 5 per hour of sleep.

Considering the parameters defined by PSG or PG, OSA may be classified as mild, moderate and severe (Table 1) (12-15, 25).

Table 1 OSA Classification

OSA CLASSIFICATION	
AHI per hour	Classification
$5 \geq \text{AHI} \leq 15$	Mild
$15 \geq \text{AHI} \leq 30$	Moderate
$\text{AHI} \geq 30$	Severe

The physical examination should focus on the cardiovascular, respiratory and neurological systems, might indicate an increased risk for the patient. Special attention should be given to the presence of obesity, narrowing of the airways, neck circumference (> 43 cm in men and > 40 cm in women) body mass index > 30 Kg/m<sup>2</sup>, presence of retrognathia, narrowing peritonsillar, tonsillar hypertrophy, enlarged uvula, high arched palate, nasal disorders (25).

The two objective acceptable testing methods are **polygraphy**, a portable device, to be done at home of the patient, and **polysomnography** to be done in a sleep laboratory.

### **2.3.1. Polysomnography**

The polysomnography (PSG) is the *gold standard* for diagnosing OSA. It is performed in a sleep laboratory by specialized professionals, consisting in a simultaneous/continuous acquisition and analysis of neurophysiologic and cardiorespiratory variables during a night sleep. This device records electroencephalogram, electro-oculograma, electromyogram, electrocardiogram, oronasal airflow, snoring, thoraco-abdominal breathing movements, body position, oxygen saturation and heart rate. The registration of these variables provides important information for the sleep study: sleep staging, cardiac abnormalities, respiratory events, respiratory effort, snoring and O<sub>2</sub> desaturations. However it has some disadvantages: high cost, the need for continuous attention and of time on the part of medical staff, these disadvantages, together with the scarcity of diagnostic resources, has required the search for alternative methods, such as cardiorespiratory polygraphy, which does not require constant attention and is much less costly than PSG. (26, 106)

### **2.3.2. Polygraphy:**

Validation studies have been carried out for some of the respiratory polygraphy systems and various groups consider them an acceptable alternative to conventional PSG.

Polygraphy (PG) is a portable recording device more economical which allows the Polygraphic study at home not requiring supervision technique. It allows cardiorespiratory registration of nasal airflow, snoring, breathing movements, body position, O<sub>2</sub> saturation and heart rate. Although there is a smaller number of variables is considered a viable and reliable for the diagnosis of OSA. (26, 27, 106)

### **2.4. Physiopathology:**

The pathophysiology of OSA is complex. There are several factors that may contribute to the manifestation of this condition. The human upper airway is a multifunctional structure involved in performing functional tasks. The anatomy and neural control of the upper airways (UA) have evolved to allow these various functions. Due to the multiple functionality of the upper airways, they have the ability to change shape and close momentarily which is essential for speech and swallowing during wakefulness, this capability also offers the opportunity for collapse at inopportune times, such as during sleep (34).



The human airway is composed of soft tissue that can collapse when the muscle tone of the body relaxes, during REM sleep.

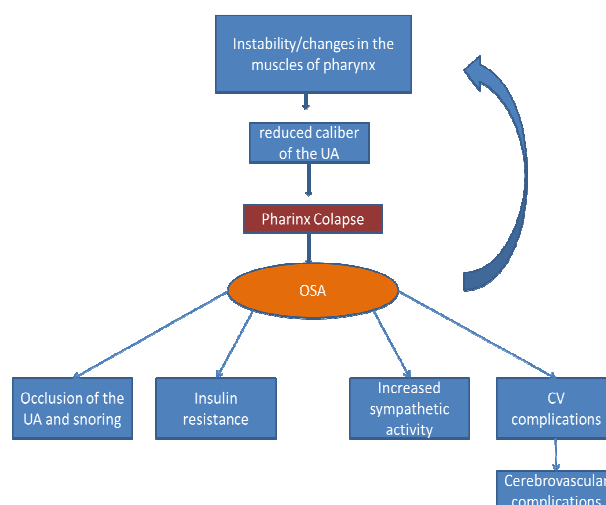
Currently it is thought that there are two main factors that contribute to the pathophysiology of OSA (35):

- structural craniofacial abnormalities may predispose patients with OSA
- deposit of high-soft tissue mass or abnormal tissue may also increase tissue pressure extraluminal and decreasing the threshold for airway collapse.

The upper airway obstruction occurs due to the collapse of the oropharynx and hypopharynx, by apposition of the tongue, by the lateral walls of the oropharynx and hypopharynx and by the soft palate. Occurring collapse of the UA and the interruption of the air flow, the muscle of the diaphragm does not interrupt your movement and the person remains breathing until it becomes sensitive to hypoxemia. This raises an awakening with the reopening of the AU, following new sleep, re-starting this cycle and thereby causing severe hypoxia and hypercapnia (23). Factors that reduce upper airway calibre lead to increased UA resistance, generating a more negative pharyngeal pressure during inspiration, and thereby predispose to UA occlusion during sleep. (36)

The narrowing of the anatomical UA is related to a neuromuscular hyperactivity of UA. Increased activity of the upper airways dilatator muscle is one important factor contributing to the improvement in severity of apnea (23, 34).

The hypoxia and hypercapnia during apneas cause a decrease in neuromuscular activity of the *genioglossus*, and *tensor palatoglossus veil palatini*, worsening UA dysfunction. These neuromuscular disorders may result from serotonergic malfunction and or central projections to the bulbar motor nucleus, generated by the repetition of the pattern caused by hypoxic apnea night (23).



**Figure 3: Scheme of the physiopathology of OSA**

## **2.5. Treatment:**

OSA should be approached as a chronic disease and requires multidisciplinary long term treatment. Thus, treatment of OSA must include generic and specific measures. Ideal therapeutic approach and development of an adequate treatment plan pass through the investigation of the etiology of OSA, the establishment of clinical severity, symptoms, presence of comorbidities relevant expectations patient and chance to improve their quality of life (25, 106).

### **2.5.1. General measures:**

General measures consist in adopting measures to combat any risk factors that enhance respiratory events. Thus, should be advised to avoid alcohol, tobacco, benzodiazepines, barbiturates and narcotics. The diet therapy should be recommended and weight reduction, as well as physical exercise and establishment of sleep routine, including a scheduled with sufficient number of hours and postural conditioning. (25, 37, 38)

### **2.5.2. Specific measures:**

In these specific measures include: pharmacological measures of positive pressure ventilation, oral prostheses and surgical measures.

#### **2.5.2.1. Pharmacological:**

The pharmacological measures have a very questionable data, as evidence scientific in its favor is scarce. There are no widely effective pharmacotherapies for OSA although there are some exceptions in case of individuals with hypothyroidism or acromegaly. However, some OSA patients, who do not tolerate CPAP and or have symptoms sufficiently severe, justify the use of pharmacological therapy. Among the drugs which act on the tonus of the upper airway, paroxetine, mirtazapine, physostigmine and donepezil improved to some extent indices OSA. Recent pharmacological approaches to the treatment of OSA, has focused on increasing the production of serotonergic neurons and enhance cholinergic activity, because both have been shown to increase the tonus of the upper airway (25, 38, 39).

In cases in which endocrine factors, such as hypothyroidism and acromegaly, are OSA substrate, it is recommended replacement therapy, which leads to significantly reducing the number of respiratory events (39, 106).

For last say that: in medical therapies to improve nasal patency Topical nasal corticosteroids can improve AHI in patients with OSA and concomitant rhinitis and thus may be useful to assist the main therapies for OSA. Moreover modafinil should be use in addition to PAP therapy for the treatment of residual excessive daytime sleepiness in OSA (38, 106).

### **2.5.2.2 Surgical**

A great variety of surgical procedures for the treatment of OSA have been described. Surgery aims to reduce obstructions of the upper airways in the nose, oropharynx, hypopharynx. It may be necessary to correct an anatomical obstruction before prescribing an oral appliance or positive airway pressure device. Surgery may be beneficial in selected cases as: usually patients with snoring and mild OSA, which have a cause amenable to surgical correction and in whom treatment with CPAP is not effective (40-42, 106).

The surgical interventions consist of the reconstruction of soft tissue and / or bone of the AU, with the aim of increasing its diameter and unblock the UA. So are several surgical procedures available, including: maxillofacial surgery, nasal surgery, uvulopalatopharyngoplasty, laser-assisted uvuloplastia, somnoplastia and radiofrequency volumetric reduction (42-45, 106).

The bariatric surgery, as adjuvant therapy is a means for achieving greater weight loss. It is indicated for patients with BMI > 40Kg/m<sup>2</sup> patients with BMI > 35Kg/m<sup>2</sup> with higher risk factors. So, this surgery, is indicated for obese patients that by this way may potentially condition the disappearance of the pathophysiology of OSA (25,106).

### **2.5.2.3 Oral appliances**

Oral appliances may improve upper airway patency by enlarging the upper airway by decreasing upper airway collapsibility. This type of device that will promote mandibular advancement are intraoral orthodontic appliances that move the jaw forward, increasing the diameter of the upper airways, reducing the possibility of pharyngeal collapse. These devices have proved effective in snoring, but in OSA their effects are not so evident. Their

efficiency tends to be lower in obese patients because skeletal and maxillofacial factors have less importance in the etiopathogenesis of apnea, compared with obesity (28, 46).

This therapy is commonly used in the treatment of mild and moderate OSA patients with few symptoms, or when other treatment modalities are not tolerated or are contraindicated. It can also be associated with CPAP or surgical measures in cases of severe OSA (106).

#### **2.5.2.4 Positive Pressure Ventilation**

Positive pressure air is intended to keep the unobstructed upper airway during sleep and thereby prevent the pharyngeal collapse (28). Positive air pressure aims to keep the upper airway unobstructed during sleep and thereby prevent the pharyngeal collapse. Applied through nasal, oral, or through an oronasal interface during sleep it is the preferred treatment for obstructive sleep apnea. There are 3 Types of PAP treatment: continuous PAP (CPAP), Bilevel PAP (BIPAP), and Automatic adjusting PAP (APAP) (47).

The use of such devices should be accompanied by patient education, adapting, adjusting and ambiance to the mask (116).

##### **2.5.2.4.1 CPAP**

Continuous Positive Airway Pressure is recommended as a treatment option for adults with moderate or severe symptomatic obstructive sleep apnea/hypopnea syndrome. (48, 49) A continuous positive airway pressure (CPAP) is currently the treatment form dominant and with more proven effectiveness in OSA. (106)

CPAP may provide different pressures. The optimum pressure is adjusted related to certain individual characteristics that include data ascertained by polysomnography. The CPAP reduces edema and congestion of the pharynx arising from microtrauma associated with snoring, and causes significant improvement in daytime sleepiness. This device has benefits in the pathology itself, improving the AHI and the reduction of risk factors. Besides that it as interference in the quality of life of patients because it improves the skills required in performing multiple daily activities, normalizes memory and cognitive function and mood. All these benefits only occur with continued and proper use (Table 2) (23, 28).

**Table 2 Benefits of CPAP , Source: Sugai, 2009**

<b>BENEFITS OF CPAP IN THE TREATMENT OF OSA</b>
<ul style="list-style-type: none"> <li>• Reduction of the number of apneas and hypopneas</li> <li>• Increase O2 saturation</li> <li>• Improvement of vigil</li> <li>• Decreased risk of cardiovascular disease</li> <li>• Decreased risk of high blood pressure</li> <li>• Improvement of cognitive functions</li> <li>• Improvement of mood and disposition</li> <li>• Decreased nocturia</li> <li>• Decreased risk of traffic accidents related to daytime drowsiness.</li> </ul>

This device also has some ancillary effects that may arise and lead to intolerance of CPAP as: mask allergy, conjunctivitis and dry eyes, facial irritation and dermatitis, rhinitis, claustrophobia, rhinorrhea, sneezing, dry mouth, sinusitis, headache, epistaxis, otitis or ear pain, belching, intolerance of the spouse, feeling of suffocation, tinnitus, aerophagia, central respiratory events, prolonged desaturations, anxiety, headache and chest discomfort and depression (Table 3).

**Table 3 Resume of Ancillary effects of CPAP. Source: Paiva, 2011**

<b>ANCILLARY EFFECTS OF CPAP</b>	
Allergy	Ear pain
Clautrophobia	Aerophagia
Rhinorrhea	Intolerance of spouse
Sneezing	Inmsonia
Dry mouth	Depression

#### **2.5.2.4.2. APAP**

The APAP has the particularity to provide an automatic adjustment of positive airway pressure during sleep. It may be initiated and self-adjusted so that unattended treatment of moderate to severe OSA in patients without significant comorbidities (25).

### **2.5.2.4.3. BiPAP**

The BiPAP allows to apply, during the respiratory cycle, two pressure levels. Usually it is indicated in OSA aggravated by respiratory failure, at that airway therapy must be implemented by choosing the ventilation mode that best suit for each case. Is an optional therapy where high pressure is needed (25, 28).

## **2.6 Anatomical and embryological overview**

### **2.6.1. Pharynx embryology:**

The development of notochord induces the overlying of embryonic ectoderm, located at the side of the midline to thicken and form the neural plate (neuroectoderme). The neuroectoderme gives origin to the Central Nervous System and to others structures. As the notochord elongates, the neural plate widens and extends cranially as far as the oropharyngeal membrane. As the notochord forms, the overlying neural plate begins folding into neural folds. The neural folds fuse to form the neural tube that separates from the ectoderm forming the neural crest. The neural crest cells (NCC) go through a transformation and migrate away from the neural tube. Some of the neural crest cells that leave the cranial neural folds will migrate along dorsolateral, ventrolateral and ventral pathways and differentiate as neurons of the sensory and autonomic ganglia, or as the melanocytes of the face and scalp (18, 19).

In the cranial region, the Cranial Neural Crest Cells (CNCC) leaves the neural folds in large fluxes to surround the primitive pharynx that will form the pharyngeal arches. (18)

It is the migration of neural crest cells into the pharyngeal arches and their differentiation into the mesenchyme that produces the maxillary and mandibular prominences, in addition to all connective tissue including the dermis and smooth muscles (19).

The CNCC from rhombomeres 1 and 2 and the caudal midbrain populate the first pair of pharyngeal arches; The CNCC from rhombomeres 4 populates the 2nd arch. The CNCC from rhombomeres 6 and 7 populate the 3, 4 and 6 arches. The NCC that migrates from cranial midbrain and caudal forebrain originate the frontonasal prominence. Other arches appear obliquely disposed, rounded grooves on each side of the future head and neck (18).

The pharynx arches contribute to the formation of the face, nasal cavities, mouth, larynx, pharynx, and neck (19).

- Palatogenesis – It begins in the sixth week and it develops in two stages: the development of primary palate and the development of a secondary palate. The palatal processes, arise as bilateral extensions from the oral aspect of the maxillary processes, reorient from a vertical position lateral to the tongue, to a horizontal position above the tongue, making epithelial contact along the anterior–posterior length of the palate (19)

Initially, the median palate process begins to develop from the medial nasal prominences. The primary palate forms the anterior/midline aspect of maxilla. The secondary palate is the *primordium* of the hard and soft palate. It begins to develop from two mesenchymal projections that extend from the interior of maxillary prominences. During the seventh-eighth week the lateral palatal processes assume a horizontal position above the tongue (159). In the primary palate, bone gradually develops, and extends from the maxillae and palatine bones into the palatal processes to form the hard palate. The posterior parts of palatal processes extend posteriorly beyond the nasal septum and fuse to form the palate, including the uvula (19).

## 2.7. Pharynx anatomy:

Pharynx is a fibromuscular tube that extends from the base of skull to the upper border of upper esophageal sphincter. It can be divided into three segments: nasopharynx, (from the base of skull to the soft palate) oropharynx (from soft palate to the pharyngoepiglottic fold) and hypopharynx (from the pharyngoepiglottic fold to the upper esophageal sphincter). The muscles of pharynx can be generically viewed as intrinsic and extrinsic; the intrinsic muscles constitute the superior, middle, and inferior pharyngeal constrictors along with thyropharyngeus and cricopharyngeus. Extrinsic muscles of the pharynx can be categorized in 3 subgroups: (20, 21).

- Group 1 — elevators and tensors of palate (levator veli palatini, tensor veli palatini, and palatoglossus);
- Group 2 — geniohyoid, stylohyoid, mylohyoid, thyrohyoid, diaphragm, stylopharyngeus, and palatopharyngeus, which cause superior and anterior movement of the larynx during swallowing;
- Group 3 — aryepiglottic, thyroarytenoid, and oblique arytenoids muscles, which close the laryngeal entry.

The 3 pharyngeal constrictor muscles, that form the outer layer, are arranged so that the bottom constrictor muscle is overlapped by the medium constrictor muscle, which in turn overlap the upper constrictor muscle. The constrictor muscles are not completely

circular. They originate from a lateral cartilage fixation, ligaments and bony points, therefore they are not present anteriorly, so there are spaces between them or between the superior constrictor muscle of the larynx and skull laterally. They are posteriorly they are complete and are inserted into the larynx raphe that extends from the pharyngeal tubercle of the occipital bone to cricopharyngeus muscle. The spaces are complemented by the fascia of the pharynx, but allow the entrance of muscles, nerves, and arteries in the wall of the pharynx. The muscle stylopharyngeus accompanied by glossopharyngeal and lingual nerve passes inferiorly to the superior constrictor muscle of the larynx. The muscle stylopharyngeus that originates medially from the region infratemporal, enters in the floor of the mouth passing through the space between the upper and middle constrictor muscles of the pharynx and joins the glossopharyngeal nerve on an external surface (20, 21).

The fascia of the larynx is located internally and externally to the muscle layer. The inner layer is pharyngobasilar fascia, it is fixed to the base of the skull, provides a firm layer which, with the help of the muscular layer, prevents distortion or collapse of the pharyngeal wall, maintaining an open airway. The outer layer of fascia is the buccopharyngeal fascia that is continuous with the pre-tracheal fascia. It extends to the skull base superiorly and laterally to cover the buccinator muscle (20).

### **2.7.1. Pharynx innervation:**

The muscles of the pharynx, except the *tensor veli palatini* and stylopharyngeus muscles, receive special visceral efferent (SVE) fibers of pharyngeal plexus that is originate in the vagus nerve, but carries fibers from the accessory cranial nerve. Sympathetic fibers originate in the superior cervical ganglion and with the branches of external plexus carotid and branches of the external carotid artery proceed to the pharynx. The sensory innervation of the upper nasopharynx is made by general somatic afferent (GSA) fibers of palatine nerve, branch of the maxillary nerve and posterior nasal branches. The rest of this region of the pharynx, the oropharynx and the upper hypopharynx is supplied with general visceral afferents (GVA) fibers of the glossopharyngeal nerve. The bottom of hypopharynx is supplied with general visceral afferent (GVA) fibers of the internal branch of the superior laryngeal nerve and recurrent laryngeal nerve (20).

The extrinsic muscles are supplied by the branches of cranial nerves V (trigeminal), VII (facial), IX (glossopharyngeal), X (vagus), ansa cervicalis, and XII (hypoglossal). Pharyngeal muscles are richly innervated, with a nerve–muscle fiber innervation, which is important for the “fine” control required for its function (21).



### **2.7.2. Vessels of the Pharynx:**

The blood supply of the pharynx is from branches of the ascending pharyngeal artery and from the Ascending palatine artery. The ascending pharyngeal artery arises from the posterior wall of the proximal external carotid artery trunk, and close to the source of the occipital artery. After a short common trunk, the ascending pharyngeal artery divides into two major trunks: anteriorly, the pharyngeal trunk, which is extracranial; posteriorly, the neuromeningeal trunk, which is intracranial and enters the posterior fossa through the foramen magnum (21, 3).

The ascending palatine artery arises close to the origin of the facial artery and passes between the styloglossus and stylopharyngeus to the side of the pharynx following between the superior pharyngeal constrictor and the medial pterygoid muscle to near the base of the skull. It divides near the levator *veli palatini* muscle into two branches: one supplies this muscle, winding over the upper border of the superior pharyngeal constrictor, supplies the soft palate and the palatine glands, anastomosing with the descending palatine branch of the maxillary artery; the other crosses the superior pharyngeal constrictor and supplies the palatine tonsil and auditory tube, anastomosing with the tonsillar branch of the facial artery and the ascending pharyngeal artery (21, 23).



### **3. Traditional Chinese Medicine Overview**



### 3. Contemporary TCM

The oldest existing therapeutic systems used by humanity for health and wellbeing are called Traditional Medicine (TM) or complementary medicine (CM). The origin of traditional Chinese medicine is uncertain. archaeological findings indicate that Chinese medicine has more than 5000 years. "*I Ging*" is one of the oldest approaches to a mathematical model and *Huangdi Neijing*, canon of Internal Medicine of the Yellow Emperor, dating back more than 2300 years (52, 53).

Always influenced by several periods of thought and acculturation in China and in world, Traditional Chinese Medicine (TCM) has been developing for centuries in clinical practice. It brings together Chinese traditional natural science and social science and combines them into an ethical and unique scientific medical system (53, 54). Since early, this biological model system, known as TCM, was based in two philosophical theories Taoism and Confucianism. So since the VII century BC, it was no longer regarded as something mystical and magical. And since the II century BC it has been perceived that the human being is a living being integrated in an environment that influences him. The two philosophies emphasized the importance of understanding the laws of nature and it was postulated that it was important that humans should integrate and respect these laws rather than to resist them. Like in the ecology laws and in science in general of our age, the human body and life was regarded as a microcosmic reflection of the macrocosm of the universe. Thus, concepts used to explain nature, such as yin/yang and Five Elements, became central to TCM theory. The goal of the clinician was to maintain the body's harmonious balance both internally and in relation to the external environment (52, 55). When practiced correctly, TCM can help protect and improve citizens' health and well-being (52, 53).

This vision of the human being attracted scientists and researchers from east to west of the world and has made great contribution to health of Chinese people for thousands years (56). In this increasingly globalized world, more than a quarter of the world seeks traditional Chinese medicine as a significant part of their health care. Part of this is due to the fact that conventional medicine and Chinese medicine does not compete with each other, on the contrary they are complementary (57). For the past 50 years, several hundreds of textbooks and monographs on TCM have been published. Nowadays, higher education is available in a substantial number of TCM universities, medical universities and faculties all over the world. This therapeutic system followed the progress of sciences and Western medicine combining contemporary diagnostic methods, such as laboratory tests and imaging, with traditional diagnostic techniques (107).

Lately the theory of Chinese medicine has been represented as a rational and simple mathematical model, which shows general laws and relationships between physiological and pathological process in human organism. As in the case of the Heidelberg model (described below), there are also other scientists who are showing that Chinese medicine can be put in a rational way (58).

Examples of that are Teppone and Avakyan. They theorized that Chinese physicians described the physiology and pathophysiology of the intercellular spaces and cavities of the body through the "*Zang Fu*" theory. Therefore the system of acupuncture points is seen as part of intercellular spaces which, due to their morphological and functional complexity, allow interactions between the interior of the body and the surroundings. They understand the Chinese view of human wellbeing and its limitation in a three dimensional space, as a kind of cybernetic model by which this complex system can have common managing or controlling parameter. In this way, they tried to explain the concept of "Qi" as a unit of measurement relatively universal. They thought "Qi" as the parameter "X" in the equation  $y = f(x, z)$ , where "z" is considered the intensity of heat produced, which describes the predominance of endothermic or exothermic chemical reactions in the human body. These authors consider that the Chinese diagnosis is necessary and sufficient to determine "excess or defect" of the conditions of the conduits  $y = f(x)$  and "excess or defect" and "hot or cold" of the pathologies of organs (zang)  $y = f(x, z)$  (58, 59).

In addition, since Gottfried Leibniz, (German scientist, mathematician and philosopher) the Yin and Yang are considered a binary system of calculation and comparison. This system is a simple way to describe the variability in the world. (58, 59) For Xiaoding Cao "the regulation of yin and yang is a fundamental principle in clinical acupuncture. Diseases result mainly from relative imbalance of yin and yang (or deficiency) or yin excess (or deficiency). The concept of yin-yang is the basic concept of all the oriental sciences it matches the precondition for the origin of all natural phenomena. The yin-yang balance in all vital processes of adaptation of the living beings and their environment is primordial (60, 61).

The concept of the movements tries to explain the evolutionary processes of nature, of the disease, of health and of the universe. it represents an analogous vision of the different correlations of the environment with Man. It Indicate the dynamic interactions between the functional units (61, 62).

Although it is important to emphasize the rational character of Chinese medicine it is significantly more relevant its great heuristic value of concepts designed according to cultural patterns of Chinese civilization. The Chinese physicians of antiquity, through

therapeutic and clinical observation and experimentation, developed explanations for the results / phenomena they found (63).

### **3.1. Acupuncture:**

In our days acupuncture more and more has been gaining attention in modern medicine (64). The research on TCM, in modern scientific ways, has “just started”. Scientific studies for endorsing its clinical effectiveness and benefit are mandatory. Researches on TCM, in the last decades have been more extensive. There has been a great effort to develop controlled clinical trials. Although with many difficulties and sometimes limitations, these results have been published. Considering this the WHO said, in its report on the research in TCM, that practitioners and researchers of TCM should be encouraged to do more research. In 1997, the National Institute of Health of the United States of America pointed out some goals for the future of Acupuncture and concludes that more research should be conducted to clarify the physiological and biological effects of this therapy. In 2007, the Society for Acupuncture investigation reiterated these goals (65, 66, and 67).

Studies in neurophysiology concluded that acupuncture has the main function to mediate the body homeostasis, acting mainly in the balance of autonomic, neurochemical and humoral functions (13).

The functional activities of needling will promote self-regulatory systems and regulate the balance of normal physiological activities. In cybernetics, a homomorphic machine, (used, for example, in biological engineering) is similar to the structures of human body. If a part of the body is slightly deviated from the balance state, the higher and lower limits of the neural network can be restored by the interactions between the different parts, so the body can return to its balance again. In other words the body has self-healing capacity. However, if the imbalance is severe, it will need additional interventions, only then, the ability to recover could be increased as well as the recovery of the primordial balance.

The regulatory action of acupuncture is not completely clear, yet. However, today it is accepted that three general mechanisms can explain this action. Energetic, neural and humoral mechanisms (61, 63, 68).

- Energetic mechanism:

A growing number of scientists see the TCM as a cybernetic model. In terms of cybernetic, the conduits (sometimes also called meridians) are information pathways that connect whole body; upper with lower parts of the body, left with right, interior with exterior and all of them together. They explain the conduits as a relationship among various parts

of the body. This corresponds to the classical conception of “Energy pathways”, the conduits. The human body has multiple levels of neural networks that transmit information of different kinds. When an organ or tissue or system, becomes imbalanced, information of these disorders are transmitted through specific areas of the body. These areas are reflex points (acupoint) or information zones. To the physiologist Guan Yuan-Jin, one of the world’s forefront medical acupuncturists, an acupoint is actually the location on the body surface outputting internal information and inputting treatment information from acupuncture. He and his network, in 1976, called to the regions of body surface, information zones (63, 68, 69).

- Neural mechanism

This mechanism made the ancient Chinese philosophical theories, known as TCM, started to have a scientific basis. Recent research on the action of acupuncture analgesia has brought significant benefits to the understanding of this mechanism. Generally, is considered as neural effects due to interaction of different sensory inputs within the Central Nervous System (CNS). The integration of the needling signals may occur at different levels of the CNS such as spinal cord, brainstem, thalamus, caudate nucleus, cerebral cortex to relieve symptoms (68).

- Humoral mechanism

It refers to the production of substances that are secreted into the blood through the action of acupuncture. Clinical facts indicate the role of the humoral factors in this TCM technique. These factors include endogenous opiate-like substances and many neurotransmitters such as: serotonin (5-HT), acetylcholine, non-epinephrine, dopamine, among others; and include hormones like prolactin, growth hormone (GH), thyroid-stimulating hormone, (TSH), cortisol, inter alia. Among the humoral factors, endorphins or enkephalins, are the most significant. The action of acupuncture can occur directly through the autonomic nervous centers and indirectly through the endocrine system to regulate various visceral functions and secretions of the glands. The release of level of the endocrine substances, found in blood, depends indirectly on the CNS (63, 68).

Acupuncture probably acts on related organs directly through effects on hormone secretion and acts on target organs through the feedback control of hormone secretion. Neural and humoral mechanisms are associated during regulatory process of acupuncture. Sometimes neural factors are primary to humoral factors, but sometimes it is in the other way round (68).

If the intensity and duration of needling is insufficient the neuro-humoral factors will not be activated to inhibit to disorder effectively. On the other hand an overly long or intense needling will become nociceptive instead of non-nociceptive (68).



In summary acupuncture change the bloodstream, promotes the release of hormones, helps to increase host resistance, resistance to disease, regulates and normalizes body functions and promotes metabolism (63)

### **3.2. Relationship between the conduits and the nervous system, blood vessels and lymphatic vessels**

#### **3.2.1. Relationship between the conduits and the Nervous System:**

The morphological observation of 324 points revealed that 323 (99%) have innervation of cranial and spinal nerves; 304 are related to superficial cutaneous nerves; 155 with deeper nerves and 137 with deeper and superficial nerves. Similarly, the acupuncture points and the nerves of its correlated organs belong to the same spinal segment or to the interior of the same nerves segment to which the organ belongs. The conduits with internal-external relationship, also belong to the same spinal segment (64, 68).

#### **3.2.2. Relationship between blood vessels and conduits:**

Observations showed that among 309 points, 24 are on top of an artery, while 262 are adjacent to an artery, and from the location of acupuncture points we can see that the conduits are closely associated with blood vessels. The arterial vascularization in the area of acupuncture points has certain ways - regular convergences, irradiation or, less regular arrangements. Those who have regular arrangements, the points are located frequently in the center of such arrangements (64).

#### **3.2.2. Relationship between conduits and the lymphatic vessels**

Research has found that the conduits are related to lymphatic plexus or to lymphatics vessels and lymph nodes. The conduits *Regens (Du mai)*, *Respondence (Ren Mai)* and *Zonal (Dai Mai)* are related to the lymphatic plexus. The conduits, Pulmonal, Stomachal, Cardial and Lienal, almost entirely in vascularization of lymphatic vessels, adapting deeply or superficially, to their corresponding distribution. It showed also that the lymphatic vessels run along the conduits yin and are fit together or in place of point *copulatio trium yin - L6 (Sanyinjiao)*, adapting both in distance, as in depth. (64)

Studies in bio-cybernetic stated that the conduits are a control system of the human body and stated that there are several species of regulation and control processes

in the body, as body temperature, blood pressure and blood sugar. Thus, the state of equilibrium of the conduits can aid in disease diagnosis and regulating the state of equilibrium of the conduits will improve the treatment of disease. Therefore, it can be considered that treatments of acupuncture, moxibustion and all techniques of Traditional Chinese Medicine have much in common with the cybernetic theory (64, 68).

### 3.3. Microsystem acupuncture

A feature of modern acupuncture is the rapid development of the principle of microsystem acupuncture. Microsystems in acupuncture correspond to reflexive areas with particular value in diagnostics and therapeutics. The microsystem acupuncture is an important ramification of the traditional acupuncture. It is based on particular somatotopic fields comprising specific points of correspondence and in the idea that in each small anatomical structures, there is a representation of the whole body or of body regions. Currently there are several microsystems recognized by practitioners of Chinese Medicine worldwide as: Auriculotherapy, Scalp acupuncture, Nasal therapy, Hand, Limbs and Face acupuncture (70, 71, 72).

Microsystem acupuncture theory arises in embryology, in concepts of physics and modern biology. In fact, microsystem acupuncture may be based on the principle of fractalization found in nature. The number of projections of this kind of acupuncture onto skin surface and mucous membrane is potentially unlimited. This projections are an extrapolation not only morphological, but also functional. It is not possible to explain such varied reflections simply by neuro-humoral connections. However, the clinical efficacy of microsystems is irrefutable. The fractal theory, a recent influence on acupuncture, relates the fractal field with the structure of the human body. This theory is able to explain the appearance and structure of microsystems of acupuncture and their activity. However, there is a need for scientific exploration and elaboration of the physiologic mechanisms involved in these microsystems to evaluate treatment effects (71, 73).

Recently, the **fractal theory** has been recognized as the basic principle behind nature's self-organization. This theory can be potentially applicable to all disciplines of new organizational phenomena (71, 74). There are several examples of fractalization in human physiology, anatomy, behavior, inter alia. The heart beat sequences, respiratory tidal volume, ion channel kinetics in cells membranes, glycolysis metabolism, DNA sequence mapping, brain, intestine and placenta linings, airways in the lungs, arterial system in kidneys, blood vessels in circulatory system, retinal vasculature, retinal vasculature, neuronal growth patterns are just some examples (75-77). Applying this model to acupuncture, it describes the conduits as the final wave cycle of an organism,

with projections onto the body surface at the level of the acupuncture points. According to this concept, the main function of the conduits is to provide an information exchange between an organism (microspace/microcosms) and its environment (macrospace / macrocosms). The final goal of this exchange is the adaptation of an organism to the changeable conditions of its environment. The pathology of an organ or of a system, within the organism, or of a traumatic injury is momentarily reflected in all acupuncture systems on the corresponding region. So, sometimes, to treat a health disorder, it is easier to use a microsystem, where all the information about an individual is concentrated on a limited surface (73).

### **3.3.1. Scalp Acupuncture**

As noted above, scalp acupuncture (SA) is part of microsystems acupuncture. This type of acupuncture is performed by punching needles into specific acupuncture points on the scalp to treat diseases. The SA, although it was already spoken in ancient china, it gains real highlight in the 20th century, when it makes the link between the classical notions of TCM and neurophysiology. Thus, SA is a contemporary acupuncture technique integrating TCM needling methods, with western medical knowledge. This kind of acupuncture often produces results just with few needles and usually brings immediate improvement (78-80).

#### **3.3.1.1. Historical overview**

The oldest book of Acupuncture known, *Huan Di Nei Jing*, described already, the relationship between the head and body, at the level of physiology, pathology and treatments of that time. In that book are also registered the first points of SA, besides more, citations of acupuncture treatments in the head can be found throughout classical literature (71, 81, 82).

The early mappings of the SA began to be drafted in 1930, through the work of *Huang Xuelong*. Since 1950, with the development of neurophysiology, several doctors have explored correlations between the brain and the human body. Then Fan's SA gives special attention to cortical *homunculus*; Tang proposed the existence of two homunculi, one in prone area and another in the supine zone; Zang and Shun formulated points of penetration in the head, and Zhu created the concept of therapeutic lines of the head (71, 80, 82).

It took 20 years until it could find a central theory that incorporates brain functions on the principles of Chinese medicine. Only in 1971, a Chinese neurosurgeon, Jiao Shunfa, systematized the SA and its correspondences. Dr. Shunfa divided scalp areas in motor and sensory stimulating, through the scalp, the different functional areas of the body (71). Another physician, Toshikatsu Yamamoto, an anesthesiologist Japanese developed a concept of SA, based on the mappings of auricular acupuncture of Nogier, where different parts of the body are represented in the scalp. These zones are regions of the scalp that may be more or less painful as the pathology in question (80, 82).

The SA quickly spread all over the world and in 1983, the WHO was requested the elaboration of a standard nomenclature for the points of SA. In 1989 the WHO recognizes the SA, which now has a standard nomenclature. Since then, the techniques and applications of this type of acupuncture has been developing with more studies and research (71, 81).

### **3.3.1.2. Scalp anatomy**

The scalp is the soft tissue envelope of the cranial vault. It is divided in four regions frontal, parietal, occipital and temporal, bilaterally. At histological level it includes five layers of soft tissue: skin, connective tissue, galea aponeurotica, loose areolar tissue and pericranium.

The skin of the scalp is thick and contains numerous sweat and sebaceous glands, a large blood supply, and hair follicles. The connective tissue is a fibro-fatty layer that connects the skin to the underlying aponeurotica and provides a passageway for the nerves and blood vessels. Galea aponeurotica (epicranial aponeurosis) is a hard connective tissue, fibrous tissue that runs from the frontalis muscle anteriorly to the occipital muscle posteriorly. The loose areolar tissue connects is between the galea aponeurotica and the periosteum. It is a zone with texture laxa and allows the three layers of the scalp to move superficially over the periosteum (71, 80, 83).

#### **3.3.1.2.1. Innervation of the scalp**

Various nerves innervate the human scalp. Roughly speaking, the set of nerves more significant of the scalp are the ophthalmic and maxillary branches of the trigeminal nerve and the ventral and dorsal branches of the upper cervical nerves (80). The sensory innervation can be separated into two components: anterior the innervation comes from supraorbital and supratrochlear branches of the ophthalmic nerve while posteriorly comes from occipital nerve, and third greater occipital. The last two subsequent nerves are

branches of C2 and C3, respectively. (20) The supratrochlear and supraorbital nerves originate from the ophthalmic division of the trigeminal nerve. The greater occipital nerve runs up to the vertex. The lesser occipital nerve innervates skin behind the ear. The third occipital nerve also provides some innervation. The zygomaticotemporal nerve, arising from the maxillary division of the trigeminal nerve, innervates the skin of the temple. The auriculotemporal nerve, derived from the mandibular division of the trigeminal nerve, innervates the posterior portion of the skin of the temple (84).

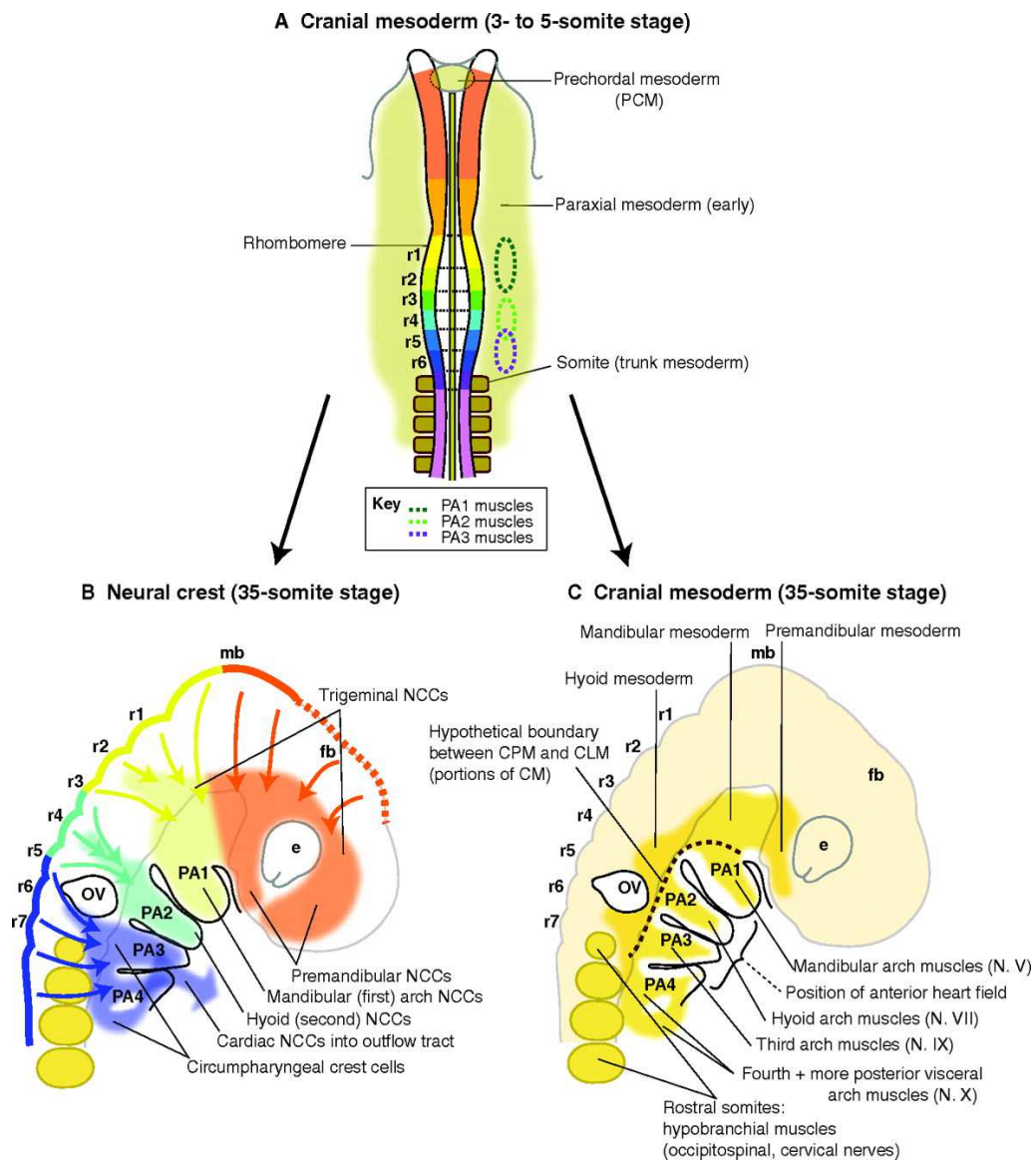
#### **3.3.1.2.2. Scalp blood supply**

The scalp has an abundant blood supply from branches of the internal and external carotid arteries. There are five pairs of the scalp arteries on the left and right. There are three pairs anterior to the ear artery supratrochlear, supraorbital artery and the superficial temporal artery. The two pairs posterior to the ear are the posterior auricular artery and the occipital artery. All originate directly from the external carotid artery, internal carotid or indirectly and all go forward to the cranial vault; all arterial branches will be anastomose forming a network that provides an abundant supply of blood to the scalp. (81, 20)

The veins of the scalp arteries follow considerably the same name, and drain, mostly, into external carotid veins (80).

#### **3.3.1.2.3. Cranial nerves embryology**

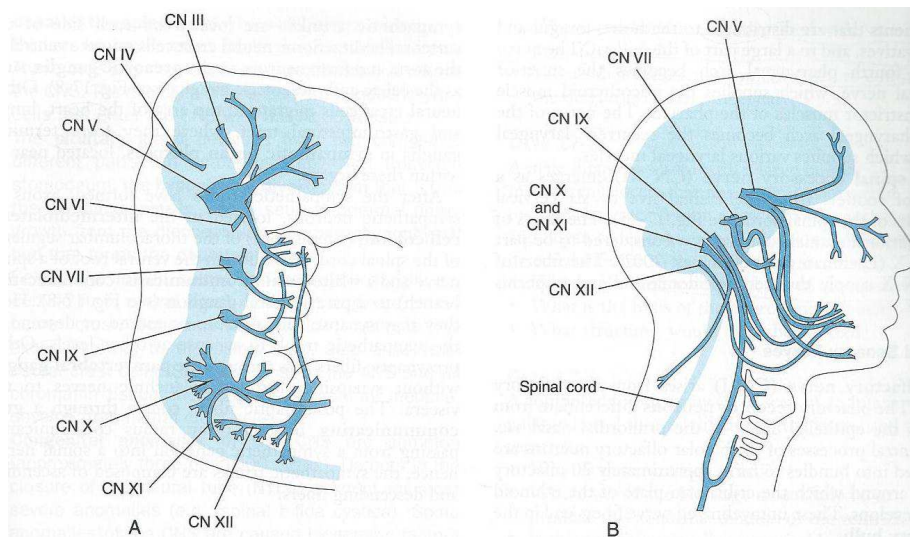
The neurulation in all vertebrate embryos is part of organogenesis. Until the phase of gastrulation, develops, mainly, the outline of the digestive system. In the subsequent stage neurulation, starts the nervous system development (Fig 4) (20).



**Figure 4: Cranial nerves embryology; Source: [www.dev.biologist.org](http://www.dev.biologist.org)**

In embryonic period which extends from the 3rd to 8th week of development, the three germ layers, including the ectoderm, endoderm and mesoderm, catalyze the formation of specific organs and tissues. The cells of the paraxial mesoderm (somitic) organize themselves in blocks, on both sides of the midline, to form somitomers which will appear first in the cephalic region. This results initially in 42 to 44 pairs of somites that appear in the occipital area until day 20. At week 4, there is a reorganization of the somites and the ventral and medial somites become polymorphic and will form the sclerotomes that form the vertebral column. Dorsolateral cells of somite comprising the dermatome, which forms the dermis and subcutaneous tissue in that segment. A dermatome represents an area of the skin supplied by a single nerve. According to Kemp, citing Dubuisson, the "field of C2 spinal root overlaps the C1 and C3 dermatomes, the trigeminal dermatomes, and the territory of the lower cranial nerves that innervate the ear." The occiput, the neck and the

submental region are related to C2 dermatome. The dermatome C3 may range from the clavicle to the mandible and extend to the ear (20, 84, 85)



**Figure 5: A, Schematic drawing of 5 week embryo showing the distribution of most of the cranial nerves, especially those supplying the pharyngeal arches. B, schematic drawing of the head and neck of an adult showing the general distribution of most of the cranial nerves. (85)**

The Greater Occipital Nerve, comes from the dorsal branch of C2 and innervates the C2 dermatome. The Third Occipital Nerve, comes from the dorsal branch of C3 and innervates the C3 dermatome. The Lesser Occipital Nerve is a sensory branch of the ventral ramus of C2. The Great Auricular and transverse cervical nerves are sensory branches of the ventral rami of C2-C3. At the root level, the dorsal segment is segregated into sensory fibers and the ventral segment is segregated into motor fibers. At the levels of the spinal nerves and rami, the sensory and motor fibers are mixed. Thus, cutaneous fibers, may arise from dorsal and ventral rami. The Lesser Occipital Nerve, the Greater Auricular Nerve, and the Cervical Transverse nerve emerge together from the cervical plexus and innervate the anterior and lateral regions of the neck (Fig 5) (84, 85).

### **3.3.1.3. Scalp acupuncture overviewing in Traditional Chinese Medicine terms:**

As in the biomedical view of SA, the vision of Chinese medicine of SA explains it by the type of SA in question. When researchers explain SA using the channels theory, they generally look at the conduits and collaterals vessels as a network, and the head as the convergence of all “yang conduits”. For this theory, stimulating points of the conduits or vessels collaterals of the head, you will make up the regulation of brain function. There

are other researchers who say that SA can be interpreted as "front-mu" points of the brain, just like the "mu" points of the belly this points regulate the related organ by stimulation of the point in the skin above the organ . There several theories about SA, some more traditional, some more biomedical, however a most recent theory, about the SA, is the holographic theory of Prof. Zhan Ying-qing Shandong University that uses concepts of fractal theory used to explain the self-organization of nature (71, 83) .

### 3.4. Heidelberg model

As already referred in this thesis, the Heidelberg model of Chinese Medicine is a rational model that explains the general laws of Chinese medicine, organic processes of human beings, physiology and pathology, unifying the contemporary medic-scientific knowledge, with the concepts of different schools of Chinese medicine. This model sees Chinese medicine as a novel vegetative medicine.

The most important characteristic of the Eastern world is the consciousness of harmony and mutual interrelation of all things and events. All things are seen as interdependent and inseparable. The quantum theory of physics, forces us to see the universe as a net of relationships between various parts of an unified whole. Within this "unicity" is recognized individuality, and the differences and contrasts are seen as the relative "unicity". The ancient Chinese civilization realized that opposites are not absolute knowledge belonging to different categories, but rather two sides of the same reality. There is a dynamic equilibrium in which opposites are interdependent which means that reality is seen as a manifestation of the interplay between opposites. To these opposites they called *yin* and *yang*. Fritjof Capra illustrates these concepts by giving the example of a ball that runs through a circular path. If this circular movement is projected becomes an oscillation between two extreme points, *yin* and *yang*. In projection, the ball velocity will change, and when approaching one extreme, it will slow and change direction, accelerating once again to slow down over again, when approaching the other extreme. (86) (Fig.6)

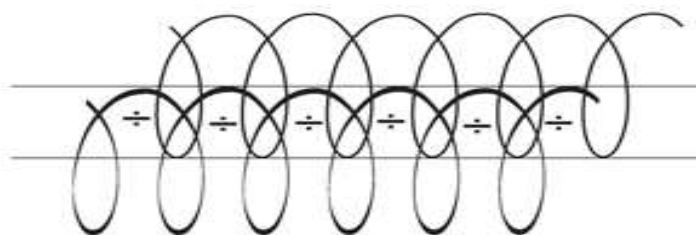
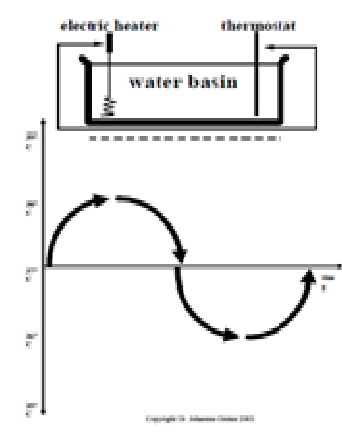
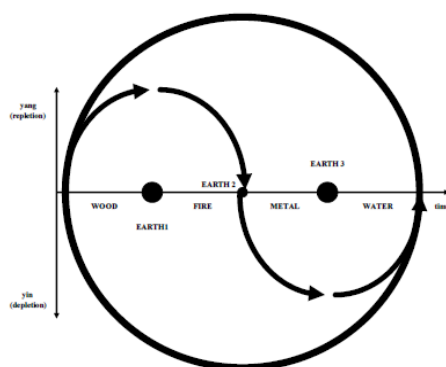


Figure 6 schematic representation of an oscillatory movement. Adapted from: Ventegodt , 2006 (87)



In Heidelberg model of TCM, *yin* and *yang* signs are considered as a mathematical expression of numbers. They are seen as a binary system which enables to describe a circular process. (66) The Heidelberg model of TCM presents a cybernetic model to systematize the diagnosis and treatment of TCM. Greten as define this medicine as “a system of sensations and findings designed to establish a functional vegetative state”. This state may be treated by 6 therapeutic disciplines: Chinese pharmacology (phytotherapy), *Qigong* (biofeedback neurovegetative exercises, dietetics, Chinese manual therapy (*Tuina*), acupuncture and psychotherapy of TCM (58). Chinese Medicine is based mainly on a system to describe functional abnormalities by their sensations (signs and symptoms). The specific malfunction/ dyssensation is felt in a specific way by the patient; symptoms come from specific dysfunctions. In a state of health, there is a harmonious balance between *yin* (structure, substance) and *yang* (function), a balance between ascending and descending vectors of human regulation (homeostasis). They are physiological aspects of the body. *Yang* represents the driving force for activities, warmth, lack of fluids. *Yin* represents deep rest, cold, dampness and it nourishes the tissue. In the *yang* phases sympathetic functions are more dominantly present, in the *yin* phases are the parasympathetic functions that are relatively more present. We can find, such paired *Yin-Yang*, at different levels in human body. The DNA strands that form the double helix; Kinases (*yang*) and phosphatases (*yin*) of cellular proteins; the pro-oxidants and anti-oxidants in lipoproteins; in the regulators Ang II, endothelin, and aldosterone (*yang*) and reciprocal counterbalanced bradykinin, prostaglandins, nitric oxide, atrial natriuretic peptide and glucocorticoids (*yin*) (58, 62, 69, 88, 89).

fou qi emblem: a symbol for the regulatory meaning of yin, yang, and the phases



**Figure 7** Fou Qi, adapted from Greten, 2008 (58) **Figure 8:** Thermodynamic system, adapted from Greten, 2008(58)

These regulatory fluctuations can be described by circular functions, in a simplistic manner, resembling a sinus wave. So, the state of health is regarded as a sinus wave.

(58, 66) and it can be represented in the famous symbol called *Taiji*. Like in a thermodynamic system, (i.e. water basin) (Fig 8) when processing this regulation, emerge internal movements or vectors (Wood, Fire, Metal, Water). There are four kinds of movements, directed to each other, in a coordinate system. The concentric force that balances the movement vectors and keeps the body regulatory function with circular characteristics is called Center. In a coordinate system this force is an axis that represents the target value of the regulation of body. Regarding to the phases, being the Centre, it has functions of assimilation and transformation, so that the continuum of the equilibrium is kept. (58)

The four movements can be allocated to body regions and the clinical indicator signs can indicate the functional state of that part of the body. This allocates the regulatory states to human anatomy. Even so, this allocation is different from the western pathophysiology. They are just patterns caused by the vegetative system. To the cluster of indicator signs, the manifestations, of this movements the HM of TCM calls it Orbs. (58, 66)

In the sinus wave of regulation there are vegetative functional tendencies that the HM calls phases. In the course of the sinus wave there are points of transition from one phase to the other. These transitions should be clear. They must allow that the power of the movement can be processed to the next phase. Thus, the transition state can be an interpretive sign of the state of health (58, 72)

### 3.4.1. Diagnostic process according to the Heidelberg model of TCM



Figure 9 Scheme of the diagnostic process. Adapted from Greten 2008 (58)

Diagnosis of traditional Chinese medicine follows two essential steps: The actual symptom and the interpretation of the symptoms.

#### **The first step – the actual symptom**

Analyzes the constitution, agent and the affected *orb*. By the constitution can be verified the patient's inner nature, his tendency of action-reaction, based on their phenotype and in his body language/communication. The agent or pathogenic factor is regarded as a functional power that causes changes in the functional properties of the

individual and produces its own clinical signs, inducing diagnostically relevant signs (*orbs*). The agent can be classified as exterior, (*ventus, algor, ariditas, aestus, ardor*) interior (*ira, voluptas, maeror, timor, pavor, sollicitudo, cogitacio*) and neutral (bad nutrition, accidents, inter alia) agents. The affected orb will indicate the clinical manifestations, the functional state of a body region, which correlates with the functional properties of a conduit. (58, 63, 66, 90,)

### The second step - Guiding criteria

It is an Interpretative approach of body regulation, according to Heidelberg Model. The body regulation is observed at four different levels: first at neurovegetative level (*repletion/depletion*), second at humorovegetative level (*Calor/Algor*), third at neuroimmunological level (exterior/interior); fourth at structural, cellular level (*yin/yang*). To this doctrine of bodily regulation, whose components allow us to perform functional diagnosis of the patient, the model of Heidelberg called **Guiding Criteria** (GC). (90)

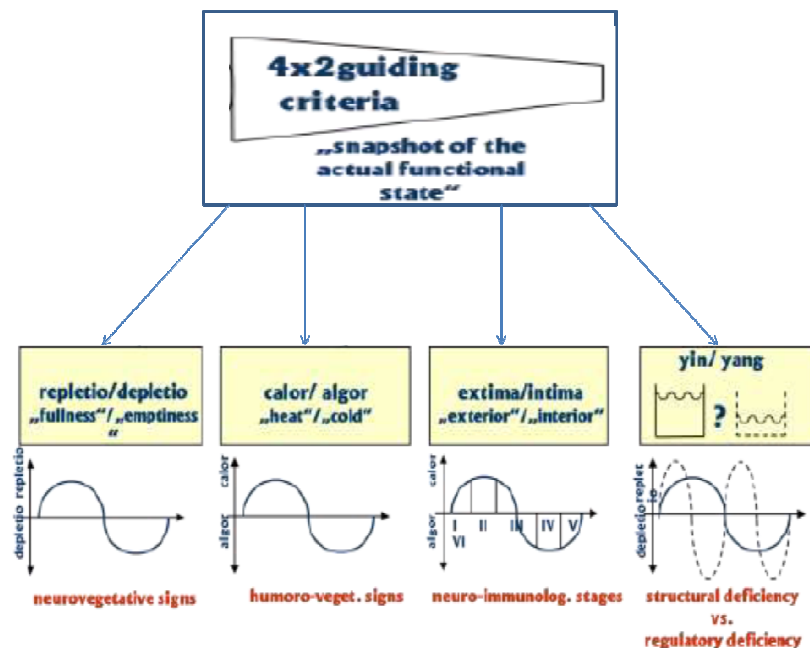


Figure 10: Four Guiding Criteria. Adapted from Greten.

**Repletion/depletion** – Quantifies and qualifies the functional capacity induced by the neurovegetative system. It evaluates the clinical signs that are believed to be originate primarily from “Qi” and Orbs. In general, signs of repletion indicate too much “Qi”, an excess of vegetative stimulation. Signs of Depletion indicate lack of “Qi”, a lack of activation, an excess of de-activation. (63, 66, 90)

**Calor/Algor** – describes the activity of “xue”. It is related to microcirculation and to humorovegetative system. It evaluates the signs that are believed to originate from the effects of “xue”. In western terms these signs include the local interdependent mechanisms of plasma, blood cells, endothelium and functional tissue of an organ and also it include an activation of body fluids, involving responses in the context of fluid distribution, supply and circulation. Calor means overactivation of “xue” (microcirculation) and algor means lack of signs of functional microcirculation. (63, 66, 90)

**Extima/Intima** - evaluates the level of achievement of the effects of an exterior agent, when it invades the body. According to Prof. Manfred Porket, from the western point of view, it refers to clinical signs induced neuro-immunologic mechanisms. (66,69,90) The most common pathophysiological model, underlying this mechanism is the model of six stages of Zhang Zhongjing, called *Shang Han Lun* (treatise on cold induced diseases). This model of the six stages describes the process of the agent *algor* damaging the body (63, 90, 91).

**Yin/Yang** – allows distinguishing whether the symptoms / signs correspond to a primary dysregulation, a functional dysregulation (yang) or if these symptoms represent a secondary dysregulation, a structural deficit, a deficit in functional tissue (yin). Therefore, allows to distinguish if the origin of the signs / symptoms is at the level of regulatory function or at a structural level. If the functional tissue is in deficiency, it will be up-regulated for achieve the proper function. However, this hyper-regulation cannot be maintained, so, after a hyper-stimulation of the functional tissue, follows a functional deficit, in other words, after a deficit of yin follows a yang deficit. (63, 66, 90)

The HM of TCM showed that the TCM diagnosis can be regarded as the vegetative state of the body, which can be defined by key symptoms. According to the HM, acupoints promote vegetative reflexes that have to match with the vegetative state of the patient, in order to the treatment be clinically effective. One clinical scenario of western diagnosis may, therefore, represent a multitude of diagnosis in TCM. That is why is not easy to do research, in TCM, when the inclusion and exclusion criteria are based in Western medicine. Usually there is a great risk that the acupuncture treatment is may be appropriate for some patients, in a certain a vegetative state, while it may not match the vegetative state of other patients. (63)

### 3.4.2. Pathogeny - Overview of the model of Heidelberg

Health is the result of a constant equilibrium of a phase (vegetative tendency). Normally there is continuity in the changes and alterations at which the body and psyche are exposed, in daily constant interactions with their environment. Nevertheless, sometimes the vegetative tendency becomes more intense and signals, the manifestations of this tendency, become more dominant. When this happens, the *continuum* of regulation is disrupted, and in the body, arises a pathological manifestation. Thus, there are two functional states: the *continuum*, in which the functional manifestations of vegetative tendency disappear, during the homeostatic process and the state of dominance of a signal which becomes a critical symptom. (58)

- Deficient transition - The vegetative tendencies, the phases, should be clearly processed one into to the other so that the equilibrium remains constant. Occasionally, it may occur a lack of functional capacity of transformation in the body. The power of transformation of a vector into the other, of the circular function is blocked, stopping the cycle of regulation, resulting in pathological signs of the blockage of one of the vectors (Phases) (58, 69, 90)
- Imbalance agonist / antagonist - when there is an imbalance of agonists and antagonists, one of the phases will be in excess in relation to the other, leading to the predominance of signals of the phase in excess. (90)
- Excess of an agent – If an agent is continuously present, the phase at which it is related is also continuously produced leading to increase of the respective vector (phase). (58, 69, 90)
- Yin deficiency - As already stated, the regulation model of the body can be compared to a thermodynamic system. Thus, when a structure with less matter is subject to variations it will manifest a more unstable variation curve, leading to higher peaks of the variable, but the turning point will be achieved faster. In terms of TCM, lack of yin means lack of substance, matter, this is why yin deficiency causes an extreme course of the curve of regulation. It leads to labile “Qi”. (90)  
There are four types of yin deficiency: lack of functional tissue (yin deficiency "sui generis"); lack of body fluids; lack of microcirculation within the tissue (lack of "Xue"); functional deficits at the cellular level (lack of "jing ")

### 3.4.3. *Algor Laedens* Theory 3<sup>rd</sup> guiding criteria

*Algor Laedens* Theory (ALT) is the latin name of *Shang Han Lun* (treatise on cold damage diseases) systematically introduced regular pattern of diagnosis for diseases due

to invasion of exogenous pathogenic factors. (92) This kind of classification of pathologies first appeared in the writings of Zang Zhongjing, flourishing during the 2nd century of our era. It may be said that Zang Zhongjing founded clinical medicine when he wrote this treatise. (69)

This theory considers that an agent faces six levels of defense when invades the body. These six levels of defense differ in vegetative functional capacity ("Qi") and "Xue". The Stages, ALT levels, are characterized by specific clinical signs that will help to identify on what level of defense lies the pathogenic agent, and therefore to classify the capacity of damage on the body. The first level of defense is consists in *Tenuintestinal* and *Vesical* conduits that depend very much on the status of "Xue". So, the lack or decrease of microcirculation (*algor*) will be the prime cause of the invasion of agents. By the western overview this theory assesses the reaction process of the body to the presence of an agent. It reflects the absence or decrease of the microcirculation which affects first the conduits that contain more "Xue" than "Qi" (58, 69, 90)

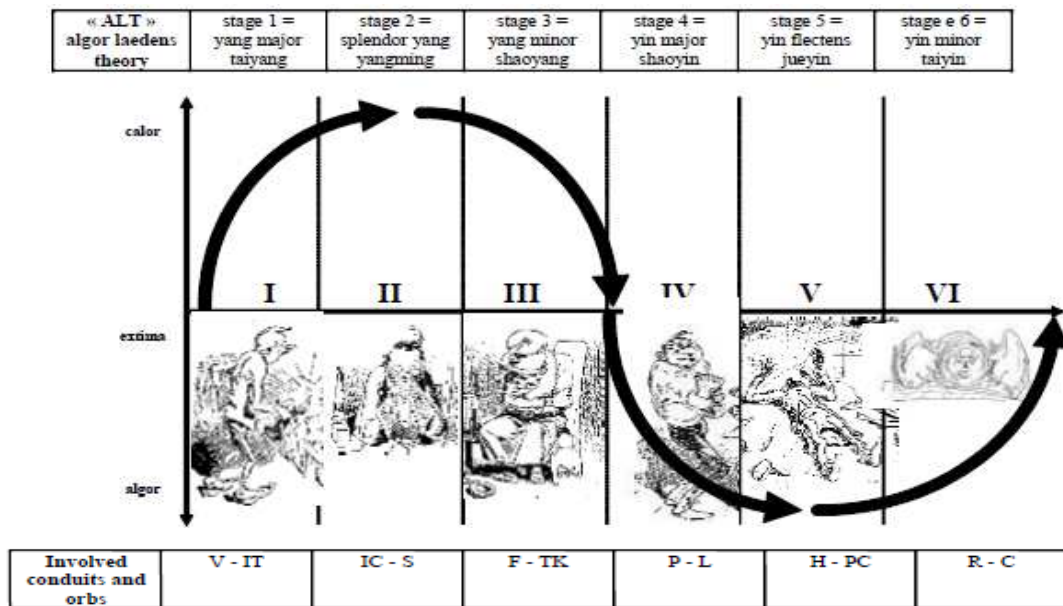


Figure 11 Scheme of Algor Laedens Theory. Adapted from Greten (58)

The ALT allows us to interpret the third guiding criteria, *extima/intimate*. As the stages I, II and III are outside the body region, and are constituted by yang conduits, their names contains termination yang. On the other hand, the stages IV, V and VI, are directly related to the body region, constituted by yin conduits, internal and contains the term yin. (90)

Due to its relative importance in OSA, is important to point out the first two stages of ALT.

Stage 1 – Yang major – in this stage the agent affects the *Qi defensivum* (Wei Qi) that resides within the extima along the surface on the outside of the conduits. The conduits directly related with *yang major* are *Tenuintestinal* and *Vesical* and indirectly related are the coupled yin conduits *Cardinal* and *Renal*. Therefore, this stage disease will affect the fluids and liquids saving mechanism, the separation of liquid and solid, excretions and production and control of *calor*. The *Yang major* conduits cross the neck, the head and shoulders; so, when an agent affects this stage the patient may show intense pain in the head and neck, pressure between the eyes, fever, shivering, no perspiration, diffuse pain, copious urine, cold hands and feet, *inter alia*. (58, 69)

Stage 2 – Splendor yang – this is the stage of conduit “Qi”. When the agent *algor* overcomes the first stage, it enters in the conduits. This leads to a blockade of flow of “Qi” and “Xue”. As in the first stage there is a deficit of “Xue”, so it will be needed to promote it. As it is the “Qi” that moves the “Xue”, it will be most affected, because it is being challenged by the lack or reduction of microcirculation of the preceding stage. The main sources of “Qi” are nutrition and breathing, thus, the Centre (responsible for the assimilation) and the Metal phase will be affected. As the yang conduits of the Centre and of the Metal phases are the *Stomach* and *Crassintestinal*, respectively, they will be most affected at this stage. The *Lienal* conduit and the *Pulmonal* conduits, they are the yin coupled conduits of *Stomach* and *Crassintestinal*; they will be indirectly affected (58, 63, 69).

The pathologies of this stage will produce disturbances in assimilation, in rhythm of all orbs and in the exchange of “energies” between the orbs. Clinical manifestations of this stage can be high fever, oppressive heat, desire to be cooled, profuse transpiration, thirst, constipation, *inter alia*. (69)

- Main symptoms of the *Stomach* orb – related to the course of conduct may arise: sinusitis or tearing pain in the face; affections of the sinuses, toothache; breathing problems; loss of appetite; weakness and pain in the thigh and Knees. Related to the impaired of stomach orb functions, may arise: swellings, edema on the eye region, unclear vision, accumulation of phlegm, swellings of the face, swellings of the mucous membranes, acute paradontosis, hoarseness and other problems in the throat, swellings of the mamma, cough, loss of appetite, anosmia, anhelitus. (69)
- Main symptoms of the *Crassintestinal* orb – related to the course of the conduct may arise some symptoms like running nose, toothache in the maxilla, pain in the neck, shoulders, forearm, tendency to develop tendinitis. Related to the

functional impairment may arise: abdominal discomfort, noisy bowel movements, constipation due to reactive *calor*, diarrhoea due to *algor*, pain in the intestines. (69)

#### 3.4.4. Upper airways in Heidelberg model of TCM

- Nose - In Chinese Medicine the nose can have different allocations. So, the nostrils are the most exterior part of the respiratory tract and are said to be the diagnostic window of the lungs. Therefore, it is primarily allocated to the pulmonary orb. As the respiratory tract, in many cases, reacts as a functional unit, the nostrils can be said to be the diagnostic window of the whole respiratory track.

The exterior of the nose has its own allocations: The rims of the nostrils and its small sebaceous glands are allocated to the Centre. Thus, on the skin of the nose, on the plateau, we see signs of the *Lienal* orb. In the wings of the nostrils we can see *Stomach* signs

The secondary allocation of the nose is the *Crassintestinal* orb. The conduit of the *Crassintestinal* orb runs underneath the nostrils, above the lip and touches the exterior side of the opposite nostril. Symptoms of exterior affections of the phase metal, like sneezing, are rather *Crassintestinal*.

- Sinuses – Due to the course of the conduit, the maxillary sinuses are primarily affected by the stomach orb. Thinking in the same way, the ethmoidal sinuses or *cellulae ethmoidales* and the feeling of pressure between the eyes are allocated to the *Vesical* orb. The root of the nose, sometimes called “the region of pads of glasses” is allocated to the contralateral branch of the *Tenuintestinal* conduit. Normally, the frontal sinuses are well treated by this conduit, considering that they are a *Yang Major* problem, but if the whole *viscerocranium* is affected, it is better to be treated by the *Stomachal* orb, considering it is a *Splendor-Yang* disease. (58)

- Pharynx – in western anatomy pharynx is conventionally divided into nasopharynx, (epipharynx) oropharynx (mesopharynx) and the laryngopharynx (hypopharynx). The nasopharynx has the same functional relations as the sinuses. The oropharynx, as part of the oral cavity, is allocated to the *Stomachal*, and the nasal cavity is allocated to the *Pulmonal* and *Crassintestinal*. The soft palate, the uvula, can be allocated to the three orbs (*Stomachal*, *Pulmonal* and *Crassintestinal*), but mostly it is related to *Splendor-yang* syndrome, as it is between the two first sections, although may show clinical signs of the three orbs. In general, all osseous structures of the body belong to the renal orb. As bone



structure that it is, the hard palate belongs to the renal orb, whereas the “fleshy” parts of the oral cavity belong to the stomach orb. As oropharynx and laryngopharynx are the prolongation of the oral cavity, most of their affections are allocated to the stomach orb. (58, 89)

- Tongue –obviously is part of the oral cavity, so it reflects the functional properties of the *Stomachal* orb. However, in Chinese medicine, the tongue is also called “the prolonged heart” which also will point to “Shen” (constellating force originated from the cardiac orb) deficiencies. (58)
- Uvula – Some inflammations of the uvula are so deep that the most effective treatment for these conditions is to use yin points, therefore some authors considered it is connected to the renal functions. This is not contradictory to the allocation to the *Splendor-yang*, because when the *Splendor yang* is long-standing, the high *Calor* produced (typical of this syndrome) will reduce the *yin* (the fluids) and over the time it will lead to a *yang* deficiency by the long standing *yin* deficiency.(58)

The Centre controls all regulation. As mentioned above, the Centre is the axis of the curve of regulation. As in the pathologies of the upper airways is required control of the surface and a good regulation, the constant action of the Centre is required, especially of its outer (yang) orb, the Stomach. In the same way, the metal phase which regulates the surfaces, is required, so, the constant action of yang orb of this phase, the Crassintestinal, is required too.

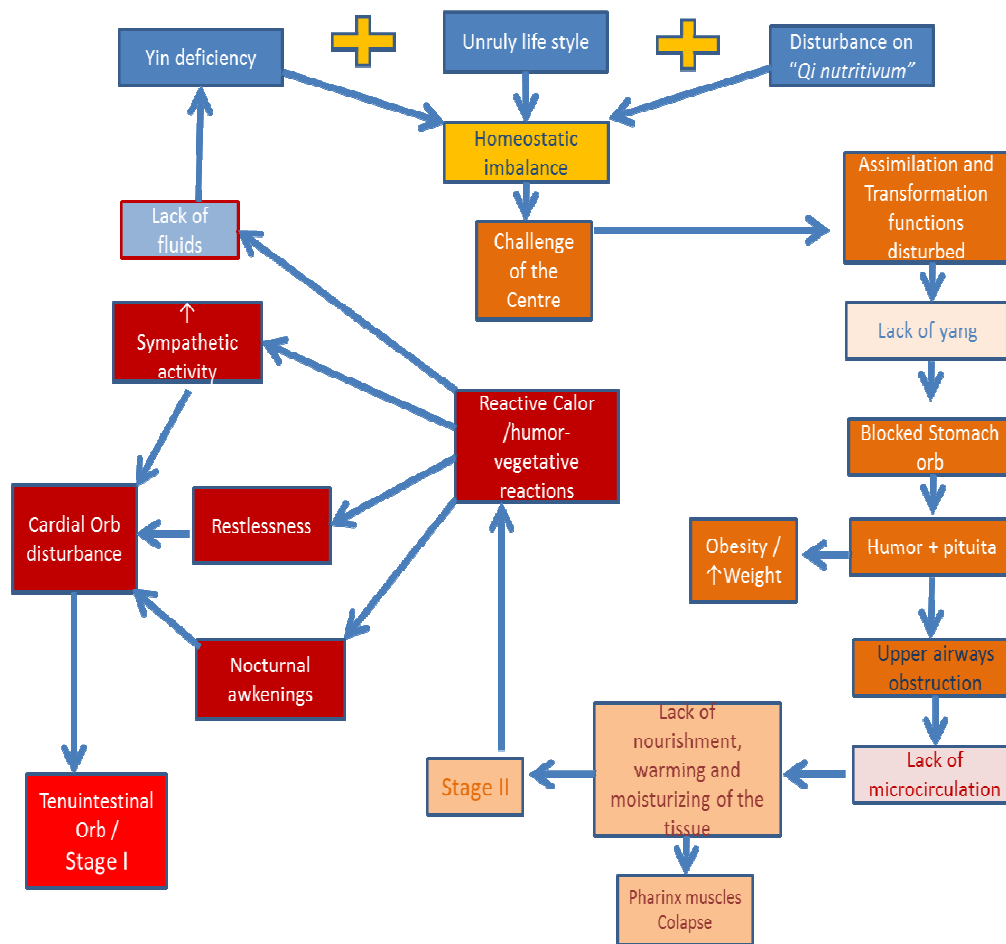
When there is a lack of microcirculation (*Algor*), there is a kind of depletion. All depletions reduce the stomach functions (to move downwards), so the downward movement of fluids, *humor* and *pituuta* (phlegm) for excretion, will be reduced. This combination of factors will lead to a blockage of *Stomachal* orb which, in Western terms, may be comparable to blocked vagal functions and thereby to various manifestations, including swelling and inflammations in the area of the face, nose, sinuses and throat.

Depletion is naturally associated to *yin* patterns. So, the *Vesical* orb, the coupled outer orb of the *Renal* orb (the most representative orb of *yin*) may be affected. Thus, the lack of “Qi defensivum” promotes stages I and II of the ALT. (58)

### 3.4.5. Physiopathology of OSA according to HM of Chinese medicine

As previously mentioned, OSA can occur at any age, but it mainly affects men between 40 and 60 years and postmenopausal women. In Chinese medicine, after 35 years, humans come into *yin* deficiency, in structural deficiency, which derives from the physiological reduction of the functional tissue. (23) Thus, there is a strong relationship between the lack or progressive loss of *yin*, often reinforced by unruly lifestyle, and OSA manifestation. This lack of *yin* will result in a homeostatic imbalance; in a disruption of the cycle of body regulation and sinus wave. Therefore, the centripetal force of the curve, the Centre, will be challenged. By this, the function of assimilation and transformation will be disturbed and thereby the *yang* orb of the Center, the *Stomachal* orb, will be challenged too.

From Chinese point of view, OSA, can be also regarded as phlegm obstructing the orifices. (93) This means that *humor* and *pituita* (phlegm) are obstructing the upper airways; there is not a vector sufficiently strong to lead the turbid down and to do the transformation and assimilation function. These obstructions will cause a blockage of *Stomachal* orb, which is the orb that moves and drains *humor* and *pituita* out; it is responsible for the downwards movements for excretion. Regarding this, upper airways obstruction can be considered a lack of *yang*, (function) based on a deficiency of *yin* (substance). As consequence, the tissues of the upper airways will not be so well nourished, warm and moisturized; the microcirculation, which is correlated with “Xue”, will decrease. Knowing that “Xue” “is a form of functional capacity bound to body fluids, with functions such as warming, moisturizing, creating “Qi” and nourishing a tissue”, (58) there will be a stage II of ALT, therefore, will arise the instability of the upper airways which will result, also, in the decreased activity of the dilator muscles of this region and in the collapse of the oropharynx. In an attempt to achieve the target value, the body will react with humorovegetative reactions, producing the so-called “reactive *Calor*”, which will lead to an increased sympathetic activity plus lack of fluids, restlessness and nocturnal awakenings, during sleep. (63, 58, 93) This will enhance the physiological activity of *Cardial* Orb and consequently its coupled orb, *Tenuintestinal*, leading to Stage I of the ALT. (Fig 12)



**Figure 12: Scheme of Physiopathology of OSA**

### 3.4.6. Treatment of OSA by acupuncture – current state of the art

TCM aims the modulation of systems responsible for the homeostasis of human body. It tries to balance the organs and systems, as well as recover the homeostatic dynamic between them, by appropriate stimulation of the acupuncture points. In TCM clinical practice can be used different acupuncture points and techniques to treat the same disease, on the other hand, one point can be used to treat different diseases. When a treatment is conducted it is taken into account the individual homeostatic imbalance of each patient. So, for the same diagnosis of conventional medicine (Western), different patients may receive a different treatment by the TCM. (23, 94)

However, scientific research requires standardization of points and acupuncture techniques, for only then we can obtain analyzable data, according to the biomedical model, for a specific clinical intervention. Only a few investigations have study the effectiveness of acupuncture in the treatment of OSA. The studies that had verified this effectiveness, had used as treatment, body acupuncture, (local and distal) one study with manual stimulation and another with electropuncture stimulation. (23, 93) The Heidelberg

model proposes, as standard treatment for OSA, the use of one microsystem, the Scalp acupuncture.

In the table below are listed the neck local points and the distal (systemic) points. In electropunctura the same points were used with 10 Hz stimulation.

**Table 4 Body acupuncture points used to treat OSA**

	Points	Chinese name	HM name	Regional anatomy
Local points	Rs23	Lianquan	Fons in angustis	Above the hyoid bone, anterior superficial jugular vein, cervical cutaneous nerve branch, nerve branch of the hypoglossal and the glossopharyngeal nerve.
	---	Shanglianquan (extra point)	---	Between the hyoid bone and the menton symphysis
Systemic points	Rg20	Baihui	Conventus omnium	Galea aponeurotica, anastomotic net formed by the superficial temporal arteries and veins and occipital arteries and veins on both sides; branch of the greater occipital nerve, and branch of the frontal nerve
	Ic4	Hegu	Valles conjunctae	Venous network of dorsum of the hand, surface of the cephalic vein, dorsal nerve of the metacarpal bone of the superficial branch of the radial nerve and in deep, palmar digital nerve, derived from the median nerve.
	S36	Zusanli	Vicus tertius pedis	Anterior tibial artery and veins; lateral sural cutaneous nerve and cutaneous branch of the saphenous nerve, deeply peroneal nerve
	Pc6	Neiguan	Clusa interna	Is related superficially with the medial and lateral cutaneous antebrachial nerve, with the palmar branch of the median nerve and, deeply with the median nerve.
	P7	Lieque	Series intermissum	Relates to the branches of the superficial radial nerve
	R6	Zhaohai	Mare illuminationis	Is related to the medial cutaneous nerve of the leg, the saphenous nerve and, deeply, with medial plantar nerve (branch of the tibial nerve)
	L6	Sanyinjiao	Copulatio trium yin	Greater saphenous vein, posteriors tibial artery and vein, medial crural cutaneous nerve, tibial nerve
	S40	Fenglong	Abundantia	Is related superficially with the lateral cutaneous nerve of the sura and, deeply, with the muscular branches of the peroneal nerve

				(superficial and deep)
	lc20	Yingxiang	Accipiens odores	Deep into the piriformis muscle edge; facial artery and vein, branches of the artery and vein of the infra-orbital; anastomotic branch of the facial nerve and orbital infrastructure

(24, 61, 64) Fig 13 and Fig. 14

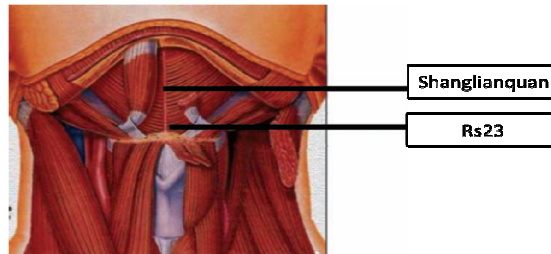


Figure 13 throat points of Body acupuncture, adapted from Freire ,2010(24)

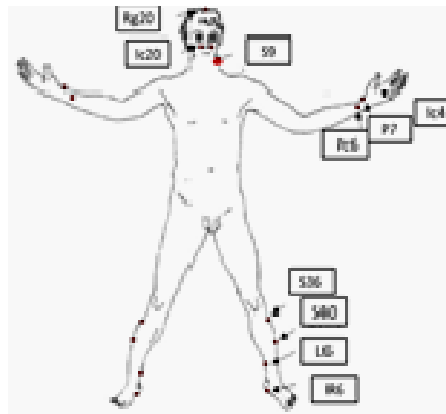


Figure 14: Body acupuncture points used to treat OSA. Source: Sugai, 2009 (23)

**Table 5: Resume of TCM research studies in OSA (23, 24, 107, 108, 109, 110)**

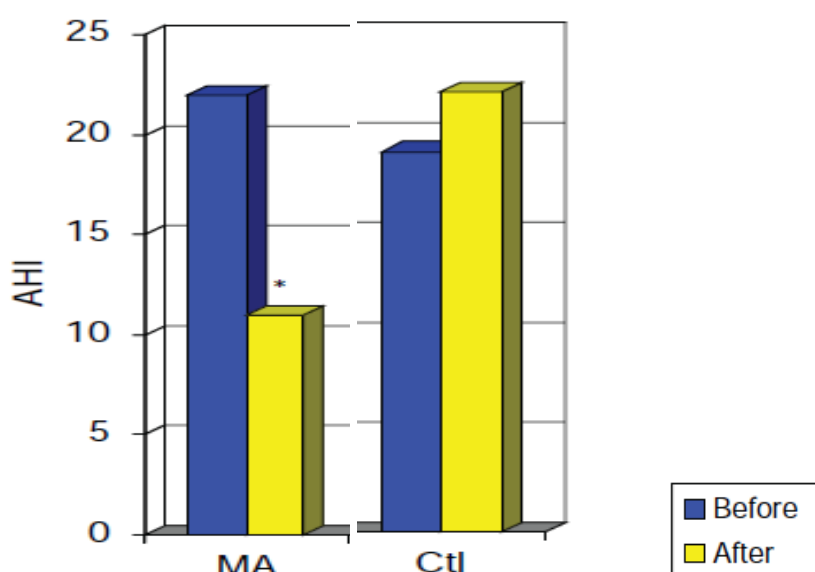
TCM RESEARCH STUDIES IN OBSTRUCTIVE SLEEP APNEA						
<b>Title</b>	<b>Immediate effect of acupuncture on the sleep pattern of patients with obstructive sleep apnoea</b>	Treatment of moderate obstructive sleep apnea syndrome with acupuncture: a randomised, placebo-controlled pilot trial	32 cases of obstructive sleep apnea-hypopnea syndrome treated by acupuncture combined with acupoint injection	Influence of auricular plaster therapy on sleeping structure in OSAS patients	Effect of acupuncture on blood oxygen saturation in patients of obstructive sleep apnea-hypopnea syndrome	A study on differences of curative effects of acupuncture and nCPAP for treatment of OSAHS
<b>Authors</b>	Freire AO, Sugai GC, Togeiro SM, Mello LE, Tufik S	Freire AO, Sugai GC, Chrispin FS, Togeiro SM, Yamamura Y, Mello LE, et al	.Xue GS	Wang XH, Xiao LY, Wang BF, Yuan YD, Pan WS, Shi YZ	Xu J, Niu YX, Piao XM, Liu Z, Wu LZ, Liang RL.	Bo C, Zhang XS, Huang H, Jia Y, Xie XM
<b>Study type</b>	Randomised, single blinded	Randomized, placebo-controlled pilot trial	-	Randomised	Clinical cases	Randomised
<b>N=</b>	40	36	32	45	30	44
<b>Control type</b>	Receiving no treatment	1) Sham acupuncture (needling in non-acupoints in nonspecified dermatomes) 2) Receiving no treatment	-	Receiving no treatment	No control	Treated by nCPAP
<b>AHI</b>	15-30/h	15-30/h	-	-	-	-
<b>Technique</b>	Manual Body acup.; Electro body acup.	Manual body acupuncture; Sham	-	Auricular plaster	Manual body acupuncture	Manual Body acupuncture

	10Hz and 2Hz	acupuncture				
<b>Conclusions</b>	<p>“In a single treatment session, both manual acupuncture and 10 Hz electroacupuncture were superior to control and to 2Hz electroacupuncture.”</p>	<p>“A major improvement in AHI with active acupuncture. We have found preliminary evidence that acupuncture is effective in the treatment of OSAS. This work, however, must be replicated and the observation period after treatment should be extended in order to evaluate the duration of the improvement obtained and also to establish well defined treatment protocols.”</p>	Not available in english language	<p>“The auricular plaster therapy significantly improved the hypoventilation index, respiratory disturbance index and other respiratory parameters as well as the sleeping parameters such as the time and rate of sleep at stage I and II, and the waking time and rate”</p>	<p>“The effective rate of acupuncture was 23.3% for OSAHS. After acupuncture, AHI and ODI4 significantly reduced (P &lt; 0.01); LSaO2 significantly increased (P &lt; 0.01); MSaO2 and the mean blood oxygen saturation of oxygen desaturation when SaO2 &lt; 90% significantly enhanced (P &lt; 0.05); the longest time of oxygen saturation &gt; or = 4% did not significantly change. The acupuncture treatment has intervenient effect on OSAHS and alleviates anoxia, so acupuncture is one of therapies improving anoxia in patients of OSAHS.</p>	<p>No significant differences of respiration, blood O2 and indexes were found in the acupuncture group during treatment (P &gt; 0.05), but hypopnea index (HI), apnea-hypopnea index (AHI), the maximal apnea duration, the maximal hypopnea duration, sleep time spent when SaO2 was below 90% (SaO2 &lt; 90%T) and the microarousal index improved significantly at the end of treatment (P &lt; 0.05 or P &lt; 0.01). The therapeutic effect in the nCPAP group was better than that in the acupuncture group during the treatment (P &lt; 0.05 or P &lt; 0.01), but no significant difference of the therapeutic effect was found between the two groups at the end of treatment (P &gt; 0.05). <b>The therapeutic effect of nCPAP on OSAHS produces during treatment and the therapeutic effect of acupuncture produces after treatment, indicating they possibly have different mechanisms.</b></p>
<b>Publication Year</b>	2010	2007	2011	2010	2009	2008

As in present study, Freire's study evaluated the immediate effect of acupuncture. The results relating to the manual body acupuncture of this study were:

**Table 6 results of Freire's study**

AHI	21.9 (8.3)	11.2 (5.5)*†
Apnoea Index	5.15 (11.9)	0.7 (1.6)*†
Hypopnoea Index	13.9 (9.3)	8.45 (4.4)*
Res Ev	120.5 (42.0)	61.0 (41.0)
Microarousal	146.0 (39.0)	88.5 (51.0)
M SaO <sub>2</sub> (%)	93.9 (1.8)	94.4 (2.0)



**Graphic 1 Comparison of AHI at baseline (before) and after procedures. Manual acupuncture versus the control group (p=0,034). P<0,05, Mann-Whitney t test. Adapted from Freire, 2010 (24)**

### 3.4.7 Treatment of OSA according to the Heidelberg Scalp Acupuncture model.

The Heidelberg Scalp Acupuncture (HSA) is a somatotopic system, related to a coordinated system that correlates some head zones with anatomical regions and concepts of TCM. (114) (Fig.15) The Heidelberg model of TCM often uses this puncture technique to treat OSA. This technique allows to take action on stages I and II of ALT; allows to act on the orbs and at the same time it has a direct action on the anatomical region where the disease is manifesting.



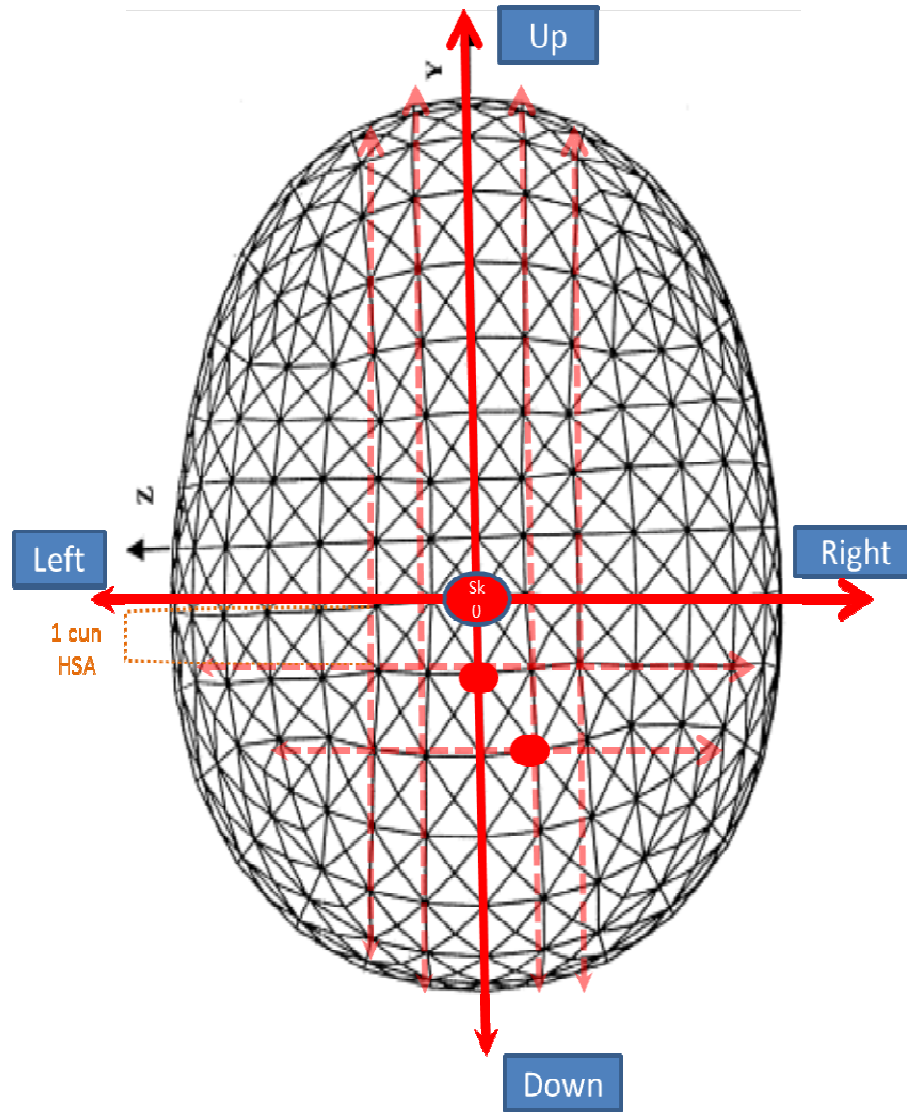


Figure 15: coordinated system of HSA (adapted from Cuffin, 2001)

Tracing a straight line from the tip of the ear lobe and the vertex, is located the point where should start the imaginary curved line that connects the two ears.

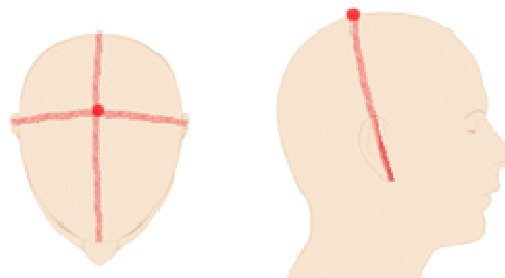
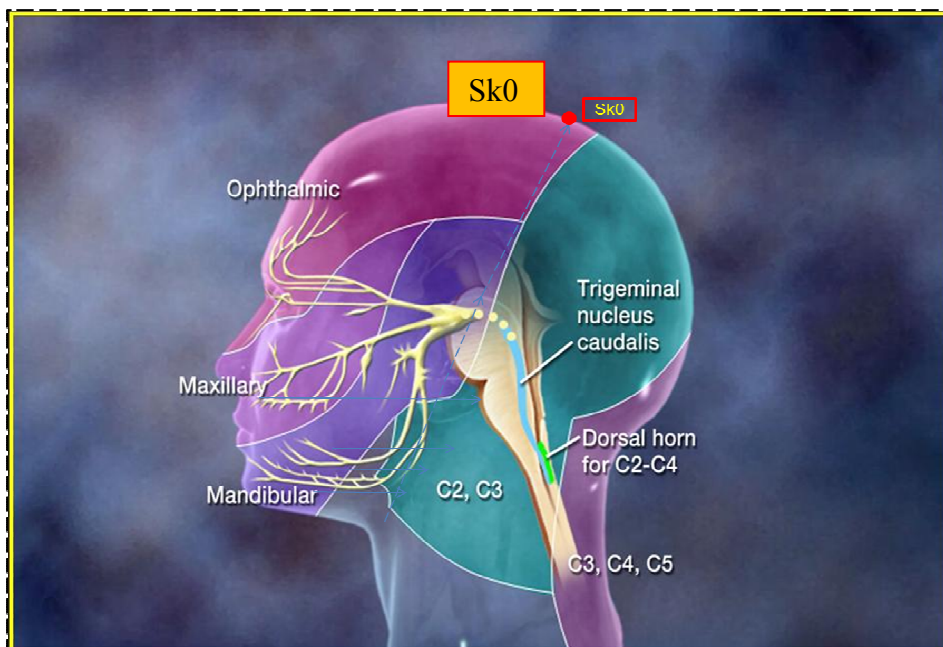


Figure 16 intersection lines to find Sk0; Adapted from [www.martialdevelopment.com](http://www.martialdevelopment.com)

This line will be intersected by an imaginary line that connects the tip of the nose to the tip of the occiput. The intersection of these lines is located the point Rg20 (*Baihu*).

This point will have the designation of Sk0, in HSA technique, it will be the reference point to find the others. This point can be, also, a projection of the extra point *Yintang*, representing the same anatomical region and the same functions. (114) (Fig 16 and Fig 17)



**Figure 17 Sk0 localization; adapted from <http://drgominak.com>**

According to this logic, the SKd1 point will correspond to point between the eyebrows in the midline; Skd2 point will correspond to the point between the eyes and the SKd2l1 and SKd2r1 points will correspond to the ethmoid cells. The point SKd3 match with *maxillary sinus ostium*; the points Skd3l1 and SK3r1 represent the compartment of *Maxillary sinus*. The SKd4 point corresponds to *inferior conchae*, and thus, the points SKd4r1, Skd4r2, and Skd4l1 SKd4l2 correspond to inferior *maxillary sinus* zone and also to the point of *Crassintestinal*, IC20. The SKd5 point corresponds to the hard palate and it especially matches with Rg26. The SKd6 corresponds to the soft palate, The Skd7 to the Uvula and SKd8 corresponds to the oropharynx. (Fig 18, Fig 19 and Fig.20)

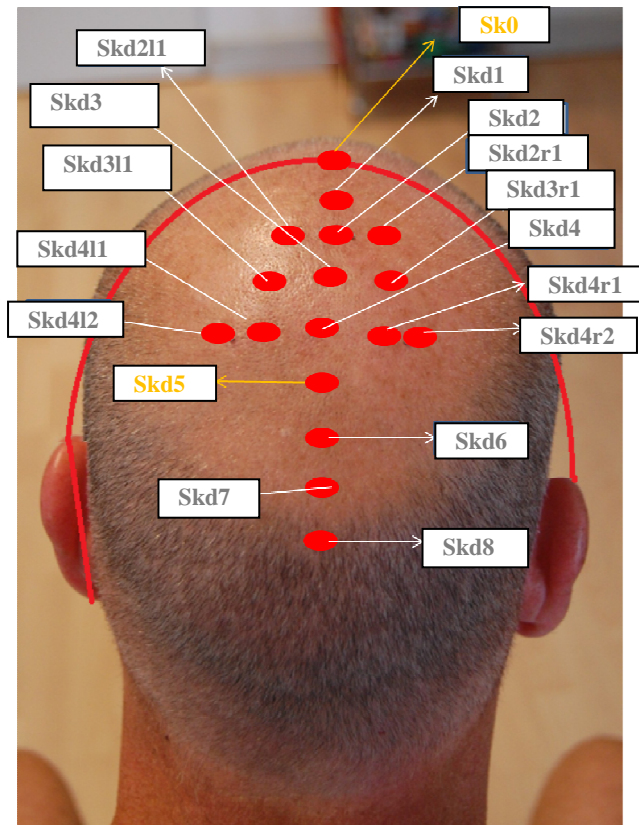


Figure 18 Localization of HSA points for OSA

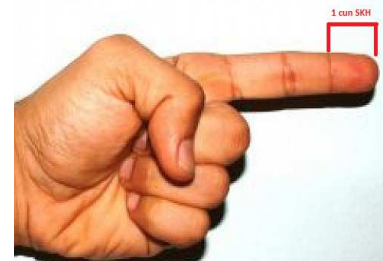


Figure 19. The cun on HSA

The 9 points of the middle Line are distant from each other 1 "cun" HSA. (Fig 19) This Cun is slightly smaller than the common "cun". The reference for this is the second distal phalanx of hand, like in the basis of the sexagesimal system. The side points, identified by letters as "R" and "L" (left and right respectively) at the point acronym, are detected by the anatomical correspondence to the region to be treated and by the method of "tender point", respecting the coordinate system. (114)

In terms of TCM, as already mentioned, some of the points have direct correspondence with points of the conduits, such as the Sk0 which corresponds to Rg20 (Rg20 = Yintang) Skd412 and Skd4r2 that correspond to IC20 and SKd6 which corresponds to Rs26. In terms of ALT, these points will correspond to the most representative area of *Splendor-yang* syndrome. (stage II) Some points, as Sk0, SKd1, Skd2, Skd211 Skd2r1 points will treat the *Yang major* syndrome, as they have correspondence with the points that are related to the *Vesical* and *Tenuintestinal*.

It is important to emphasize that point Sk0 and point Skd5, in particular, have direct relationship with the *Cardial* Orb and all midline points are directly related to the "Regens", therefore are related to *Renal* orb. This feature is especially important because the Cardio - Renal relationship is important for all the pathologies of sleep and for a good organic and tissue regeneration.

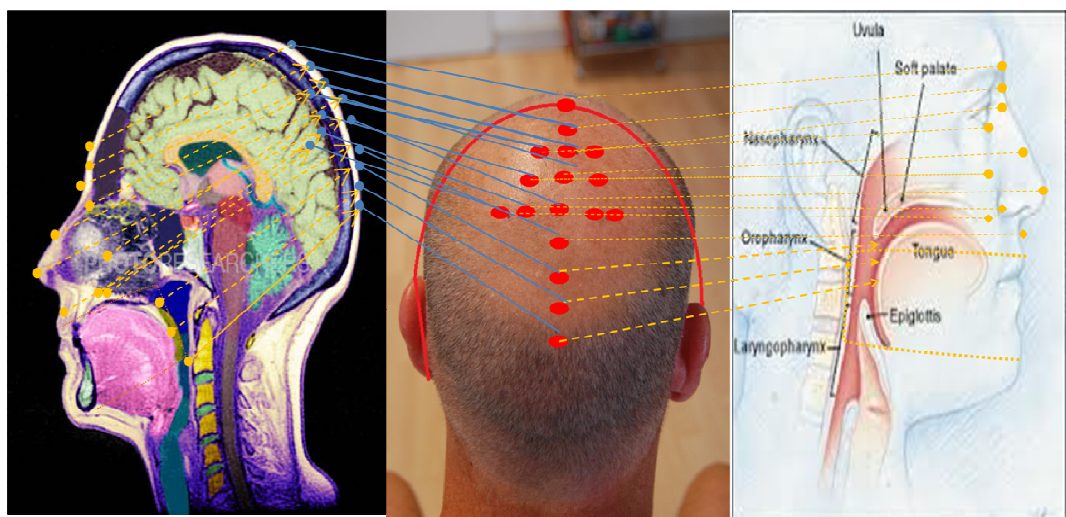
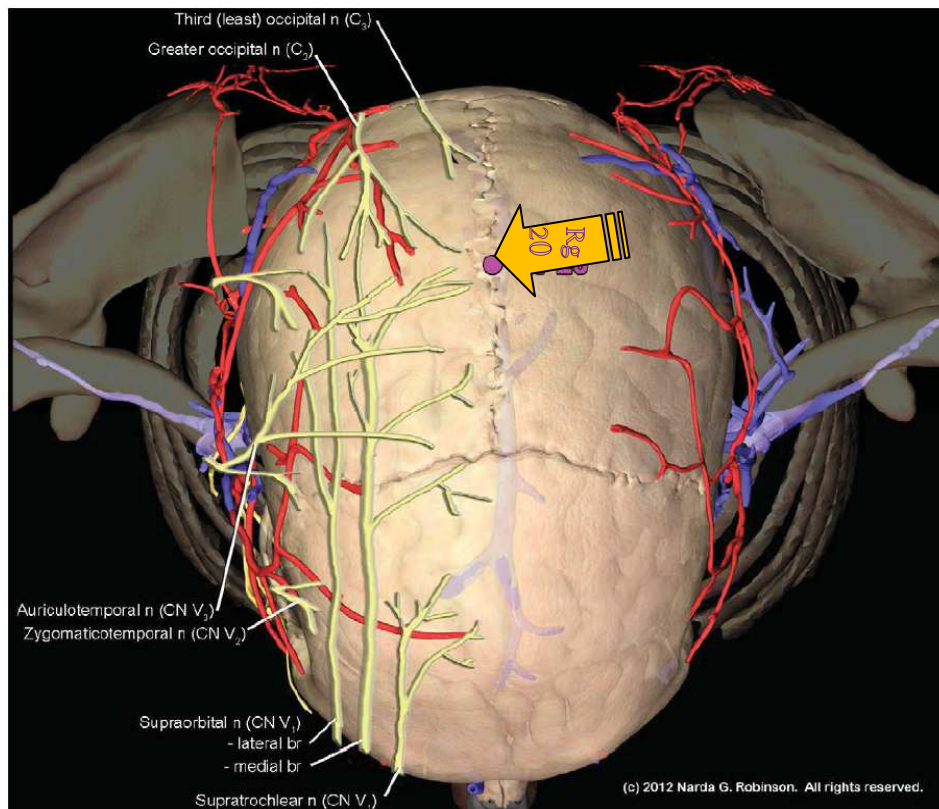


Figure 20: Projection lines (adapted from [www.photoresearchers.com](http://www.photoresearchers.com) (97) , Greten 2012 and [www.aafp.org](http://www.aafp.org)) (98)

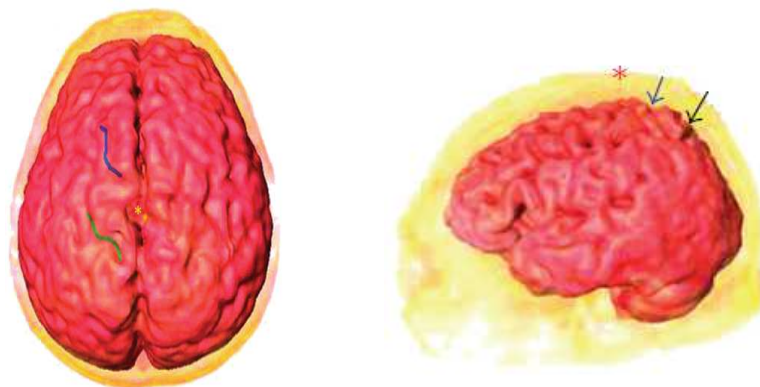
✓ **Sinarteria Regens/Leading sinarteria (Du mai):** Majority of points of HSA is located in this conduit. Thus, it is particularly important in this therapy. This conduit is one of 8 Odd conduits which are closely related either on *yin* (structure) either on *yang* (bodily functions). The *Regens*, through *reticulares*, communicates with *Renal* orb and therefore it has a great influence on the "*Qi primum*", the inborn vital resource. In addition this *sinarteria* (conduit) establish the communication between the reproductive system, all *yang* conduits and the head. Thus, this Odd conduit lifts up this kind of "energy", from the *Renal* orb into the surface. As it is the conduit that rules all *yang* of the body and it is connected with all *yang* conduits, ruling over primordial *yang*. *Regens* regulates the *yang* of all conduits, the "*Qi*" and the "*Xue*", and nourishes the brain and marrow. Furthermore, *Regens* enter in the brain, so, if it is affected by pathology, symptoms and diseases of the nervous system, of sensorimotor system and digestive system, may arise. (61, 64, 69)

Like the others conduits, it also has two trajects. The main traject arises in the kidneys and adrenals, interrelating with *yin* (structure) and *Yang* (function), it follow to the perineum, rising up to the point Rg16 in the nape, where it diverges into a secondary branch that penetrates the brain and reappears at the top of the skull, at the point Rg20. At this point it intersects the main branch which follows the dorsal midline, within the spinal cord, and down the forehead to the columella of the nose, to the point Rg28, where it joins the *tendinomuscular* conduit of the *Stomachal* orb, entering in the throat and in laryngopharynx. Moreover, the internal branch has the same starting point but diverges into an abdominal branch that goes to the heart and reappears in the chest, to join to the anterior branch of the *Vesical tendinomuscular* conduit, then follows to the throat and face, entering in the center of the eye and then in the brain. (61, 64)

✓ **Sk0/Rg20 point** (*Conventus omnium*, whose the chinese name is *BaiHui*) = *Yintang* - Is one of the most important points of the *Regens*. It is located at the vertex of the head. It is the meeting point of the *Regens* with *Vesical* and *Hepatic* conduits, and it is a convergent point of all *yang* functions. In this point it is possible to restore the *yang*, to overcome depletion; awake the mind and open the orifices. Stimulating this point it is possible the stabilization and regulation of the *Hepatic orb*, support the *Cardial Orb*, clear and opening the senses and bring up the "yang Merum" ("pure *yang*") from the lower to the upper caloric. It restores the yang; awake the mind and the orifices. (64, 69, 99) (Fig21, Fig 22)



**Figure 21: Regens 20 Localization. Adapted from Robinson, 2012 (100)**



**Figure 22 Regens 20 Projections on the brain. Source: Shen, 2011 (101)**

It is responsible for enhancing nitric oxide (NO) increasing of the local circulation and normally it is indicate to a great restlessness, tension of the muscles, fainting, dizziness, obstruction of the ears, obstruction of the nose, running nose, gastroptosis, respiratory failures, asphyxia, stress, nervousness, nausea, and some kinds of prolapses and collapses. This point has a stimulating effect on the central nervous system in addition to just peripheral nerves. It stimulates the brain and spinal cord, chemically, which alters the pain sensation and/or leads to the release of other chemical substances, such as hormones, that influence the self-regulation system of the body. (64, 99, 101)

In terms of regional anatomy this point is located on the *galea aponeurotica*, anastomotic net formed by the superficial temporal arteries and veins and occipital arteries and veins on both sides; branch of the greater occipital nerve, and branch of the frontal nerve. (64)

*Yintang* - Like other extra points, is an important vegetative action point, located between the medial ends of the two eyebrows. In terms of regional anatomy over the *piramidalis nasi* muscle; branches of medial frontal arteries and veins, supratrochlear branch of the trigeminal nerve. It calms down and clears the mind. Among other actions acts on psychological agitation, nightmares, state of numbness, it decongests the nose and it is a structural point of vegetative functional capacity of *Pulmonal orb.* (61, 64)

✓ **SKd5point = Rg26 point** (*canalis aquae*, whose the Chinese name is *Shuigou*) Regarded as one of the human center; it regulates and stabilizes the Centre, thus, it may act transforming *humor* or *pituita*, unblocking the senses and checking *calor*. It is the crossing point of *Regens* with *Crassintestinal* and *Stomachal* Conduits; is one of the most important points of the body. It has the function to awake the mind and open senses, relieve convulsions and tranquilize the mind. Normally, it is indicated to infantile asphyxia, carbon monoxide poisoning, facial paralysis, swollen face, acute lumbar sprain, carsickness, seasickness and coma. (99, 102) Friese, in 1993, show that this point can enhance respiration in animals; when respiration comes to an instant pause, acupuncture at this point could help to restore breathing. (99, 102) It can also improve brain blood pressure, and brain activity by afferent excitation, stimulating the ascending activating system of reticular structure of the brain stem. (99)

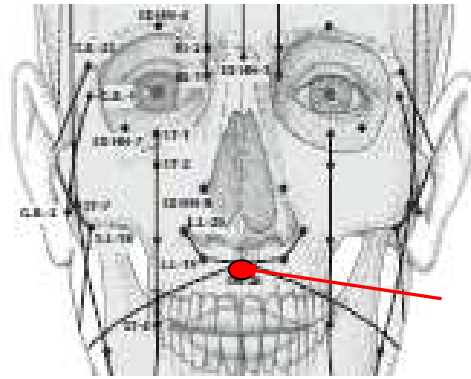


Figure 23: Localization of Rg 26. source: Focks, 2008 (103)

It is located underneath the nose, over the midline, in the upper third of the sulcus, between the root of the nose and the upper lip margin. In terms of regional anatomy, over the *orbicularis oris* muscle, superior labial arteries and veins, buccal branch of the facial nerve and branch of the infraorbital nerve. (64, 99, 104) (Fig 23)

- **Skd4l2/ Skd4r2 = Ic 20 points** (*Accipiens odors*, whose the Chinese name is *Yingxiang*) -

It is the crossing point of the conduits of *Splendor-yang* (*Crassintestinal* and *Stomachal*) and is Located in the nasolabial groove, at the midpoint of the lateral border of the wing of the nose. In terms of regional anatomy it is located about quadratus muscle of the upper lip, deep into the *piriformis* muscle edge; facial artery and vein, branches of the artery and vein of the infra-orbital; anastomotic branch of the facial nerve and orbital infrastructure. (It is indicated for Splendor-yang syndrome, especially in nasal obstruction, forced breathing, nasal discharge, nosebleeding, loss of smell, pareses of facial muscles. (90, 69) (Fig 24)

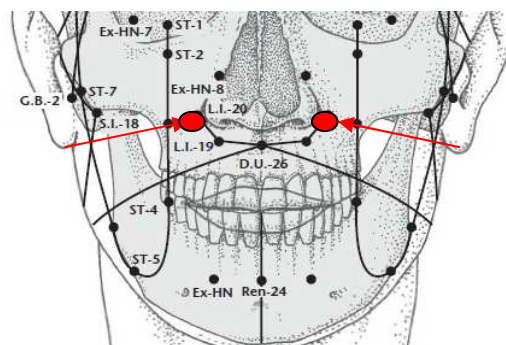


Figure 24: Localization of IC20. Source: Focks, 2008 (103)





## CHAPTER 2



## 4. CLINICAL RESEARCH PROTOCOL

#### **4.1 Title: “Effects of Heidelberg Scalp Acupuncture on Obstructive Sleep Apnea”**

#### **4.2. Organizational structure:**

In collaboration with the master's program of the Institute Abel Salazar for Biomedical Sciences, in Traditional Chinese Medicine, this research project was conducted in the Consultation of Respiratory Pathology of Sleep and Sleep Laboratory of the Department of Pulmonology of SJHC. The study had the technical support of ResMed that has provided the equipment and consumables items. The research project did not have any external funding.

#### **4.3. Research team:**

##### **Main investigators:**

Maria João Rodrigues Ferreira Rocha dos Santos

- Therapist of Traditional Chinese Medicine at A.R.PHARMA
- Master student of Traditional Chinese Medicine at Abel Salazar Institute for Biomedical Sciences

Sofia Isabel Martins Milhano

- Physiotherapist at Clinica Ortopedica Nuno Alegrete
- Master student of Traditional Chinese Medicine at Abel Salazar Institute for Biomedical Sciences

##### **Research supervisor:**

Prof. Doctor Henry Johannes Greten. Head of the Heidelberg School of Traditional Chinese Medicine; President of the German Society of Traditional Chinese Medicine (DGTCM), Heidelberg, Germany.

##### **Co-supervisors:**

- Prof. Dr. João Carlos Winck responsible for the consultation of pathology of sleep and sleep laboratory of the Department of Pulmonology SJHC; associate

Professor in Faculty of Medicine of Oporto University; editor in chief of Portuguese journal of pulmonology

- Dr. Nuno Correia, Specialist in Internal Medicine at the Department of Internal Medicine - SJHC; Master in Chinese Medicine - ICBAS/UP; Board member of Traditional Chinese Medicine Scientific Society. Professor of Physiopathology – Nursing School of Oporto.

#### **4.4. Research co-workers:**

Dr.<sup>a</sup> Maria João Lima, specialist in internal medicine, responsible for the hypertension consultation at Department of Internal Medicine - SJHC; Dr.<sup>a</sup> Anabela Marinho, physician at consultation of pathology of sleep and sleep laboratory of the Department of Pulmonology SJHC; Technician of Cardiopneumology Patricia Teles; Marcia Sá physician at Family Health Unit - ACeS Grande Porto III

#### **4.5. Study objectives:**

##### **General objective:**

To evaluate HSA effects on OSA using objective measurements of standard sleep study

##### **Specific objectives:**

- Related to OSA:
  - ✓ Verify the effects of the main parameters of cardiorespiratory polygraphy:
  - ✓ Agitation / movement
  - ✓ Snoring
  - ✓ O<sub>2</sub> saturation
  - ✓ Fatigue
  - ✓ Breath threshold
  - ✓ Apnea index; Hypopnea index; Apnea-Hypopnea index
- Related to HSA technique:
  - ✓ Analyzing the mechanisms of action of the HSA technique
  - ✓ As projections "front - mu" type of the brain region
  - ✓ As sensorial stimulation and neurophysiological action
  - ✓ As embryological relationship with the upper airways

#### 4.6. Study design:

##### Phase 1 - Preliminary study:

Study design: non-blinded pilot, case series type.

##### Phase 2- Randomized Control Trial

Study design: randomized control trial including comparison of two groups (HSA treatment group vs Control, no treatment, group).

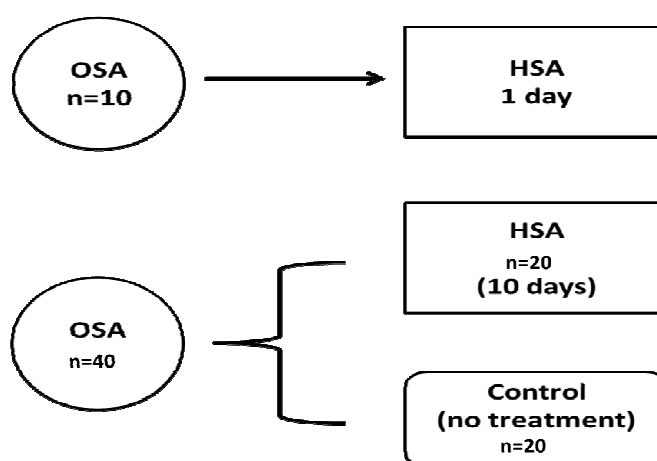


Figure 25: Diagram of the research protocol phases . OSA – Obstructive Sleep Apnea. HSA – Heidelberg Scalp Acupuncture.

**Setting:** This study will focus on patients followed on the Department of Pulmonology - Pathology of Sleep and Sleep Laboratory.

#### 4.7.1. Eligibility criteria

Table 7: Eligibility criteria:

<u>Inclusion criteria:</u>	<u>Exclusion criteria</u>
✓ Individuals with OSA (AHI> 5).	History of elevated consumption of alcohol
✓ aged between 30 and 70 years.	History of neurological
✓ Male or female sex	History of psychiatric disease
✓ Naïve for acupuncture.	History of thyroid disease
✓ Informed consent	Needles phobia
	Pregnant and lactating women.

#### 4.9. Procedure for Data Collection:

- **Phase 1 (preliminary study):**

At baseline, prior to intervention, measurements included: cardio-respiratory polygraphy (PG).

After treatment, PG was reevaluated during the sleep period of the same day of needling.

In the morning after treatment, needles were removed and patients answered to adapted “morning questionnaire” of Sleep Disorders Clinic, School of Sleep Medicine of Stanford Medical Center (post-sleep study) (see attachment) that allows to check the patient's perception of sleep (96)

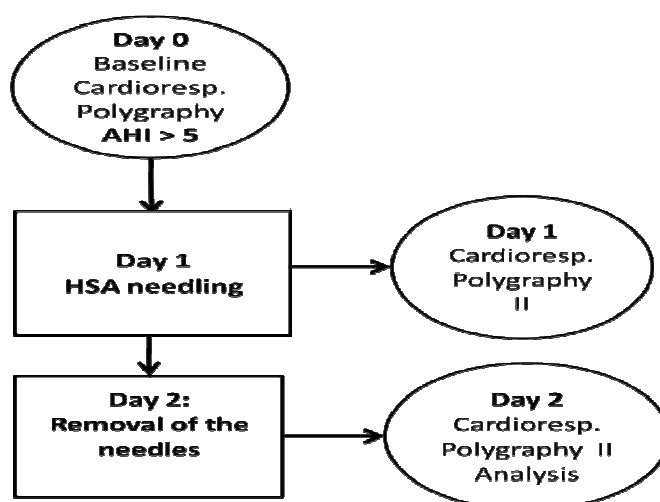


Figure 26. Flow-chart of phase 1 experimental protocol.

- **Phase 2:**

Baseline measurements: PG; Sleep questionnaires (Sleep Disorders Questionnaire version 1.2, Epworth scale, adapted “morning questionnaire” and the adapted questionnaire from Treatment Credibility Scale of Borvkovec and Nau.)

During HSA, a VAS is performed to evaluate scalp point tenderness.

Needles are left in place for 10 days.

On 10<sup>th</sup> day, PG is performed on the same night during the sleep period.

On 11<sup>th</sup> day, needles are removed and patients questionnaires are repeated.

Control group: same procedures and measurements as intervention group.

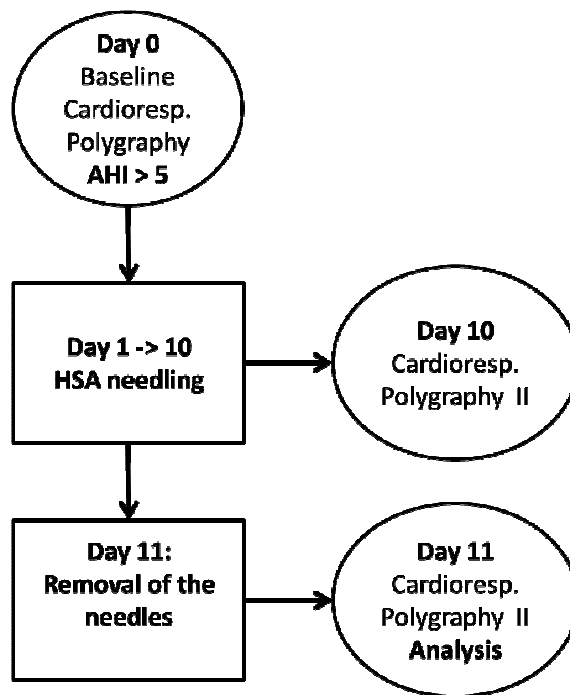


Figure 27. Flow-chart of phase 2 experimental protocol.

Patient's data is coded to respect confidentiality.

#### 4.9.2. Cardiorespiratory Polygraphy:

Each cardiorespiratory polygraphy was performed, with the needles placed, on the night after the application of needles. The programming of the equipment was performed according to the time of sleep of the patients and took place between the 23 pm and 6 am.



Figure 28: Polygraphy device. source: [www.resmed.com](http://www.resmed.com)

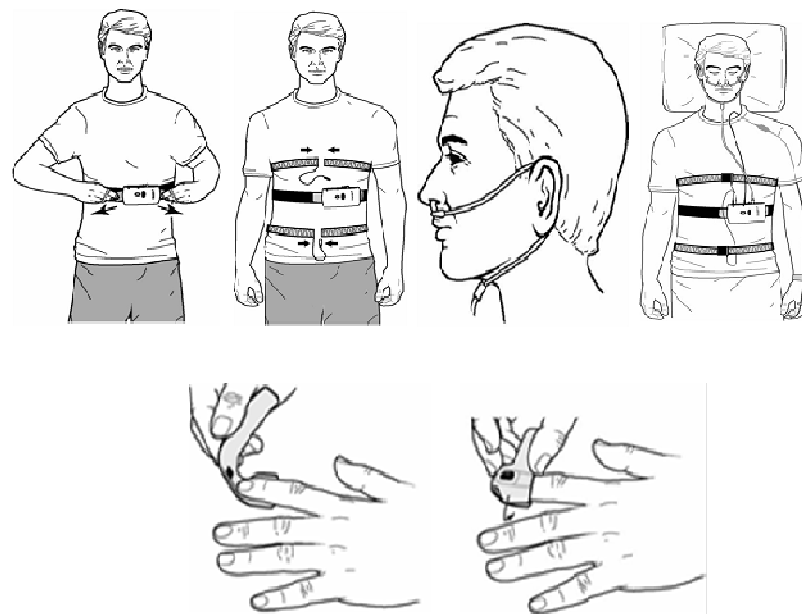
The diagnosis of OSA always involves the analysis of the patient's sleep, using polysomnography (PSG) or through cardiorespiratory polygraphic study.



Currently the inability to respond of health services, to the increasing number of patients who use the sleep lab, regarding the PSG, is increasing.

Thus, increasingly health services resort to domiciliary cardiorespiratory polygraphic study, portable registration, viable, reliable and more economical for the diagnosis of OSA and that requires no technical oversight. Dingli in 2003, compared domiciliary studies done by the device Embletta with polysomnographic studies, classifying Embletta as satisfactory, noting that enables costs reductions. However, this study has limitations regarding PSG, since a lesser number of registers variables. (105, 111)

The equipment used for this study was Embletta ® Gold™, (Fig. 27) 8 channels with digital signal acquisition. Respiratory monitoring was conducted by nasal cannula, thoracic-abdominal bands and oximeter placed on the index finger. This equipment allowed record nasal airflow, snoring, breathing movements, body position, O2 saturation, heart rate and pulse rate per minute. To this end, this equipment had the consumables waist belt, chest belt, nasal cannula and pulse oximeter.



**Figure 29: How to put the device of Polygraphy: Source: (Ohio State Medical Center ) (112)**

In the morning after the polygraphy, registers were analyzed and it was proceeded the adapted “morning questionnaire” of the Sleep Disorders Clinic, School of Sleep Medicine of Stanford University (Attachment 2). This questionnaire has identified particular features of the routine of individuals and data relating to sleep.

#### **4.10. Acupuncture intervention**

The acupuncture points of this technique were detected using a detector of points with two metal tips. We found the acupuncture points, with this detector, pressing the scalp near an angle of 90°. This angle reduces the possibility of providing more force in some points than in others. This question is fundamental because the most tender points of that reflex micro-region corresponds to a true point. As pain intensity corresponds, in terms of Chinese medicine, to a level of repletion, (excessive vegetative stimulation)

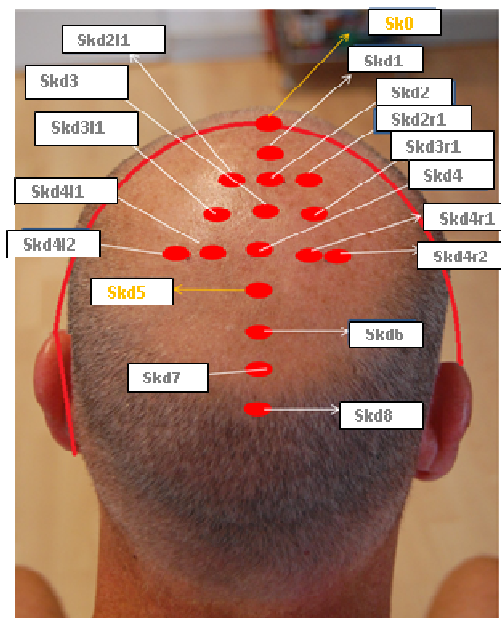
To each patient were placed 17 semi-permanent micro-needles of acupuncture. In Sk1 point and in SK6 point were placed two golden needles, so it was enhanced the vegetative function of these two points that correspond to Rg20 and Rg26. In the other points were placed silver needles.

**Phase 1:** Needles remain placed in the patient during 24 hours. In the following morning, needles were removed.

**Phase 2:** HSA is performed as described above and needles are left in the scalp during 10 consecutive days and removed on 11<sup>th</sup> day morning.

#### 4.10.1 Heidelberg Scalp acupuncture (HSA) treating OSA

Used points: SK0; Skd1; Skd2; SKd211, SKd2r1, SKd3, Skd3l1, Skd3r1, Skd4, Skd4l1, Skd4r1, Skd4l2, Skd4r2, Skd5, Skd6, Skd7 and SKd8 (Fig. 29)



**Figure 30: Localization of HSA points for OSA**

#### 4.11. Statistical analyses

Data was analyzed using XL-Statistics, version 5.0., and Microsoft Excel 2010. Tests used were Spearman correlation for association of continuous variables and Kruskal-Wallis test to compare continuous variables (Polygraphy1-Polygraphy 2)

#### **4.11. Ethical considerations:**

The research protocol followed the guidelines of the declaration of Helsinki of the World Medical Association. All general ethical principles were respected according to international standards.

The participation of individuals in the study was voluntary and did not constitute any health risk. Phase 1 lasted 3 weeks, offering a therapeutic technique (Heidelberg Scalp Therapy) with low clinical risk, and with therapeutic potential.

All participants were informed about the purpose of the study, objectives and procedures, acupuncture technique, side effects and possible adverse effects of acupuncture. A written informed consent was obtained. (Attachment 5)

Data collection respects confidentiality and is only used by the principal investigators of the study. Patients do not cease their conventional medical treatment.

Prior to phase 1, approval by the Ethics Committee of the S. João Hospital Center (SJHC) was obtained (Attachment 1).

#### **4.12. Study finances:**

The study subjects were invited to participate at no cost. The material of acupuncture was supported by the main investigator. The cardiorespiratory polygraphy equipment was supplied by ResMed. The study had no significant additional cost to the patients' usual medical approach in SJHC.

#### **4.13. Conflicts of interest:**

None of the elements of the research team are involved in activities that can represent conflicts of interest.



## CHAPTER 3



## 5. RESULTS





## 5.1. Sample characterization

By the time of this thesis deadline, phase 1 was completed.

Initially 18 patients were recruited. Due to technical problems, 8 were excluded.

Finally, data from 10 patients was retrieved and analyzed.

10 patients were included with a mean age of 56 years old (44 minimum-66 maximum); 6 men and 4 women and regarding OSA classification 4 patients had mild; 4 had moderate and 2 patients had severe OSA.

## 5.2. Descriptive analysis

Following tables show general data regarding AHI, Respiratory Events; Apnea Index (A/H) Hypopnea Index (H/h); Oxygen saturation and Snoring relative time, concerning both measurements (before and after polygraphy)

**Table 8: Descriptive analysis of: Apnea-hypopnea index; Respiratory events; Hypopnea index; Apnea Index – P1 vs P2**

	AHI - P1	AHI - P2	Resp Ev. P1	Resp. Ev. P2	H/hP1	H/hP2	A/hP1	A/hP2
<b>Mean</b>	20,14	12,49	141,5	84	6,34	4,68	14,51	8
<b>Min</b>	5	3	34	21	0	0	0,7	0,6
<b>Max</b>	37,2	31,7	314	214	12,3	14,8	44,6	26,3
<b>Median</b>	18,9	11,6	128	79	8,05	4,4	10,45	8
<b>Q1</b>	14,3	5,25	95,25	43	2,8	1,85	7,15	3,175
<b>Q3</b>	25,6	16,775	172,5	109,75	8,775	6,475	20,65	9,25

AHI – Apnea- Hypopnea index; Resp Ev. – respiratory events; H/h – Hypopnea index; A/h-Apnea index;

Min – Minimum; Max-Maximum; Q1-Quartile 1; Q3-Quartile 3

P1 – Polygraphy 1; P2- Polygraphy 2

**Table 9: Descriptive analysis of: Oxygen saturation; Dessaturation Index – P1 vs P2**

	A. O2 sat% P1	A. O2 sat% P2	(OD/h) P1	(OD/h) P2
<b>Mean</b>	93,31	94,03	16,73	12,91
<b>Min</b>	89,5	91,9	3,4	2,2
<b>Max</b>	95,5	97	24,4	23
<b>Median</b>	93,4	93,8	19,2	14,7
<b>Q1</b>	92,6	93	14,475	6,125
<b>Q3</b>	94,4	94,7	20,225	17,825

A. O2 sat% - Average of O<sub>2</sub> saturation; OD/h – Oxygen desaturation index

Min – Minimum; Max-Maximum; Q1-Quartile 1; Q3-Quartile 3

P1 – Polygraphy 1; P2- Polygraphy 2

**Table 10: Descriptive analysis of; Snoring relative time – P1 vs P2**

	Sno time%P1	<b>Sno time%P2</b>
<b>Mean</b>	19,67	<b>21,97</b>
<b>Min</b>	1,2	<b>0,4</b>
<b>Max</b>	47,8	<b>56,8</b>
<b>Median</b>	14,9	<b>16,3</b>
<b>Q1</b>	8,825	<b>5,7</b>
<b>Q3</b>	28,725	<b>35,725</b>

Sno Time% - Snoring relative time

Min – Minimum; Max-Maximum; Q1-Quartile 1; Q3-Quartile 3

P1 – Polygraphy 1; P2- Polygraphy 2

**Table 11: Improvement percentage \***

	AHI P1-P2	A. O2 sat% P1-P2	(OD/h) P1-P2	Resp Ev. P1-P2	S. time% P1-P2	H/h P1-P2	A/h P1-P2
<b>Median</b>	-51,4%	0,4%	-14,8%	-51,3%	-28,8%	-73,2%	-34,9%
<b>Q1</b>	-73,7%	-0,4%	-61,1%	-69,2%	-66,5%	-80,7%	-64,4%
<b>Q3</b>	-8,0%	1,4%	-8,5%	-7,8%	204,8%	-31,8%	6,8%

\*Improvement percentage= (P2-P1)/P1

### 5.3. Perception of sleep quality

**Table 12: Resume of Morning Questionnaire of Sleep Disorders**

MORNING QUESTIONNAIRE										
Evaluation parameter	Patients									
	1	2	3	4	5	6	7	8	9	10
Time to sleep (min)	5	5	30	5	10	10	15	5	10	10
Classification of the time to sleep*	AU	MLU	AU	MLU	AU	AU	AU	MLU	AU	AU
Awake up times	1	2	5	3	2	4	3	3	2	1
Hours of sleep/night	9	9	7	6	7	7	8	7	7	8
Feeling on the morning	A	R	F	A	A	R	R	A	R	R
Quality of sleep classification	AU	AU	BU	AU	AU	AU	AU	BU	BU	AU

MLU – Much lesser than usual; MBU - much better than usual; SU - Shorter than usual; MLU - Much longer than usual; LU- Longer than usual; AU – As Usual; BU- Better than usual; F- Fatigue; A-Alert; R- Rested;

#### 5.4. Inferential analyses – study outcomes

Before (polygraphy 1, P1) and after (polygraphy 2, P2) intervention with HSA.

- **Polygraphy Parameters**

We present data from: AHI; respiratory events; apnea index; hypopnea index; O2 saturation and snoring relative time.

##### 5.4.1 Apnea Hypopnea Index:

**Table 13: Apnea Hypopnea Index – P1 vs P2**

Patient	AHI -P1	AHI - P2	Improv. (%)
1	20,8	4,9	-76,4%
2	14,3	19,8	38,5%
3	37,2	9,3	-75,0%
4	33,9	31,7	-6,5%
5	5	13,9	178,0%
6	14,3	3,7	-74,1%
7	17	14,9	-12,4%
8	22,9	6,3	-72,5%
9	9,5	3	-68,4%
10	26,5	17,4	-34,3%

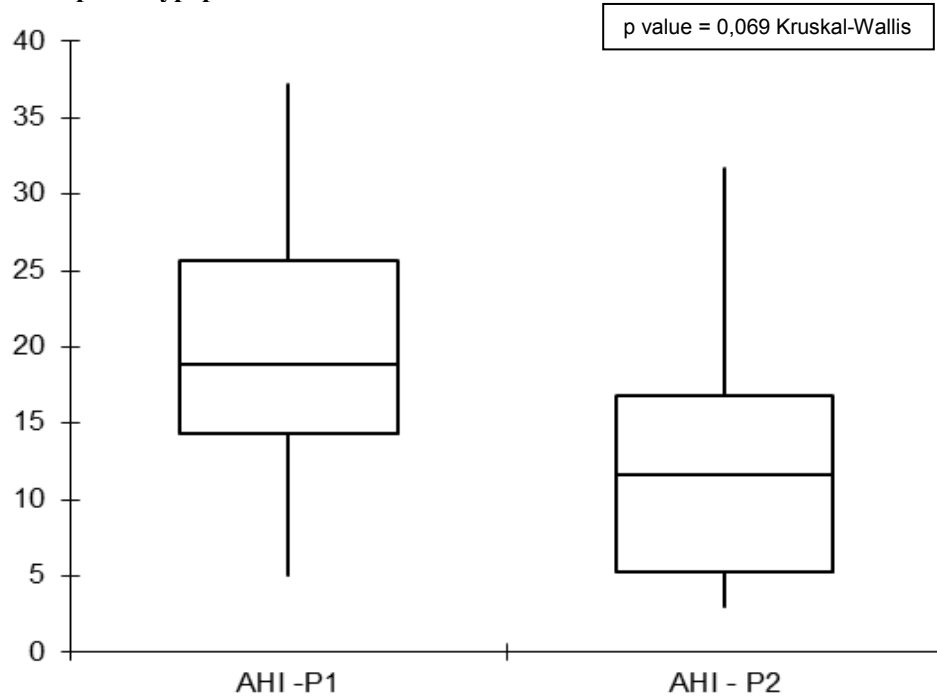
AHI – Apnea – Hypopnea Index

P1 – Polygraphy 1

P2 – Polygraphy 2

Improv. (%) – improvement percentage: (P2-P1)/P1

**Graphic 2: Apnea-Hypopnea Index – P1 vs P2**



P1 – Polygraphy 1  
P2 – Polygraphy 2

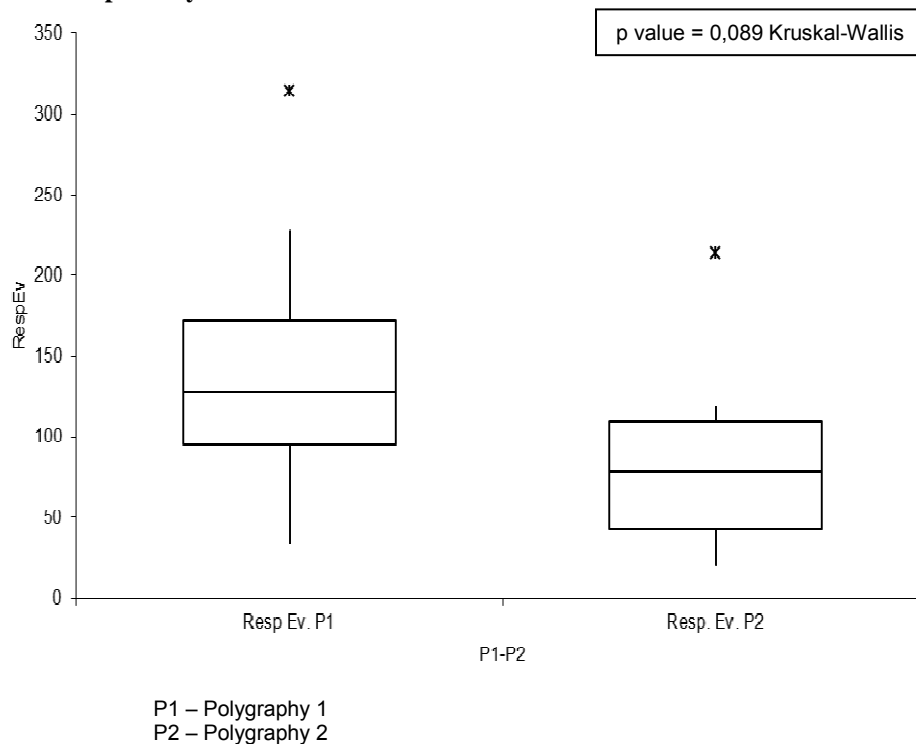
**5.4.2 Respiratory Events:**

**Table 14: Respiratory Events – P1 vs P2**

<b>Patient</b>	<b>Resp Ev. P1</b>	<b>Resp. Ev. P2</b>	<b>Improv. (%)</b>
<b>1</b>	144	46	<b>-68,1%</b>
<b>2</b>	95	112	<b>17,9%</b>
<b>3</b>	314	62	<b>-80,3%</b>
<b>4</b>	228	214	<b>-6,1%</b>
<b>5</b>	34	96	<b>182,4%</b>
<b>6</b>	96	25	<b>-74,0%</b>
<b>7</b>	118	103	<b>-12,7%</b>
<b>8</b>	138	42	<b>-69,6%</b>
<b>9</b>	66	21	<b>-68,2%</b>
<b>10</b>	182	119	<b>-34,6%</b>

Resp. Ev. – Respiratory events  
P1 – Polygraphy 1  
P2 – Polygraphy 2  
Improv. (%) – improvement percentage: (P2-P1)/P1

**Graphic 3: Respiratory events – P1 vs P2**



### 5.4.3 Apnea Index:

**Table 15: Apnea Index – P1 vs P2**

Patient	A/hP1	A/hP2	Improv. (%)
1	12,1	0,6	-95,0%
2	11,6	8,7	-25,0%
3	44,6	9,3	-79,1%
4	24,8	26,3	6,0%
5	3,3	7,3	121,2%
6	6,7	3,7	-44,8%
7	8,5	9,1	7,1%
8	9,3	3	-67,7%
9	0,7	1,3	85,7%
10	23,5	10,7	-54,5%

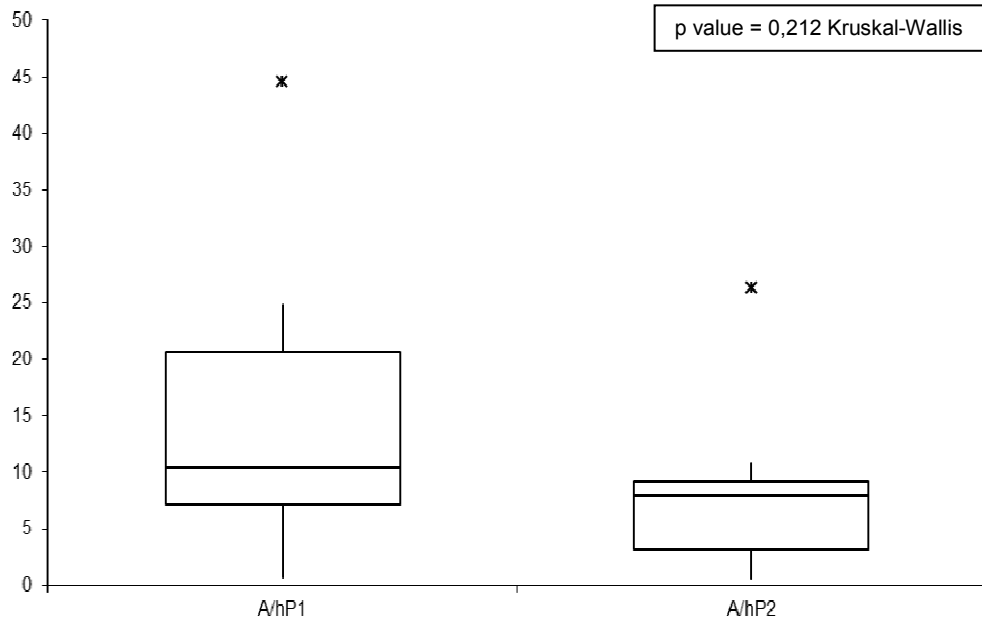
A/h – Apnea index (number of apneas per hour)

P1 – Polygraphy 1

P2 – Polygraphy 2

Improv. (%) – improvement percentage:  $(P2-P1)/P1$

**Graphic 4: Apnea index – P1 vs P2**



P1 – Polygraphy 1  
P2 – Polygraphy 2

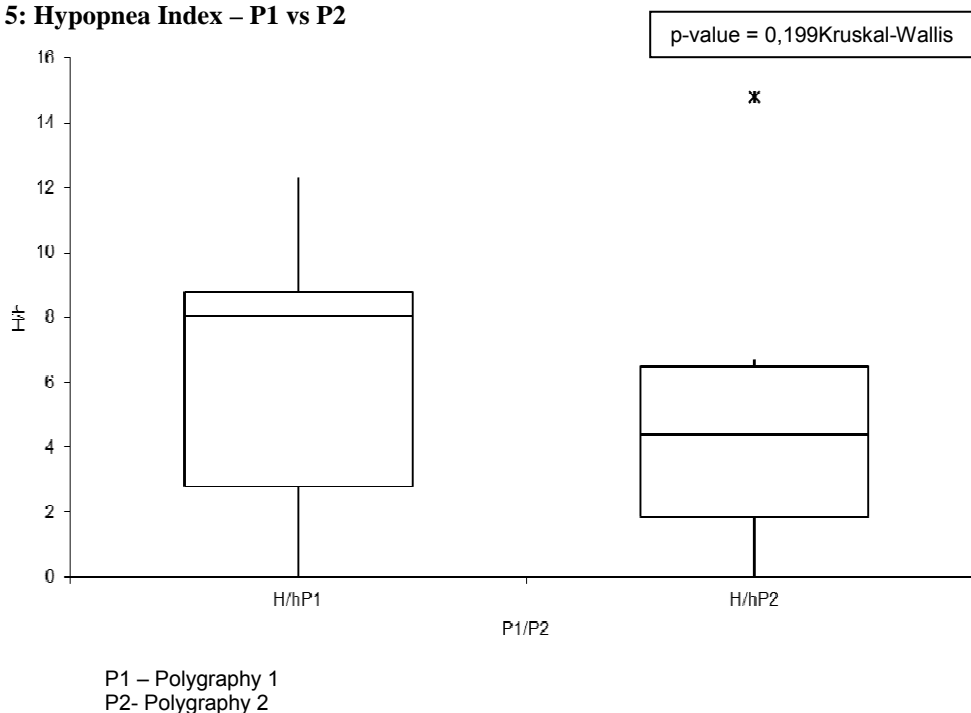
#### 5.4.4. Hypopnea Index

**Table 16: Hypopnea Index – P1 vs P2**

Patient	H/hP1	H/hP2	Improv. (%)
1	8,7	2,3	-73,6%
2	2,7	14,8	448,1%
3	2,6	0	-100,0%
4	9,1	5,5	-39,6%
5	0	6,7	
6	7,6	0	-100,0%
7	8,5	5,8	-31,8%
8	12,3	3,3	-73,2%
9	8,8	1,7	-80,7%
10	3,1	6,7	116,1%

H/h – Hypopnea index (number of Hypopneas per hour)  
P1 – Polygraphy 1  
P2 – Polygraphy 2  
Improv. (%) – improvement percentage:  $(P2-P1)/P1$

**Graphic 5: Hypopnea Index – P1 vs P2**



### 5.4.5 Oxygen Saturation

**Table 17: O2 saturation – P1 vs P2**

Patient	A. O2sat(%) P1	A. O2sat(%) P2	Improv. (%)
1	92,8	93	0,2%
2	92,6	91,9	-0,8%
3	95,5	96,1	0,6%
4	95	93,7	-1,4%
5	94,5	93,9	-0,6%
6	92,6	94,1	1,6%
7	89,5	93	3,9%
8	94	97	3,2%
9	92,5	92,7	0,2%
10	94,1	94,9	0,9%

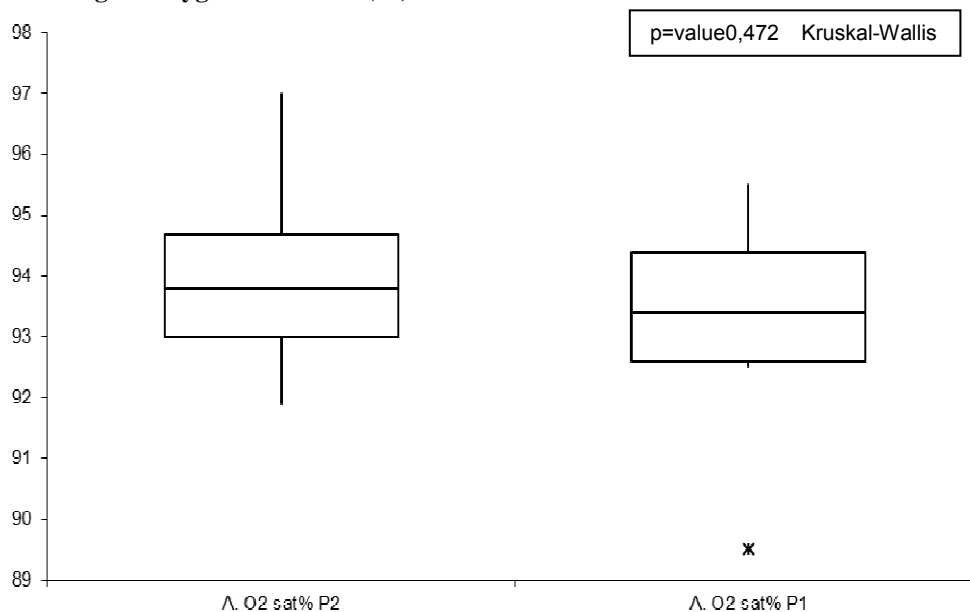
Av. O2sat% - Average of O2 saturation

P1 – Polygraphy 1

P2 – Polygraphy 2

Improv. (%) – improvement percentage:  $(P2-P1)/P1$

**Graphic 6: Average of oxygen saturation (%) – P1 vs P2**



P1 – Polygraphy 1  
P2 – Polygraphy 2

**Table 18: Oxygen dessaturation index – P1 vs P2**

Patient	(OD/h) P1	(OD/h) P2	Improv. (%)
1	19,6	18,3	-6,6%
2	21,4	23	7,5%
3	20	8,6	-57,0%
4	24,4	20,8	-14,8%
5	3,4	16,4	382,4%
6	14,1	5,3	-62,4%
7	15,6	13,4	-14,1%
8	20,3	5,1	-74,9%
9	9,7	2,2	-77,3%
10	18,8	16	-14,9%

OD/h – Oxygen dessaturation index ( O<sub>2</sub> dessaturation per hour)

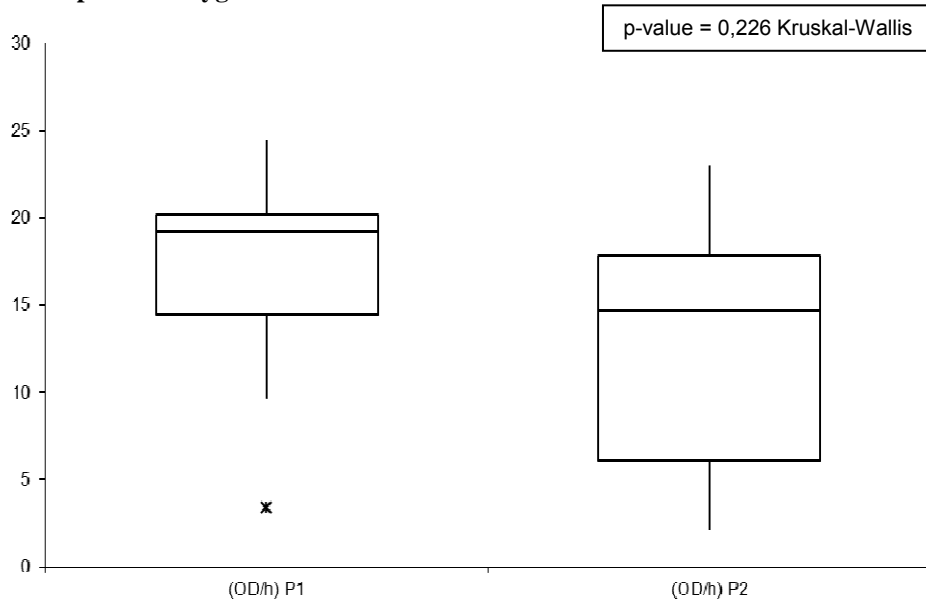
P1 – Polygraphy 1

P2 – Polygraphy 2

Improv. (%) – improvement percentage: (P2-P1)/P1



**Graphic 7: Oxygen dessaturation**



**5.4.6 Snoring**

**Table 19: Snoring relative time – P1vs P2**

<b>Patient</b>	<b>S.time%P1</b>	<b>S. time%P2</b>	<b>Improv. (%)</b>
<b>1</b>	24,6	16,3	<b>-33,7%</b>
<b>2</b>	7,9	51,8	<b>555,7%</b>
<b>3</b>	11,6	2	<b>-82,8%</b>
<b>4</b>	2,7	8,4	<b>211,1%</b>
<b>5</b>	15,8	56,8	<b>259,5%</b>
<b>6</b>	47,8	16,3	<b>-65,9%</b>
<b>7</b>	14	40	<b>185,7%</b>
<b>8</b>	41	4,8	<b>-88,3%</b>
<b>9</b>	1,2	0,4	<b>-66,7%</b>
<b>10</b>	30,1	22,9	<b>-23,9%</b>

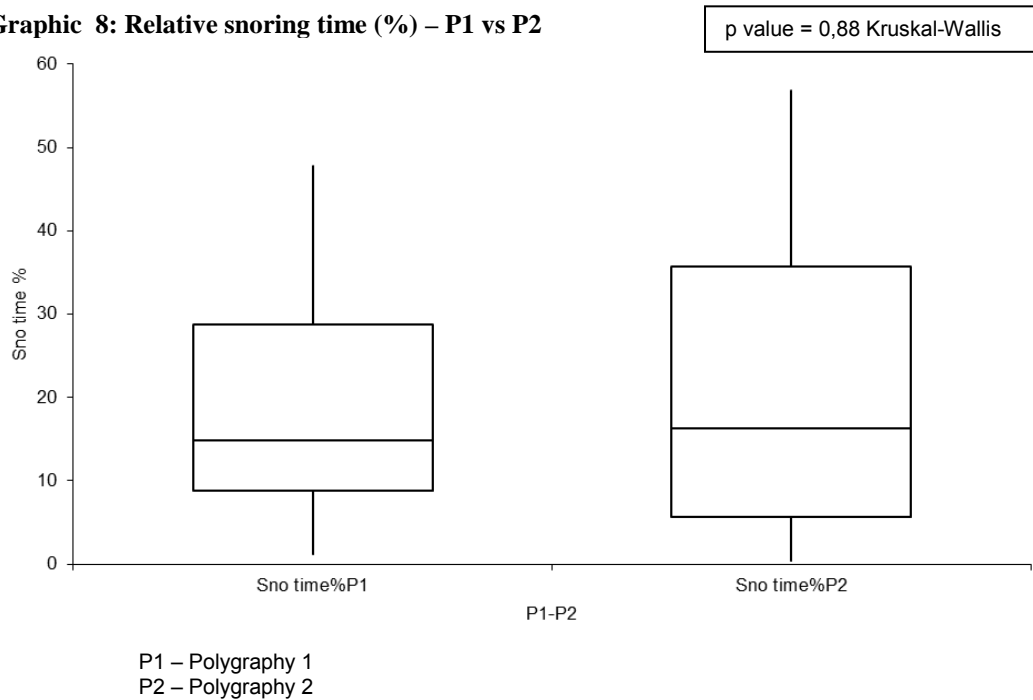
S.time% - Snoring relative time (%)

P1 – Polygraphy 1

P2 – Polygraphy 2

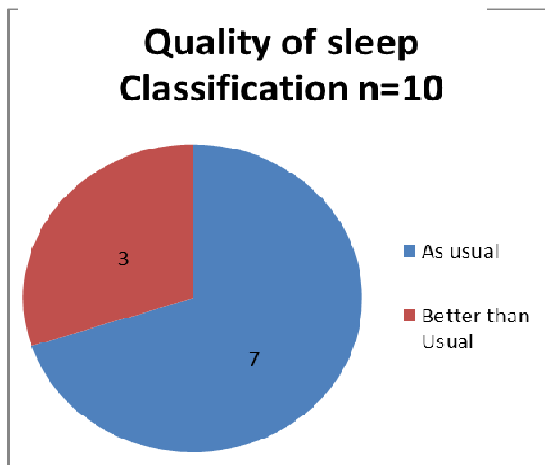
Improv. (%) – improvement percentage:  $(P2-P1)/P1$

**Graphic 8: Relative snoring time (%) – P1 vs P2**

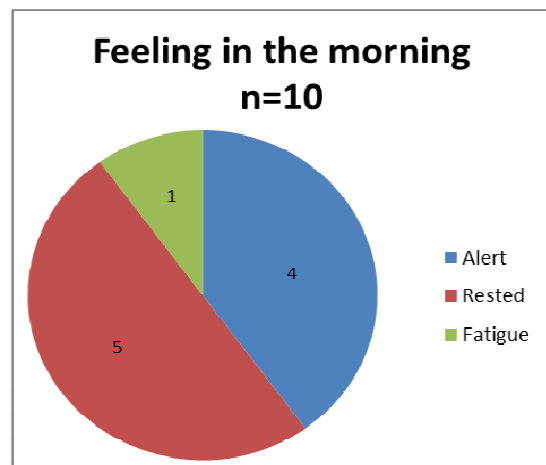


- Perception of sleep quality

**Graphic 9: Quality of sleep (n=10)**



**Graphic 10: Feeling in the morning (n=10)**



### 5.5 Sample size estimation:

Based on the above data on the AHI, we estimated the sample size needed to achieve statistical significance.

If the total of 66 patients would enter a two treatment parallel-design study the probability is 80% that the study will detect a treatment difference at a two-sided 0.05 significance level. This is based on the assumption that the standard deviation of the AHI is 10.9

## CHAPTER4



## 6. DISCUSSION:

Due to the small sample size on phase 1, no statistical significance was achieved on any outcome. However, these preliminary results suggest that HSA may improve OSA. We further discuss the main findings.

- **Scalp acupuncture acute effects:**

The Western treatment for OSA includes general measures that include diet therapy and change patient behavior and specific measures that can pass through pharmacological actions, surgical, oral appliances and oral Positive Air Pressure.

These measures have certain limitations. The pharmacological measures have been subject to many discussions and their evidence is supported by very questionable data (39). Indication to surgery occurs only in selected cases after failure of CPAP as therapy. These surgeries frequently have a post-operatively painful course and can lead to impaired swallowing and speech. (25) The oral appliances are prescribed in cases of patients with mild and moderate apnea. (28) The Positive Air Pressure devices are the gold-standard treatment for OSA, however they have some significant side effects such as depression, claustrophobia, insomnia, marital conflicts and allergies that lead to abandonment and intolerance of this device. (116)

The acupuncture therapy is a low cost and with few adverse effects. Regarding OSA, there is a paucity of studies on the effect of acupuncture, including auriculotherapy. (23, 24, 107, 108, 109, 110). The only study available, in English, on immediate (acute) effect of acupuncture on OSA showed that a single treatment session, of manual body acupuncture was superior to control group and that it was a major improvement in AHI with active acupuncture. They have found preliminary evidence that acupuncture is effective in the treatment of OSA. (23, 24). This study used a local approach and a systemic treatment, using 19 cooper-handle needles, 40 x 0,25 mm, into 19 points distributed throughout the body (body acupuncture): 1 point in the region of scalp, 1 point in the face (bilateral), two points in the neck region, three points on the forearm region (bilateral), 3 points in the tibial region (bilateral) and 1 point in the foot (bilateral). In terms of comfort for the patient, by clinical experience it is known that patients are not comfortable with manipulations or insertions of needles in the neck, and that they feel more comfortable with smaller needles. Using this technique the placement of needles is in the ventral part of the body, with the patient lying down. The Clinical experience from our group suggests that scalp acupuncture may have a beneficial effect in OSA, based on a new model – Heidelberg Scalp Acupuncture. This technique is more comfortable for the patient. In this technique the needles are much

smaller (micro-needles with 3mm) placed with the patient in the sitting position, with clothes on, and without the patient notice the needles, which reduces the normal apprehension of the puncture); it is less invasive than previous acupuncture, and so it is more tolerable by the patients. In addition, the stimuli may be permanent, since the needles are permanent in the selected scalp points. Therefore, we decided to conduct a research study on the effect of scalp acupuncture in OSA in order to investigate these field observations.

Interestingly, no previous studies on Scalp Acupuncture on Obstructive Sleep Apnea are available in the literature.

The Heidelberg Scalp Acupuncture can present itself as an alternative or complementary therapy for the treatment of OSA. This preliminary study, with 10 clinical cases, showed that 8 out of 10 patients, with individual treatment, responded to the therapy approach, which is demonstrated by an improvement of: 51.4% (p value = 0,069) in AHI; 51.3% (p value = 0,089) in the number of respiratory events; 14,8% (p value = 0,226) in Oxygen Desaturation Index and 28.8% (p value = 0,88) in Snoring relative time. In terms of perception of sleep, no patient reported that sleep quality had worsened; 3 of 10 patients indicated that sleep quality was better than in the regular days. 7 patients classified the quality of sleep as the same as usual. Regarding the feeling in the morning, 4 patients reported that they felt alert; 5 reported that they felt rested and only one answered that he felt fatigue. All patients did not report any kind of discomfort or complaints regarding the permanence of the needles.

In our perspective, these preliminary data supports the need for further research. A prospective randomized control trial, in a double blinded assay ("Heidelberg assay") method, is currently in course.

**If our research shows improvement of OSA by HSA, we may speculate of positive effects on the other OSA associated diseases and sub-health problems, such as cardiovascular diseases, hypertension, cerebrovascular complications, and psychosocial consequences.**

- **Neurophysiological basis for HSA – a theoretical proposal**

The four patients reported that the most painful points pointing to greater pathology, were SKd5, SKd6, SKd7 SKd8 and which project the hypoglossal triangle, vagal triangle, cranial nerve and cervical accessory nerve, respectively.

By doing line projections between points of HSA to treat OSA and the structures to which each point corresponds we found relevant intersections on the thalamus and brain

stem. The facial somatotopic system of Heidelberg Scalp Acupuncture apparently correlates with the major anatomical projections of the points such as (114) (Fig 30):

Thus the line of:

- SK0 point intersects the line of Yintang in the region of the thalamus.
- SKd1 point intersects the line of the root of the nasal pyramid in the upper midbrain.
- SKd2 point intersects the line of the nasal bone in the region of trochlear nucleus.
- SKd2r1 point intersects the line of the ethmoid cells in the region of trochlear nerve.
- SKd2l1 point intersects the line ethmoid cells in the region of trochlear nerve.
- SKd3 point intersects the line of the maxillary sinus ostium medial region of the trigeminal nucleus.
- SKd3r1 point intersects the line of Maxillary Sinus in the region of Trigeminal nerve
- SKd3l1 point intersects the line of Maxillary Sinus in the region of Trigeminal nerve
- SKd4 point intersects the line of lower conchae in the region abducen motor nucleus.
- SKd4r1 SKd4l1 points and intersects the line of lower maxillary sinus zone in the region of vestibulocochlear nerve.
- SKd4r2 and SKd4l2 points intersects the line of the points IC20 in the region of Glossopharyngeal nerve
- SKd5 point intersects the line of Rg26 in the region of Hypoglossal triangle
- SKd6 Point line of intersects the soft palate in the region of Vagal triangle
- SKd7 point intersects the line of uvula in the region of the Cranial accessory nerve
- SKd8 point intersects the line of oropharyngeal in the region of Cervical Nerve 1 (C1)

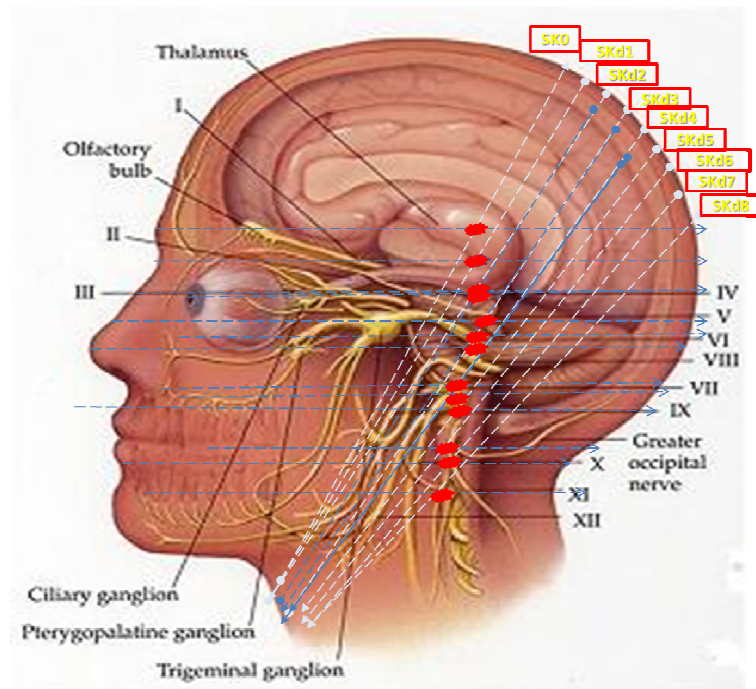


Figure 31 Scheme of the intersection points of facial somatotopy of HSA. Adapted from [www.michigan-headache-tmj-doctor.com](http://www.michigan-headache-tmj-doctor.com)

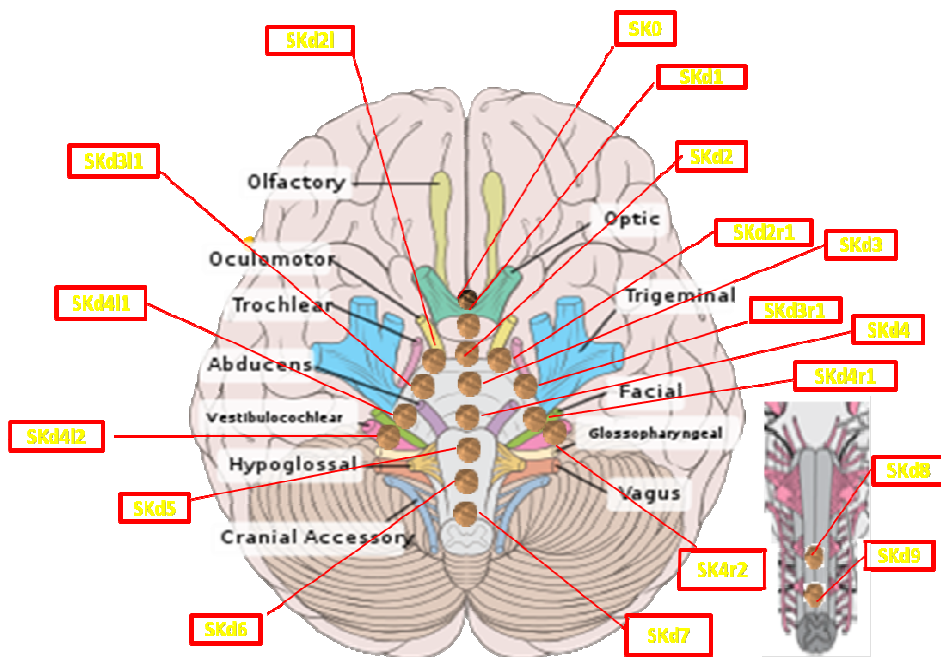
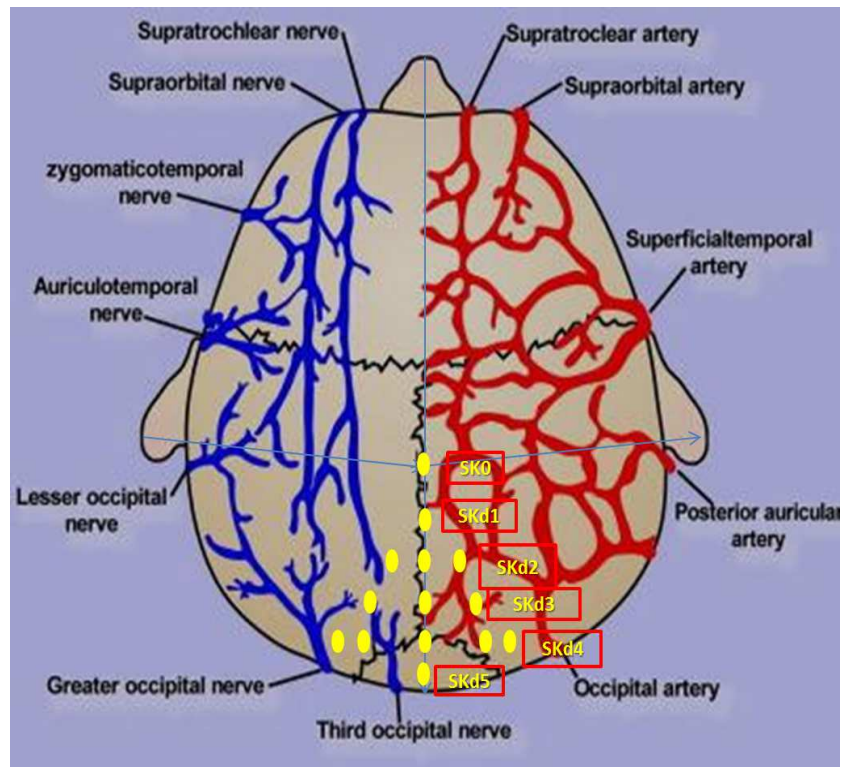


Figure 32: Intersection points, inferior view, adapted from Patrick J. Lynch (118)





**Figure 33: Innervation and vascularization structures possible involved in HSA**

In terms of innervation of the scalp, there seems to be an involvement of Supratrochlear Nerve branches, the Great Occipital Nerve branches and branches of the Occipital Third Nerve. (Fig.32)

In terms of vascularization was found involvement of the anastomotic net formed by the Superficial Temporal arteries and veins, and of the occipital arteries and veins. (Fig 30)

Thus, this type of projections suggests a kind of "Front-Mu" relationship with the brainstem and with the cranial nerves related to it. (Fig. 32)

The brainstem has three main functions: serves as conduit for the ascending and descending tracts connecting the spinal cord to the different parts of the higher centers in the forebrain; it contains important reflex centers associated with control of respiration and the cardiovascular system and with the control of consciousness; contains important nuclei of cranial nerves III through XII. (85)

The Somatic efferent cranial nerves III, IV, VI and XII have origin in cells (derived from the basal plates) located in the somatic efferent column. Their axons are distributed to muscles derived from head myotomes. The nerves of pharyngeal arches V, VII, IX and X supply the embryonic pharyngeal arches. (85)

These nerves have significant importance in the innervation of the upper airways and underlines a possible relationship to scalp stimulation by HSA. (Fig. 31)

These relationships can also verify the fractal theory applied to human physiology and ontogeny, so, it is suggest a study to investigate and verified these embryonic and neurophysiological relationships.

### **7. Limitations:**

This study is the preliminary step of a research project that aims to verify the effects of Heidelberg Scalp Acupuncture on Obstructive Sleep Apnea. In this preliminary study we only recruit ten patients. In this phase there are obvious limitations such as the number of patients and lack of control group. However, data suggested a positive tendency of beneficial effects secondary to scalp needling, according to our model, supporting further research. A randomized controlled trial is currently in course.

## CHAPTER 5



## 7. Future Perspectives:

Scalp acupuncture has demonstrated beneficial effects in several diseases mostly dependent on neurological pathology (e.g. stroke, Parkinson disease, psychiatric diseases, speech disturbances, etc).

It is a field on Microsystems's acupuncture with a high research potential, because anatomically may be correlated with various structures, plus it is a simple technique to apply, painless, and with reduced financial costs.

It is therefore necessary further investigation to have some enlightenment in:

- **The biological mechanisms of this technique** (that can involve various areas such as neurophysiology, embryology, endocrinology and ontogeny), **particularly in the OSA physiopathology.**
- **The magnitude of the therapeutical effect in different degrees of OSA (mild, moderate and severe) and possible side effects**
- **The cost-benefit of the integration of this technique in the treatment approach of OSA in order to complement conventional treatment.**
- **The type of permanent needles to use in OSA. Commercially available implantable needles may be developed to be a long term complement to CPAP treatment.**
- **The optimal time of permanent needling on the scalp on OSA.**

## **8. Conclusion:**

Despite our preliminary evidence, the Heidelberg Scalp Acupuncture (HSA) seems to have some therapeutically benefits on OSA. Our study suggests that HSA may improve sleep apnea as measured by polygraphy.

This technique may implicate several neurophysiological, embryological and ontogenetic factors. More research is needed to assess the long-term effect of HAS on OSA and to explore the mechanism of action of this treatment technique.

Further research in HSA on OSA is needed to evaluate long-term effects of scalp acupuncture. This future research may also enlighten HSA effects on comorbidities that benefit from OSA improvement such as: HTN, HF, cerebrovascular disease.

At the end, an *integrative* approach to OSA, joining conventional to complementary therapies, may be established with a superior therapeutic benefit to the patient and possibility avoiding higher costs and medical side effects.

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## ATTACHMENTS





## Attachment 1



### Declaração

Para os devidos efeitos se declara que a Dra. Maria João Rodrigues Ferreira Rocha dos Santos entregou um projecto de investigação denominado “*Efeitos da acupuntura no Síndrome da Apneia Obstrutiva do Sono*” para ser apreciado pela Comissão de Ética para a Saúde do Hospital de S. João / Faculdade de Medicina da Universidade do Porto. Este projecto foi aprovado pela Comissão de Ética na Reunião Plenária de 31 de Julho de 2012, e enviado para o Conselho de Administração para autorização em 2 de Agosto de 2012.

Porto, 26 de Setembro de 2012

O Secretário da Comissão de Ética para a Saúde

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Dr. Pedro Brito

## Attachment 2

### QUESTIONÁRIO MATINAL (PÓS-ESTUDO POLIGRÁFICO DO SONO)

Nome: \_\_\_\_\_

Data: \_\_\_/\_\_\_/\_\_\_

Hora : \_\_\_ h \_\_\_ min

1) Quanto tempo demorou a adormecer na última noite, desde o momento em que as luzes foram apagadas? \_\_\_\_\_ min

2) Como compara este tempo com o que habitualmente demora a adormecer em casa?

Muito mais longo que o habitual

Mais longo que o habitual

Igual

Mais curto que o habitual

Muito mais curto que o habitual

3) Quantas vezes se recorda de ter acordado na última noite? \_\_\_\_\_ vezes

4) Ao todo, quanto tempo dormiu na última noite? \_\_\_\_\_ horas.

5) Como é que se sente neste momento?

Muito cansado e sonolento

Acordado mas não alerta

Descansado

Alerta e bem acordado

6) Tem algumas queixas esta manhã?

Não

Sim

Quais? \_\_\_\_\_

\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

- 7) Classifique de 1 a 7 a qualidade do seu sono da última noite, marcando com um círculo em todas as características abaixo:

*O meu sono da última noite foi:*

Leve	1	2	3	4	5	6	7	Profundo
Curto	1	2	3	4	5	6	7	Longo
Interrompido	1	2	3	4	5	6	7	Contínuo
Sem sonhos	1	2	3	4	5	6	7	Com muitos sonhos
Cansativo	1	2	3	4	5	6	7	Repousante

- 8) Lembra-se de algum sonho da última noite?

Não  Sim

Se sim descreva-o resumidamente:

- 9) O que o acordou esta manhã?

Barulho  Desconforto  Técnico  Espontâneo

Outro  Qual? \_\_\_\_\_

- 10) Em termos gerais, como classificaria a sua última noite de sono, quando comparada com o habitual em sua casa?

Muito pior que o habitual

Pior que o habitual

Igual ao habitual

Melhor que o habitual

Muito melhor que o habitual

- 11) Caso queira fazer mais algum comentário ou dar mais alguma informação, use as linhas seguintes.

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## Attachment 3

### Questionário 1

Relativamente ao tratamento que efetuou responda as seguintes questões assinalando com um X.

(1) Qual a sua expectativa sobre o efeito do tratamento de acupunctura no alívio da sua patologia?

Muito Baixa\_\_ Baixa\_\_ Satisfatória\_\_ Alta\_\_ Muito Alta\_\_

(2) Da lista seguinte indique fatores que influenciaram as respostas anteriores.

Melhoria (ou ausência de melhoria) no sono\_\_

Melhoria (ou ausência de melhoria) da roncopia\_\_

Melhoria (ou ausência de melhoria) da fadiga matinal\_\_

Bem estar geral\_\_

Comentário do cônjuge/familiar\_\_

Uma sensação “particular” durante o tratamento de acupunctura\_\_

Localização dos pontos que foram picados\_\_

Respondi ao acaso\_\_

### Questionário 2

Relativamente ao tratamento que efetuou responda as seguintes questões assinalando com um X.

(1) Recomendaria o tratamento de acupunctura a outras pessoas?

Não\_\_ Talvez\_\_ Sim\_\_

(2) Na sua opinião faz sentido utilizar acupunctura no tratamento da SAOS?

Não\_\_ Talvez\_\_ Sim\_\_

(4) Qual a sua expectativa sobre o efeito da acupunctura no tratamento de outros problemas de saúde?

Muito Baixa\_\_ Baixa\_\_ Satisfatória\_\_ Alta\_\_ Muito Alta\_\_

## Attachment 4:

### INFORMAÇÃO AO PARTICIPANTE

**Caro Participante,**

O presente estudo no qual participará designa-se “**Comparação de duas estratégias de acupuntura no tratamento da apnéia do sono obstrutiva. - Estudo preliminar-**”.

O objectivo do estudo é perceber se a terapia complementar da Medicina Tradicional Chinesa, a acupuntura, leva a melhoria de sintomas associados ao síndrome de apneia obstrutiva do sono e quais as alterações levadas a cabo por esta terapia quer ao nível da fisiologia, quer ao nível da qualidade de vida.

No sentido de estudar os efeitos fisiológicos será sujeito a avaliação registada por poligrafia.

No sentido de avaliar a qualidade de vida será pedido o preenchimento questionários: Questionário Matinal; Questionário de credibilidade do tratamento. Durante estes procedimentos estará acompanhado por médico e/ou enfermeiro, além da terapeuta de Medicina Tradicional Chinesa.

A sua participação será voluntária. I

Irá proceder-se à técnica de acupuntura designada por craniopunctura. Esta técnica consiste na inserção de microagulhas semipermanentes no couro cabeludo. Estas agulhas permanecerão no couro cabeludo 24 horas. Durante a colocação da agulhas será sujeito à avaliação visual da dor da punctura. Na noite após a colocação das agulhas irá repetir a poligrafia cardiorespiratória para avaliar os efeitos da técnica terapêutica. Na manhã seguinte serão realizados dois questionários simples para avaliar a sua percepção da qualidade do sono.

O tratamento com acupuntura será efectuado por um profissional de saúde com formação em Medicina Chinesa Tradicional certificada por Universidade pública portuguesa.

Com o tratamento de acupuntura **esperamos contribuir para melhoria da sua doença**, nomeadamente, melhoria do índice de apnea-hipopnea que avalia a gravidade do Síndrome da Apneia do Sono e da qualidade do sono.

Note que não se espera que a acupuntura prejudique o tratamento convencional a que será sujeito nem haverá qualquer interferência no seu plano de tratamento habitual.

Todas as **agulhas de acupuntura são esterilizadas e descartáveis** (ou seja, de uso único). Antes da inserção das agulhas, a pele será desinfectada com uma solução anti-séptica alcoólica.

Os **riscos associados a acupuntura são mínimos**. Poderá sentir algum grau de dor ou desconforto e formigueiros no local das picadas com as agulhas de acupuntura. **Mais raramente**, poderá sentir tonturas, ansiedade ou náuseas. É possível que após o tratamento possam surgir ligeiros sangramentos, em particular se estiver a tomar a tomar medicamentos anti-agregantes (ex.: Aspirina, ácido acetilsalicílico) ou hipocoagulantes (ex.: Varfine® (varfarina); Sintrom®, acenocumarol) e/ou aparecerem ligeiros hematomas num local onde foram inseridas as agulhas que se resolverá espontaneamente. Caso esteja a tomar a medicação acima referida deverá informar a equipa de investigação.

Note que durante estes procedimentos estará sempre acompanhado por Médico e ou Enfermeiro com treino em suporte avançado de vida e que o Hospital de São João está dotado de uma Equipa de Ressuscitação Interna durante 24 horas de actuação rápida, caso seja necessário, que é activada por telefone interno.

Sendo a sua **participação voluntária** terá o que tempo que necessitar para ponderar sobre a sua participação neste estudo. É livre de consultar a opinião dos seus familiares ou amigos. **Caso decida aceitar, poderá posteriormente, a qualquer momento recusar continuar no estudo.**

**Se recusar continuar neste estudo, o tratamento médico convencional não será afectado e toda a assistência habitual é-lhe garantida pelos profissionais de saúde.**

Ao entrar neste estudo será **garantida a sua privacidade**, através de confidencialidade dos dados e regras do sigilo médico. Todos os resultados obtidos serão devidamente codificados. Caso pretenda, poderá ter acesso aos resultados, mas não os poderá divulgar ou usar para fins científicos. Os dados serão apenas do conhecimento dos investigadores principais e dos orientadores do estudo e do eventual patrocinador do estudo e poderão ser posteriormente publicados em revistas científicas ou apresentados em eventos científicos. Será sempre mantido o seu anonimato.

Note ainda que este estudo foi aprovado pela Comissão de Ética do Hospital de São João.

Para seu conhecimento, as investigadoras principais deste estudo são as mestrandas Maria João Santos e Sofia Milhano

**Para qualquer esclarecimento poderá entrar em contacto com a Mestranda Maria João Santos telemóvel 91 3563504.**

A equipa de investigação agradece a sua participação e está ao seu dispor para qualquer esclarecimento.

Hospital São João, Data: \_\_\_/\_\_\_/\_\_\_

Com os melhores cumprimentos,

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Maria João Santos

Com os melhores cumprimentos,

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Sofia Milhano

## Attachment 5

Comissão de Ética para a Saúde do Hospital de S. João – EPE Modelo CES 05.A

### DECLARAÇÃO DE CONSENTIMENTO

*Considerando a "Declaração de Helsínquia" da Associação Médica Mundial*

*(Helsínquia 1964; Tóquio 1975; Veneza 1983; Hong Kong 1989; Somerset West 1996 e Edimburgo 2000)*

#### **Designação do Estudo (em português):**

"Comparação de duas estratégias de acupuntura no tratamento da apnéia do sono obstrutiva.

-Um estudo preliminar-".

**Eu, abaixo-assinado, (nome completo do participante)** -----

-----, compreendi a explicação que me foi fornecida, por escrito e verbalmente, da investigação que se tenciona realizar, para qual é pedida a minha participação. Foi-me dada oportunidade de fazer as perguntas que julguei necessárias, e para todas obtive resposta satisfatória.

Tomei conhecimento de que, de acordo com as recomendações da Declaração de Helsínquia, a informação que me foi prestada versou os objectivos, os métodos, os benefícios previstos, os riscos potenciais e o eventual desconforto. Além disso, foi-me afirmado que tenho o direito de decidir livremente aceitar ou recusar a todo o tempo a minha participação no estudo. Sei que se recusar não haverá qualquer prejuízo na assistência que me é prestada.

Foi-me dado todo o tempo de que necessitei para reflectir sobre esta proposta de participação.

Nestas circunstâncias, decido livremente aceitar participar neste projecto de investigação, tal como me foi apresentado pelo investigador(a).

Data: \_\_\_\_ / \_\_\_\_\_ / 20\_\_\_\_

**Assinatura do(a) participante:**

\_\_\_\_\_  
**O(A) Investigador(a) responsável:**

Nome:

\_\_\_\_\_  
Assinatura: