Hypertension and Osteopathic Treatment: A Literature Study

Literature Study for the Acquisition of the Diploma Osteopathy (D.O.)
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Declaration

I hereby confirm that the presented work is compiled by my own hands and has not been submitted elsewhere for examination/review. Foreign sources are identified and labelled with information about their origin.

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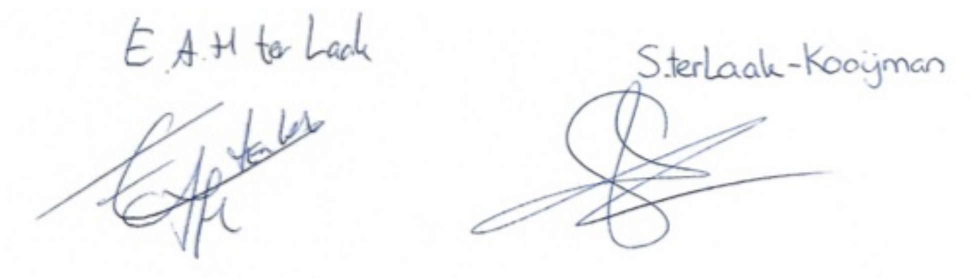
‘s-Hertogenbosch 26/10/2019



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Abstract

This thesis sets out to determine if there is a relationship between osteopathy and a change in the health of adult patients with hypertension (HTN), and if it is safe to treat these patients using osteopathic treatment (OT). It is important to note that osteopathy is not a form of medicine that concerns itself with the treating of disease, as is the case with allopathic medicine.

After a description and discussion of the anatomy, physiology and embryology of the vascular system, relevant scientific papers are described and discussed. From the appraisal and criticism of the included papers, it is apparent that in no singular occurrence of OT was it reported as causing harm to any patient. This alone is an important factor when considering OT as a viable treatment as part of a multi-disciplined approach to patient care within the group of vascular hypertensive patients. Patient safety should always be at the forefront of any healthcare providers mind.

With regard to the results of this literature study, the most promising evidence was found in studies where patients underwent full osteopathic treatment. These studies originate mainly in Italy. The results showed both improvements in the blood pressure and structural changes which are commonly seen in pathologies relating to HTN.

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1. Foreword

I first came into contact with osteopathy circa 2009 in England, where I was treated by Edward Jones BOst to whom I remain very grateful. He helped me recover from a neck injury that I incurred whilst practicing somersaults on a trampoline with a snowboard duct-taped to my feet. It was, after all, summertime and therefore too hot for wearing snowboard boots! Landing on my head was the straw that broke the camel's back in my case. This new form of therapy certainly made a huge impression on me. In 2012 I was receiving treatment for lower back pain in the Netherlands at the practice of Pieter Achten D.O. in Den Bosch. It was at that time that I told Pieter I wanted to learn his profession. Luckily, he took me seriously and a few weeks later I was following lessons in the foundation year at Sutherland College of Osteopathy in Amsterdam. Since then I haven't looked back.

Learning osteopathy has brought me to many new places and has occupied a great deal of my time and energy in the past 7 years, I'm no longer the person who had a limited understanding of Dutch and almost constantly had my hand in the air to ask questions in the class. My colleagues will verify the hand in the air behavior; even now I'm eager to know the finer details and, if I disagree with what is being said, I'll readily put my hand up. After many years of asking questions and getting into numerous discussions with tutors and colleagues, I've definitely changed as a person and how I approach others. My thanks to Therapist – Patient Relationship (TPR) tutor, Toos Bartlema for the latter - from initially regarding TPR lessons as silly and unnecessary in the first year to becoming the most important lessons for my personal development in the last years of study.

William John Robertson
Den Bosch May 2019

2. A Brief History of Osteopathy and its Implications for this Thesis

There is a discrepancy in the approach of osteopaths around the world. This discrepancy is greatest between practitioners in the USA, where allopathic medicine is fully integrated into the teachings of osteopathy, and European and UK schools of osteopathy, which developed, for the most part, outside the confines of allopathic medicine.

Dutch and Belgian schools of osteopathy are typical examples of osteopathy that developed outside of the confines of allopathic medicine and may be seen as being at the opposite end of the spectrum to that of osteopathy in the USA. In the rest of the world the osteopathic approach varies between these two polarities of osteopathy. To list each country and its form of osteopathy would be lengthy and not of any real value to this thesis. This modern-day discrepancy is most likely due to a few factors:

1. The presence of MDs in the first schools of osteopathy in Kirksville USA from 1892 onwards, where A.T. Still* was based.

2. Two of Still's students, brothers John Martin and James Buchan Littlejohn. are important to mention in the development of the profession of osteopathy, they represent an early schism which is still present to this day. James Buchan was a strong proponent for the inclusion of surgical practice within the profession. O'Brien (2017) states "Although James's distinct vision has never been recognised, he laid out a blue-print for osteopathy to evolve into osteopathic medicine. His path was protecting major surgery as an integral subject within the core curriculum". O'Brien also suggests that James Buchan was at the vanguard of the USA osteopathic philosophy to fully integrate with allopathic medicine. John Martin on the other hand was a strong supporter of the complementary allocation of osteopathy, and believed that the causative factors were not only to be found in spinal (osteopathic) lesions. John Martin's ideals were rejected outright by the mainstream of the profession at the time.

3. John Martin brought osteopathy over from the USA to the UK in 1913 after studying for 10 years in Chicago, USA. At this time the healthcare system in the UK was already regulated by allopathic medicine. This meant that the profession of osteopathy in the UK operated outside of

*Still is widely viewed as the founding father of osteopathy. Referenced from: https://www.johnwernhamclassicalosteopathy.com/what-is-classical-osteopathy/a-t-still-j-m-littlejohn/ (2019, 19th October) allopathic regulation in its origin. This also rings true with John Martins philosophy of osteopathy being a profession in its own right and not a part of the allopathic approach. This philosophy of osteopathy as a complementary healthcare system is very much present at the Sutherland College of Osteopathy in Amsterdam, The Netherlands

4. Osteopathy arrived in France in 1917 by way of an American osteopath serving in the First World War, he taught osteopathy to Doctor Lavezarri, a physician practicing in Nice and Paris at the time. Osteopathy then spread from the UK and France to the rest of Europe. (Barillon 2003)

Osteopathy in the modern age is still a form of therapy that seeks to improve the functionality of the body through better mobility, tone and tension. As taught at College Sutherland, Amsterdam, this should include all structures in the body. The criteria for an osteopathic treatment are only decided upon following a physical examination, carried out by the osteopath. The physical examination determines which OT is to be applied at that time, not the presence of disease or symptoms with which the patient presents. This is crucial in understanding the way in which an osteopath performs his or her profession. Bresciani, Boscagli, & Zhang (2010) state:

> Osteopathy (also called osteopathic medicine) relies on manual contact for diagnosis and treatment. It respects the relationship of body, mind and spirit in health and disease; it lays emphasis on the structural and functional integrity of the body and the body's intrinsic tendency for self-healing. Osteopathic practitioners use a wide variety of therapeutic manual techniques to improve physiological function and/or support homeostasis that has been altered by somatic (body framework) dysfunction, i.e. impaired or altered function of related components of the somatic system; skeletal, arthrodial and myofascial structures; and related vascular, lymphatic, and neural elements. (pp.1)

There are multitudes of studies relating to singular osteopathic techniques, the vast majority of which are not included in this paper as they do not conform to the principles of holistic osteopathy as taught at Osteopathy College Sutherland, Amsterdam.

3. Acknowledgements

My heartfelt thanks to my family, especially my wife Susanne. For her continuing support and understanding on my path to becoming an Osteopath, through the hard times and the good. She remains my best friend and the person I can turn to when I'm lost or struggling, to Susanne I am eternally grateful. Also, many thanks to my children: Samuel; Tristan and Elias. They allow me to play the fool and are a great source of enjoyment and silliness. This is a very important factor to me in remaining sane!

My "clean mother and father" Frans and Ceciel Thijssen for their willingness to help out with the children, both routinely and when we aren't able to arrange childcare. Thanks too for being made to feel at home in their house and the numerous delicious dinners. Many thanks also to my family overseas, for their visits to us in the Netherlands on various occasions and to have a safe haven in diverse countries in Europe and further afield. Not to mention coming to Sutherland College in Amsterdam for treatment, to facilitate my total number of treatments for my final year: Mum; Brian; Dad; Ilze; George; Sarah; Thomas; Siani; Joseph & Annabel.

My thanks to my mentors: Erwin & Sylvia ter Laak for their help in writing this thesis. Sylvia for the willingness to help out following Erwin's CVA and to Erwin himself for years of lessons covering important and difficult subjects concerning both anatomy and osteopathy, and for making these subjects enjoyable with his comedic talent and light heartedness! My gratitude extends to the entire staff at College Sutherland, be it the secretaries or teaching staff, a place where I am able to feel at home amongst the eclectic mix of personalities. Every member of the team has a unique role. Without you all, Sutherland College Amsterdam wouldn't be the wonderful place that it is today. Keep up the good work!

Kindest regards,
William

4. Introduction

The goal of this literature study is to determine if osteopathic treatment (OT) can have a beneficial effect on the health of patients with hypertension (HTN). Those responsible for increasing access to osteopathic medicine, whether they be legislators or purchasers of healthcare services, need to know that osteopathy is safe, effective and cost beneficial. (Vogel et al 2013)

Due to its high prevalence, and negative effects, hypertension and its treatment can play an important role in individual health, healthcare costs and ability to work. "The WHO rates hypertension as one of the most important causes of premature death worldwide. HTN is directly responsible for 57% of all stroke deaths and 24% of all coronary heart disease deaths in India. (Sriloy, Pradeep, Nair, Pranav & Sathyanath, 2015)

4.1 Normotension, Hypotension and Hypertension

Normal resting blood pressure is within the range 60-90 mm Hg diastolic blood pressure and 90-140 mm Hg systolic blood pressure. Therefore, the patients discussed in this paper will have a blood pressure in excess of 140/90mm Hg at rest. Patients with blood pressure under 90/60mm Hg are termed as hypotensive, risks associated with this phenomenon are syncope, typically orthostatic hypotension and insufficient tissue perfusion. (NHS 2019)

4.2. Primary Hypertension

In cases of primary hypertension, the causative agent is not known. This is termed idiopathic. Primary hypertension is a synonym of essential hypertension. In this study the term primary hypertension will be used unless directly quoted from literature when it is stated as essential hypertension. Primary hypertension is the most frequent type of hypertension in adults (95%) and is diagnosed when there is a sustained elevation of BP greater than 140/90mm Hg and when no etiology can be determined for the hypertension. (Lenfant, Chobanian, Jones, & Roccella, 2003).

The presence of primary hypertension (PH) is a result of several different factors, a family history being a strong indicator of the likelihood of a patient developing PH. "Children of hypertensive patients are twice as likely to develop hypertension as are children of normotensive patients, and more blacks than whites are hypertensive” (Marieb & Hoehn 2013)

Other key predisposing factors include:

1. age
2. diabetes mellitus
3. diet
4. smoking
5. stress
6. obesity

4.3. Secondary hypertension

Secondary hypertension accounts for 10% of cases, the causative agent is known. Common causes of secondary hypertension are:

1. Kidney pathologies:
    a. diabetic nephropathy
    b. polycystic kidney disease
    c. glomerular pathology
    d. stenosis of renal arteries.

2. Endocrine disorders:
    a. Cushing’s syndrome, either due to medication or pituitary tumor
    b. disorders which affect the secretion of cortisol
    c. thyroid disorders
    d. Conn’s syndrome (hyperaldosteronism)
    e. hyperparathyroidism.

3. Other structural conditions can cause secondary hypertension:
    a. coarctation (narrowing) of the aorta
    b. obesity

4.4. Possible Complications of Hypertension

1. Intima-media thickening, arteriosclerosis (stiffening of the arterial wall)
2. Intima-media roughness
3. Atherosclerosis: plaque forming, narrowing of the lumen and hardening of artery wall
4. Arterial aneurysm
5. Angina pectoris (chest pain)
6. Arrhythmias
7. Coronary arterial disease
8. Left sided cardiac hypertrophy
9. Heart attack
10. Heart Failure

4.5. Infantile Hypertension is Excluded from this Study

The emphasis of this study will be on adults with hypertension.

Literature pertaining to the osteopathic treatment of children with hypertension, due to ethical reasons is scarce.

4.5.1. Table showing hypertension in relation to age:

09/03/2019

Table 3. Most Common Causes of Secondary Hypertension by Age*

Age groups	*Percentage of hypertension with an underlying cause*	*Most common etiologies†*
Children (birth to 12 years)	70 to 85	Renal parenchymal disease Coarctation of the aorta
Adolescents (12 to 18 years)	10 to 15	Renal parenchymal disease Coarctation of the aorta
Young adults (19 to 39 years)	5	Thyroid dysfunction Fibromuscular dysplasia Renal parenchymal disease
Middle-aged adults (40 to 64 years)	8 to 12	Aldosteronism Thyroid dysfunction Obstructive sleep apnea Cushing syndrome Pheochromocytoma
Older adults (65 years and older)	17	Atherosclerotic renal artery stenosis Renal failure Hypothyroidism

*—*Excluding dietary and drug causes and the risk factor of obesity.*
†—*Listed in approximate order of frequency within groups.*

Information from references 2, 3, and 30 through 34.

(Viera, A.J. & Neutze, D.M. 2010)

4.6. Malignant Hypertension is Excluded from this Study

Malignant hypertension, when blood pressure exceeds 180/120mm Hg, is a medical emergency, and requires immediate medical attention, in order to limit damage to the renal system and the eyes (hypertensive retinopathy).
Other risks associated with malignant hypertension include: aortic dissection; unstable angina; heart failure with the potential for organ damage; heart attack causing myocardial necrosis; cerebrovascular accident; pulmonary edema; eclampsia (during pregnancy).
Hypertensive crisis is a synonym of malignant hypertension, for this study malignant hypertension is excluded as treatable with OT due to the immediate need for treatment with antihypertensive drugs in order to reduce the chances of one or more of the conditions mentioned above from happening.
(Heart.org 2019)

5. Methodology

Various sources of information are used in this literature study:

1. Osteopathy congresses
2. Scientific papers
3. Online databases such as PubMed
4. Syllabi from College Sutherland archives; theses from the Sutherland College library
5. Quotes from relevant articles both online and from the personal library of the author.

This is in order to determine if there is a relationship between OT and changes in the systemic blood pressure in patients with HTN and its complications, whether that be primary hypertension or secondary hypertension. Also, to determine, if there are any changes, whether those changes are chiefly of short- or long-term effect.

6. Farmaceutische Kompas

The Farmaceutische Kompas is an independent online resource developed by general practitioners in the Netherlands for information pertaining to healthcare and pharmacology. Below are the recommendations for Patients with hypertension, translated from Dutch to English retrieved from the Farmaceutische Kompas website on the 29th of May 2019:

1. Discuss lifestyle changes, non-drug derived solutions
2. Cessation of smoking
3. Reduce alcohol intake
4. Restrict salt intake
5. Reduce intake of glycyrrhetinic acid- containing products such as liquorice and some chewing gums
6. Reduce intake of some herbs (Ephedra, ma huang)
7. Suitable amount of physical activity
8. Stress reduction
9. Promote healthy eating habits and optimal bodyweight (BMI <25 in adults up to 70 years old)

If it is shown that osteopathic treatment (OT) can have a positive effect on hypertensive patients, the benefits could be far-reaching. The relatively low risk, and non-invasive nature of OT, could provide a safer alternative for patients than anti-hypertensive medicines alone. In a recent study by Bliek (2018), an assessment of the safety of a singular osteopathic technique, the liver pump was assessed as to its safety relative to the cardiovascular system. “It therefore seems that the technique can be applied without risk” (pp.4)

Side effects are common with anti-hypertensive medicines, to take an example of two commonly prescribed medicines and to compare this to the relatively safe OT. (Vogel et al 2013).

Farmaceutische Kompas

6.1. Side effects Lisinopril (most frequently prescribed ACE inhibitor):

Often (1-10%):

1. dizziness
2. headache
3. orthostatic hypotension
4. syncope
5. dry cough
6. renal impairment
7. diarrhea
8. vomiting
9. increased blood lipid content (Farmaceutische Kompas 2019)

6.2. Side effects Amlodipine (most frequently prescribed Ca^{2+} channel blocker):

Often (1-10%):

1. visual disturbance (e.g. double vision);
2. palpitations;
3. flushing;
4. dyspnea;
5. abdominal pain;
6. nausea;
7. dyspepsia;
8. diarrhea;
9. constipation;
10. ankle edema;
11. muscle cramps;
12. fatigue;
13. asthenia.
14. Early onset side-effects also include: somnolence; headache; dizziness (Farmaceutische Kompas)

7. Null- and Alternative Hypothesis

Null Hypothesis (H_0): No relationship between OT and changes in BP and complications of hypertension. Discernable complications include: intima media thickening; arteriosclerosis and roughness of the intima media (common carotid artery).

Alternative hypothesis (H_1): there is a relationship between OT and a change in BP of patients with hypertension, and a change in complications related to hypertension, such as those mentioned above in the H_0 hypothesis.

If OT is seen to have a positive effect on patients with hypertension, it has the possibility of influencing a large population and the benefits can be far-reaching for the health of the individual.

8. Physiology of Circulation, Regulation of Blood Pressure and Hypertension

Circulation of blood throughout the human body is essential for maintaining homeostasis. Without an adequate circulation tissues and organs would receive insufficient blood-borne oxygen and nutrients, the body would not be able to function properly, ultimately leading to organ failure and death. It is clear that proper maintenance of the circulatory system is essential to life and health.

8.1 Important terms relating to blood circulation

8.1.1. Blood Flow

Blood flow is the volume of blood passing through a blood vessel. In terms of the entire vascular system, blood flow is equivalent to cardiac output. It is relatively constant when the body is at rest. Different body organs will have different needs and therefore different rates of perfusion. For example, the kidneys are richly vascular and receive a relatively high volume of blood in comparison to other bodily organs at rest. They alone receive approximately 20% of cardiac output. at rest, the brain receives about 13% of total blood flow, the heart 4%*, the* kidneys 20%, and *the* abdominal organs 24%. Skeletal muscles...20%. (Marieb, & Hoehn 2013). These values vary widely due to the demands placed on the body by exercise and on individual organs by factors such as digestion or psycho-emotional demands.

8.1.2 Blood Pressure

Blood Pressure is the force exerted by the contained blood on a vessel wall, expressed in millimeters of mercury (mm Hg). The term blood pressure refers to the systemic arterial pressure in the largest arteries near to the heart. Blood pressure follows the laws of physics of flow from an area of high pressure towards an area of low pressure., This is the blood pressure gradient. The end blood vessels within the tissues, the capillaries, have a much lower pressure than that of the largest arteries. The collecting venules and veins have a lower pressure still. In this way the blood flows from areas of high pressure in the arteries to areas of low pressure in the veins through the network of:
arterioles → capillaries → venules.

8.1.3. Peripheral Resistance

The peripheral resistance opposes blood flow and is a measure of the amount of resistance that the blood encounters when moving through the blood vessels. Three important factors governing peripheral resistance are:

1. Blood viscosity
2. Vessel length
3. Vessel diameter

Arterial hypertension is the result of an abnormal flow-resistance relationship. Resistance to outflow consists of different components: the systolic component is generated by conductive vessels, whereas the diastolic component consists of peripheral resistance, which regulates peripheral blood supply due to the run-off of conductive vessels during left ventricular diastole. An increase in systemic resistance results in a rise in diastolic blood pressure. If the elasticity of conductive vessels decreases, diastolic run-off also decreases and diastolic blood pressure goes down. When this loss of elasticity occurs, the ejection force can no longer be offset by arterial distension, the pulse wave velocity increases and reflex waves to the heart arrive earlier, causing the systolic blood pressure to increase. (Simone, & Pasanisi, 2001)

8.1.4 Blood Viscosity

Blood viscosity is a measure of how sticky or thick a fluid is, a high viscosity causes a fluid to flow more slowly. Low viscosity means that a fluid flows more freely. Because blood contains many compounds necessary for maintaining homeostasis, it is much more viscous than water. As a general rule, the more components carried within the blood, the more viscous it becomes. However, blood viscosity in vivo is not constant, but is subject to change as is blood pressure during the diastolic and systolic phases of the heart. Blood is a non-Newtonian fluid, and its viscosity changes at different velocities. During the diastolic phase the blood is subject to lower pressure, or shear. In this phase the blood flow slows and cell aggregation increases, resulting in an increased viscosity. The systolic phase, on the other hand, exerts higher pressure on the blood, shear increases and blood components are dispersed from their aggregated state. Larsen, (2019) writes “Blood at diastole can be anywhere between 5 and 20 times as viscous as the same blood at systole” The relationship between blood viscosity and blood pressure during systole and diastole are mentioned in the following studies [see paragraph 8.2.1.]. (Fowkes & Lowe, 1993) and (Ciuffetti & Schillaci, 2005)

Further factors influencing blood viscosity are:

1. The hematocrit
2. Erythrocyte deformability
3. Erythrocyte aggregation
4. Temperature
5. Total blood lipid content; LDL: HDL ratio (most applicable to blood returning to the liver by way of the portal vein via the mesenteric root, lymphatic vessels via the thoracic duct to the subclavian vein)
6. Plasma viscosity
7. Some medications (including contraceptives) (Sullivan 2017)

Myers and Jones, (2019) state "blood viscosity can increase because of many factors, such as certain medications, too many red blood cells, high lipid levels, and other conditions, including diabetes and cancer".

Several studies have been conducted to expand further on the hypothesis of blood viscosity in relation to blood pressure and in relation to complications of hypertension. Three separate studies are highlighted in the following subchapters

8.2. Direct Relationship Between Blood Viscosity and Blood Pressure

The earliest study was by Letcher and Chien, (1981). Taking a normotensive subject group n=49 and an untreated essential hypertension group n=49, they showed a direct correlation between BP and blood viscosity among both the normotensive and hypertensive subjects with a p value of $p<0.001$. Subgroups were also compared of subjects with matching hematocrit values n=25. The viscosity remained significantly higher in hypertensive subjects ($p<0.05$).

8.2.1. Edinburgh Artery Study

A later study, from 1993, of a random population sample n=1,592 in the Edinburgh Artery Study showed that systolic BP was univariately related to blood viscosity in males (p<0,001) and diastolic BP was univariately related to blood viscosity in both sexes ($p<0.001$). The authors suggest a strong independent relationship between viscosity and BP that cannot be explained by hematocrit and plasma content alone. (Fowkes, et al 1993)

8.2.2. Prognostic Impact of Low-shear Whole Blood Viscosity in Hypertensive Men

The most recent highlighted study, from 2005, of a subject group n=331 males followed men recently diagnosed with primary hypertension for up to twelve years. Subgroups were formed by way of the diastolic blood viscosity levels: high; medium; low. The high viscosity subgroup were more than three times as likely to have cardiovascular events than the low viscosity subgroup p=0,006. The authors concluded that both blood viscosity and hematocrit were univariate predictors of cardiovascular morbidity in hypertensive men, but only viscosity came out as an independent risk factor in a multivariate analysis. They further stated that blood viscosity is dependent on several factors, such as: cell concentration; cell aggregation; cell deformability; plasma protein concentration. (Ciuffetti et al 2005).

Plasma protein concentration is an important factor in plasma viscosity, and it especially includes the high molecular weight proteins such as immunoglobulins and fibrinogen. An over-active immune response as seen in autoimmune disorders and/or an increased inflammatory response due to damage or imbalance in the sympathetic- and parasympathetic nervous systems, can significantly influence plasma viscosity. Another factor in plasma viscosity is hydration, less water in the blood = greater viscosity, dehydration is common, over-hydration less so. (Sloop & Garber 1997), (Fossum, Høieggen, Moan, Nordby, Velund, Kjeldsen 1997)

8.2.3. Blood Doping: Erythropoietin and Equivalents

Modern-day examples of increased blood viscosity can be seen in blood doping where erythropoietin, or an equivalent drug, is used by athletes trying to improve their performance by temporarily increasing their blood count. (World Anti-Doping Agency 2019).

This allows more oxygen to be carried by the blood but carries the risk of increasing the erythrocyte count, which increases blood viscosity and thereby increasing the risk of blood clotting and stroke. This is far from a new phenomenon, in the times of the Ancient Greeks the spleen would be removed to increase stamina (due to higher red blood cell count) as less erythrocytes would be filtered out by the spleen. (Dionigi, Boni, Rausei, Rovera, Dionigi 2013).

8.2.4. Pathologies Which Increase Viscosity or Cause Hyperviscosity

Pathological conditions relating to increased blood viscosity and hyper-viscosity syndrome can be subdivided into those which affect the hematocrit and those which affect the plasma viscosity. Peres, Rogers & Estes (2019) state:

> Conditions responsible for hyperviscosity syndrome that involve cellular components of blood include polycythemia vera, leukemia, and thrombocytosis…diseases include myeloma, Waldenstrom macroglobulinemia, and cryoglobulinemia. Rheumatic conditions … compromise polyclonal causes of hyperviscosity syndrome as well as Castleman disease and HIV infection.

8.3. Vessel Length

The longer the network of vessels the greater the resistance it exerts on the contained liquid, increased surface area is proportional to the amount of friction encountered. The friction increases as the surface area increases. An infant has far less total vessel length than an adult and therefore the child has less peripheral resistance than an adult.

8.4. Vessel Diameter

Smaller diameter vessels have a greater surface area to volume ratio than larger vessels, so they exert more friction on the contained liquid which in turn reduces the flow rate. If the radius of the vessel doubles, the resistance encountered by the contained fluid drops to one sixteenth of its original value. This is an important factor to take into account with regard to the total peripheral resistance. The small diameter arterioles are the major players in peripheral resistance regulation when it comes to vasoconstriction or dilation in response to neural and chemical controls. For example, if arterioles serving a particular tissue dilate, blood flow to that area increases without an increase in systemic blood pressure. If the cardiac output were to stay the same during this period of vasodilation, systemic blood pressure would actually decrease. An extreme example of this can be seen during anaphylactic shock when a colossal number of vessels dilate causing a life-threatening drop in systemic blood pressure.

Physiology of Circulation, Regulation of Blood Pressure and Hypertension

8.5. Laminar and Turbulent Flow

Laminar flow is predominant in the center of the blood vessel lumen and in vessels with a smooth wall. Turbulent flow tends to occur close to the vessel wall and where the wall is rough or the blood is otherwise impeded; for example, at vessel branches or due to pathologies such as vascular plaques partially blocking the lumen. Turbulent flow greatly increases peripheral resistance.

8.6. The relationship between Blood Flow, Blood Pressure and Peripheral Resistance

Blood flow is dependent on the blood pressure gradient mentioned briefly in [8.2]. above. The greater the blood pressure difference between two given points the steeper the gradient and the faster the flow rate. If the blood pressure increases at point A (central) while the pressure remains the same at point B (peripheral), the blood flow will increase. Conversely, if the pressure increases at point B while the pressure at point A remains the same, the blood flow will decrease. This phenomenon of increasing the pressure in the peripheral structures plays an important role in the understanding of hypertension which will be discussed in later chapters. This relationship can be succinctly expressed by the formula:
Blood flow = Blood pressure/peripheral resistance

The venous return of blood is the more susceptible to impairment due to several factors:

1. A thinner vessel wall than that of arteries, causing lower resistance to pressure in the surrounding tissue.
2. Lower venous blood pressure than arterial blood pressure and a higher viscosity of venous blood than arterial blood.
3. A linear increase of the whole blood viscosity due to an increase in carbon dioxide level.
4. Oxygen level has an inverse relationship with whole blood viscosity. (Nagashima 2019)

Physiology of Circulation, Regulation of Blood Pressure and Hypertension

Further factors are: the degree of dependence on muscle activity for venous blood flow (e.g. reliance on physical activity, correct breathing technique). In turn, an increase in venous pressure has been shown to increase the total blood viscosity. In this way the relationship between venous pressure and venous blood viscosity can be regarded as a feed-forward system in which the two positively influence each other. Langstroth (1919) stated

> A rise in venous pressure caused by application of a loose binder to the arm results in a marked increase in the viscosity of the whole blood which is primarily due to a concentration of the blood in the capillaries. This concentration is shown by an increase in the viscosity and total nitrogen of the plasma, an increase in the relative volume of the red blood cells, and an increase in the relative percentage of hemoglobin.

In this way, if left unchecked, increased venous pressure will in turn increase total blood viscosity. This has the effect of decreasing blood flow if the BP remains the same, or increasing BP in order to maintain the same level of blood flow. Possible mechanisms for an increased venous pressure are hypertonic muscle tissue in the immediate surroundings of a venule or vein, edemic tissue in the immediate surroundings of the vessel; stiffening of the vessel wall; increased turbulent flow inside the vessel due to venous valves, roughness or branching. In contrast arterial blood has a higher likelihood of turbulence due to increased flow rate. This is a factor contributing to the damage of arterial linings. Stone (2007) elucidates “Maintaining an even, soft, tissue environment for the vessels not only helps to maintain the patency of the arterial and venous system but also reduces local neural irritation to sympathetic fibers travelling with, and serving the arterial tree”.

Physiology of Circulation, Regulation of Blood Pressure and Hypertension

8.7. Nervi- and Vasa-Vasorum

8.7.1. Nervi-Vasorum

These nerves contain generally sympathetic fibers. Sympathetic activation constricts arteries and arterioles which causes an increase in peripheral resistance and a decrease in distal blood flow. When this happens on a large scale, systemic pressure increases. During the sympathetic activation of veins, venous compliance decreases and venous pressure increases as a consequence. Klabunde (2014) explains “Most blood vessels in the body do not have parasympathetic innervation”.

8.7.2. Vasa-Vasorum

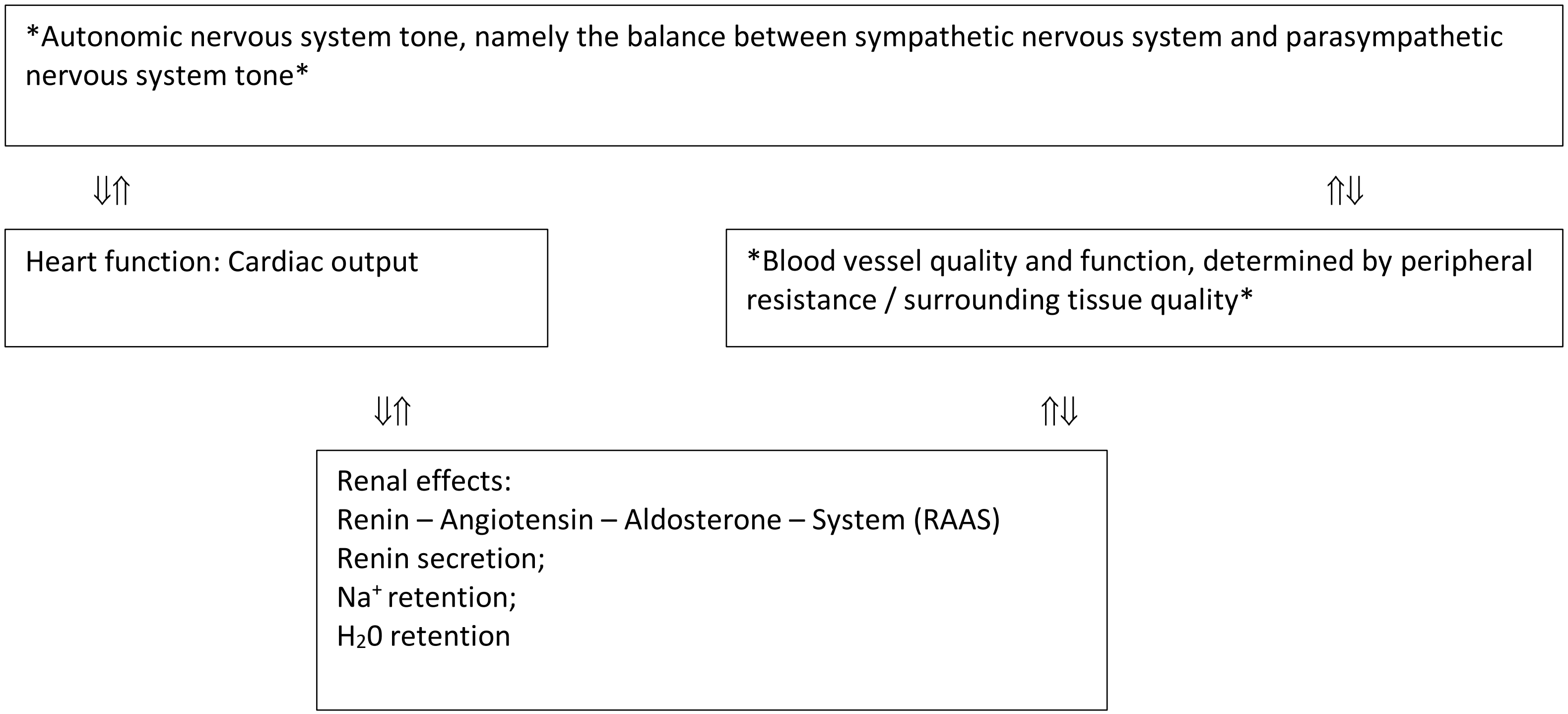
These blood vessels serve vessels with a large lumen. They supply blood and nourishment to the tunica adventitia and outer parts of the tunica media of larger vessels. Examples of these large vessels are the aorta, including its proximal branches, and the vena cava, including its proximal branches. Vasa-vasorum and vasa nervorum are particularly susceptible to external mechanical compression and can be involved in the pathogenesis of peripheral vascular and nerve diseases. (Moore, Dalley, & Agur, 2010)

Haverich (2017) proposed that the formation of plaques is not from inside the vessel, but the result of inflammation of the vasa vasorum. He noted that arteries fed by vasa vasorum are subject to the development of arteriosclerotic plaques. He postulated that inflammation compromises the integrity of the arterial wall and suggested that arteries with thin walls, not having vasa vasorum, do not develop arteriosclerosis.

Consider the fascial and myofascial web as integral to the abluminal surface of the blood and lymphatic vessels and their surroundings and it is the membranous and fibrous supporting structure for afferent and efferent neurovascular structures of all tissues within the body. Treatment forms such as, but not limited to, osteopathy may have an effect on the metabolism of the fascial and myofascial web. Treatment may therefore cause changes in the vasa vasorum pathologies as described by Pries, Reglin & Secomb (2005). In their study of the changes to the abluminal wall, brought about by changes in the metabolism of the surrounding tissues. If the tissue metabolism improves in HTN patients following prolonged (e.g. 12 months) of OT, it may be a form of alternative therapy that can improve patient health. Progress could be measured by a decrease in or cessation of arteriosclerotic plaque formation. This pathology is discussed by the author in section [12.1] below. (Cerritelli et al 2011)

9. Graphics Showing Regulatory Mechanisms Relating to Blood Pressure

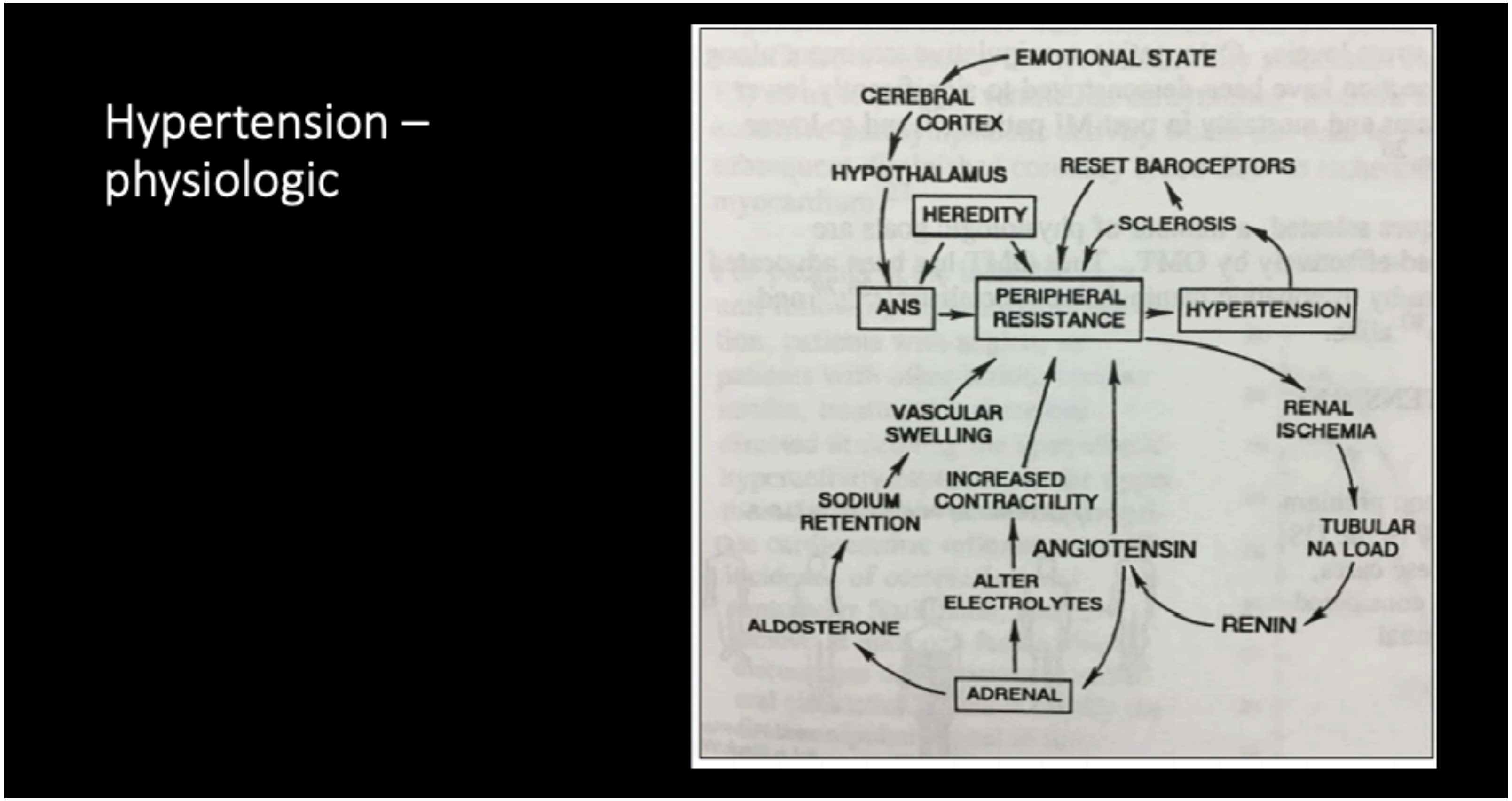
9.1. Graphic by the Author



*Suspected areas of greatest influence of osteopathic treatment on systemic blood pressure.

Graphics Showing Regulatory Mechanisms Relating to Blood Pressure

9.2. Physiology of Hypertension Diagram



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10. Possible Mechanisms of Influence of Osteopathic Treatment in Hypertensive Patients and Anatomical Areas of Interest

The author hypothesizes a few mechanisms whereby osteopathic treatment may have its greatest influence on the circulatory system.

10.1. Vascular and Neural Level

At both the vascular and neural level, a change could be initiated by an improvement in the veno-lymphatic drainage to the supporting tissue around either a blood vessel or nerve.

10.1.1. Vascular Level

At the vascular level, the mechanism of action in veins may be a reduction of pressure within the vessel lumen, caused by a decrease in proximal blood pressure; and in arteries, by a decrease in distal pressure. Another possibility is in an increase in the venous return flow rate by decreasing the edematous state of the surrounding tissues via lymphatic vessel drainage.

10.1.2. Neural Level

Improvement in intervertebral and costovertebral joint mechanics at areas of sympathetic chain ganglia located along the length of the spine from the base of the cranium to the coccyx. The paravertebral ganglia are the sites where preganglionic fibers synapse with postganglionic neurons

10.1.3. Glossopharyngeal Nerve

The glossopharyngeal nerve (CN. IX) communicates with both the vagus nerve and the sympathetic chain ganglia. It leaves the skull through the jugular foramen along with the vagus (CN. X) and accessory (CN. XI) nerves.

The glossopharyngeal nerve carries impulses from chemoreceptors and baroreceptors situated in the carotid body and the carotid sinus respectively. Therefore, the activity of the glossopharyngeal nerve is important when considering patients presenting with hypertension. Is the hypertension functional for this patient, in the sense that visceral perfusion requires a higher than normal BP or, is there a dysfunction in the glossopharyngeal nerve, or in its vicinity which may be implicated in the hypertension? Examples of this might be a hyper- or hypotonicity of myofascial structures of the neck which could affect the relative pressure detected at the carotid sinus, leading to an abnormal neurological response. This will possibly cause a change in systemic blood pressure due to a regional effector. Dysfunctions of the nerve itself are termed glossopharyngeal neuralgia. (Kandan, Khan, Jeyaretna, Lhatoo, Patel & Coakham 2019).

10.1.4. Vagus Nerve Activity, Proposed Areas and Mechanisms of Effect

Stimulating the vagus nerve (CN. X) by techniques directed to where the nerve leaves the base of the skull by the jugular foramen may have an effect on hypertension. Stimulation at the cervical level, where the vagus nerve courses inside the carotid sheath, could also affect heart activity. Osteopathic techniques of the thoracic region could have an effect on the right and left vagus nerves, which innervate the atrio-ventricular and sino-atrial nodes respectively. In the region of the esophagus, the vagus nerve forms the celiac plexus and continues further into the abdomen as the dorsal and ventral vagal trunks, through which it innervates much of the abdominal viscera.

As a nerve containing efferent cardiac parasympathetic fibers, the vagus has an influence on the myocardium of reducing heart rate, heart rhythm and affecting heart contractility. Vaseghi et al (2017) stated:

> Augmenting the parasympathetic drive with vagal nerve stimulation reduced ventricular arrhythmia inducibility by decreasing ventricular excitability. Multiple studies have shown that vagal nerve stimulation reduces inflammation and ischemia-driven ventricular arrhythmias if initiated at the time of or before onset of coronary artery occlusion.

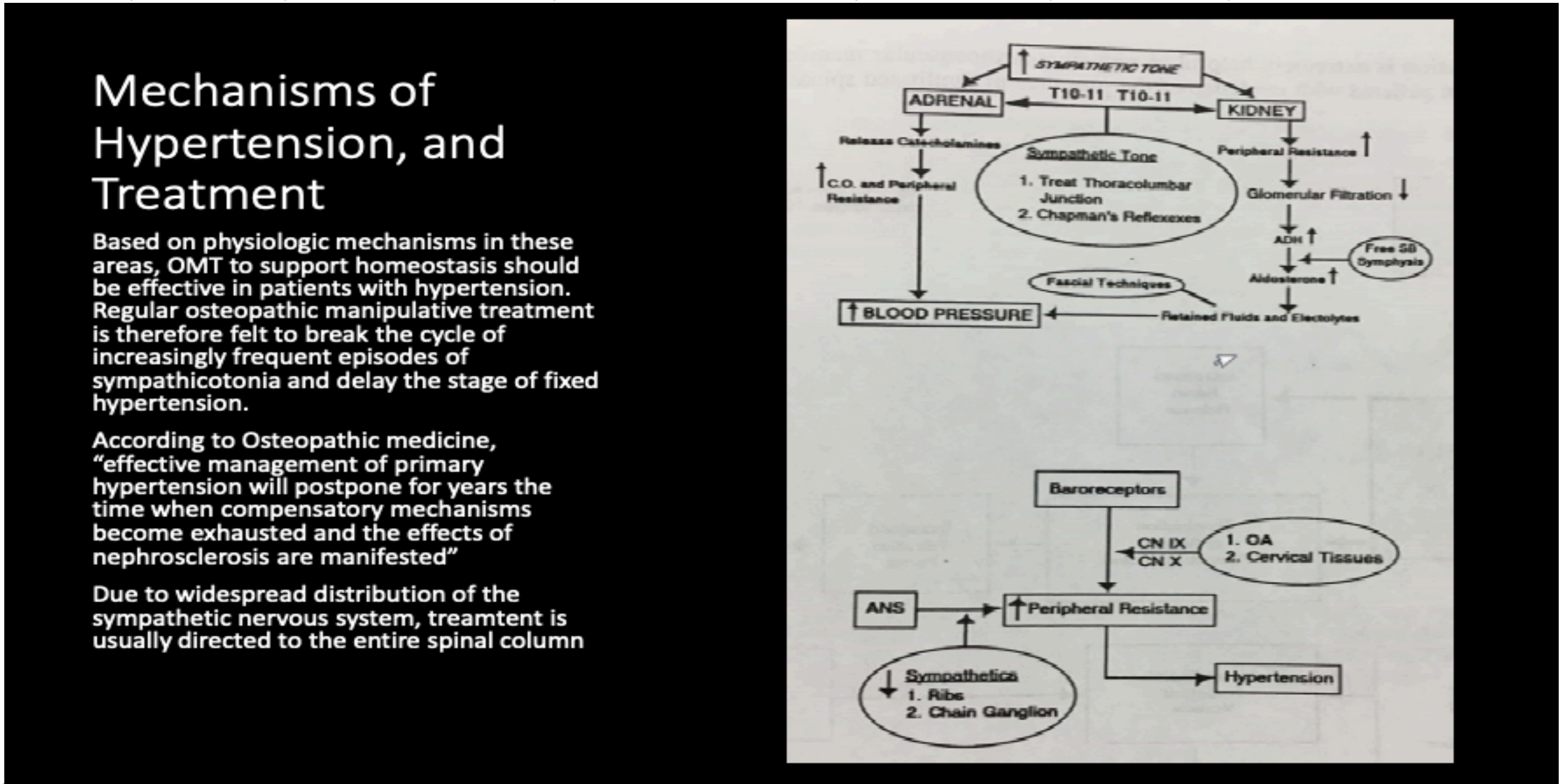
10.2. Osteopathic Techniques of the Viscera

Although not as widely researched, techniques directed toward the viscera may influence the systemic blood pressure. Such treatments can be directed at organs involved in the regulation of blood pressure such as the heart, kidneys and lungs. Techniques aiming to improve the mobility of richly vascular organs and structures such as the kidneys, liver, spleen and mesenteric root can also have an effect on the systemic blood pressure. A suggested model is the improvement of the veno-lymphatic drainage of the given organ or its surrounding connective tissue. Other proposed mechanisms of action are the easing of restrictions in serous membranes covering organs. This could have an action at the level of their roots containing both afferent and efferent nerves, blood and lymphatic vessels

Possible Mechanisms of Influence of Osteopathic Treatment in Hypertensive Patients and Anatomical Areas of Interest

10.3. Mechanisms of Hypertension, and Treatment

This diagram shows possible areas and mechanisms of influence on the systemic blood pressure via OT, this graphic seems to focus on spinal techniques and unfortunately there is no mention of possible techniques which may influence the viscera.



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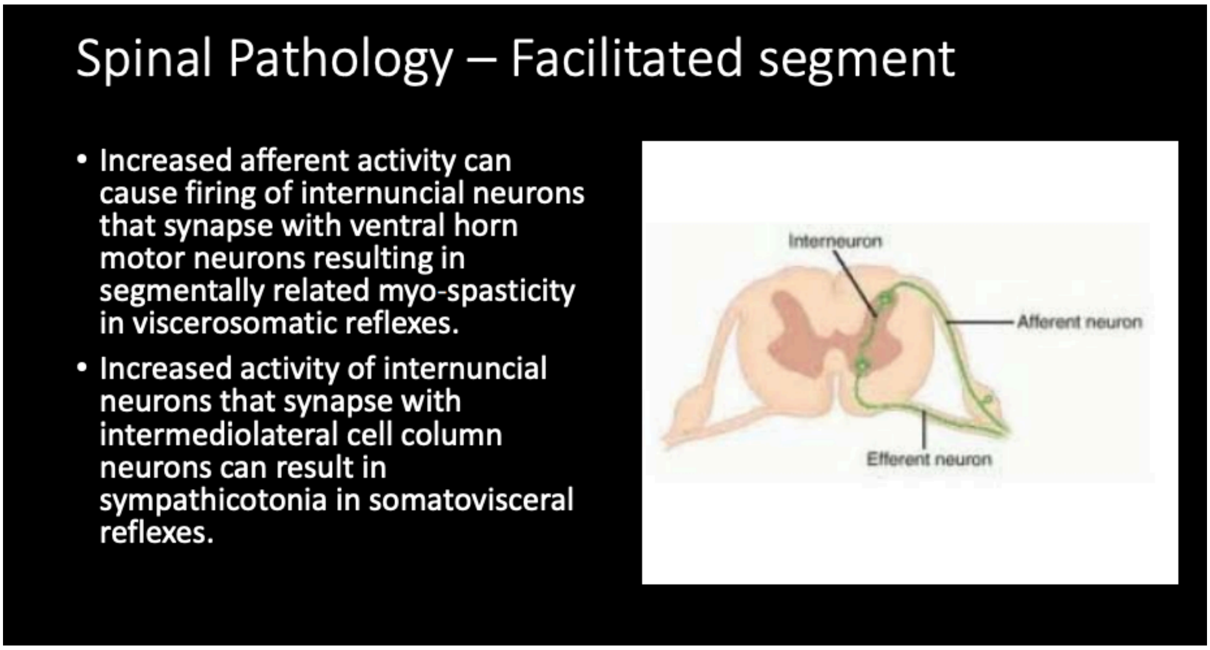
10.4. Viscerosomatic and Somatovisceral Reflexes, Facilitated Segment

One or more of these viscerosomatic or somatovisceral reflexes may be implicated in patients with hypertension, and osteopathic treatment directed toward these visceral and somatic areas may influence the systemic blood pressure. In viscerosomatic reflexes, visceral inflammation activates general visceral afferent neurons. In somato-visceral reflexes primary somatic dysfunction activates somatosensory nociceptive neurons. These afferent neurons enter the spinal cord and synapse in the dorsal horn. Ongoing afferent stimulation results in a state of irritability (facilitation). The stimulation threshold is lowered for any efferent input in this hyper-excited segment.

Viscero-somatic reflexes of the myocardium are capable of causing hyper-excitability of somatic areas innervated from thoracic spinal segments at T1 – T4. Upper and lower limb vascular beds are also a possible region of influence at T2-T8 and T11-L2 respectively. At the thoracolumbar junction there is possibly an influence from the sympathetic plexus (renal, aortic and celiac plexuses, lowest splanchnic and first lumbar nerves). (Stone 2007)

10.4.1. Graphic Showing Facilitated Segment



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11. Embryology of the Cardiovascular System

To understand the influence of osteopathic treatment on hypertension, an understanding of embryological development is essential. The correlation in both positional, and chronological, development and possible interactions during the embryonic, fetal and post-partum stages of the development is key in understanding possible influences of the various techniques as part of a holistic osteopathic assessment and treatment. The mesoderm is the germ layer which gives rise to the main structures of the cardiovascular system, but to discuss structures originating from this germ layer alone would be an oversight. For this reason, structures of non-mesodermal origin will also be discussed, as their development is of great importance to the cardiovascular system. Some examples of structures of endodermal origin are the lungs and liver. Structures of ectodermal origin, namely the autonomic nervous system, regulate vasodilation and vasoconstriction which in turn have a great influence on peripheral vascular resistance and its effects on systemic blood pressure, its regulation and/or deregulation leading to HTN and associated pathologies.

Osteopathy concerns the whole body, including that of all three embryonic germ layers. But the tissues derived from the mesodermal layer are considered to be most influenced by OT. Some notable advocates of this theory are: Robert Muts D.O. (College Sutherland) and Jean-Paul Hoppner D.O. (post graduate tutor of osteopathy)

Not all osteopaths around the world believe that tissues of all origins are possible sites of OT influence, some examples are the USA and the majority of osteopaths operating within the United Kingdom where OT is chiefly limited to the musculoskeletal system. In the teaching at the Amsterdam College Sutherland, osteopathy is taught as an approach to the entire body, not limited to the musculoskeletal system alone but also to that of its nearest neighbor, the visceral system and its fascial web which in turn supports the neurovascular system containing both efferent and afferent pathways.

11.1. Carnegie Classification of Development

The Carnegie scheme of embryonic development is used out of preference and, for precision, only relevant stages and information will be given in order to avoid reader being overwhelmed with unnecessary information. The last Carnegie stage (23) ends at approximately 8 weeks gestation and gives rise to the fetal stage which in turn is characterized by the development and maturation of organ systems.

> The fetal period that begins after the 8th week is characterized by the growth and maturation of the organs. The inner and outer morphologic alterations are less noticeable. For this reason, one no longer divides the fetal period into Carnegie stages. (Human Embryology.CH 2019)

Only the relevant parts of Carnegie stages will be described. For further information the reader is directed to the websites:
http://embryology.ch/dutch/iperiodembry/carnegie01.html
https://embryology.med.unsw.edu.au/embryology/index.php/Main_Page

11.1.1. Relevant Carnegie Stages

Stage 5a: Formation of the bilaminar disc.
The bilaminar disc consists of epiblast (which will form the entire embryo, and an epithelial lining of the amniotic cavity) and hypoblast which forms from the inner cell mass. Hypoblast is the primitive endoderm, which later gives rise to, amongst others, the lungs and liver which are a major factor in the systemic blood pressure due to their rich vascularization in the fully developed body.

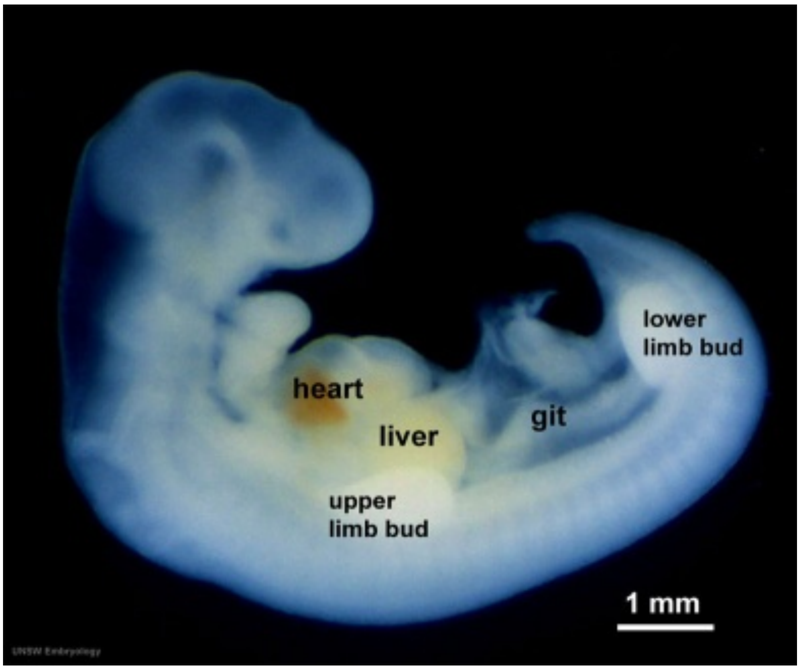
Stage 5c: Extraembryonic mesoblast formation
The extraembryonic mesoblast is the precursor to the mesoderm (endothelium, heart) layer in the trilaminar disc.

Stage 7: Genesis of the blood vessel system and formation of blood.
Gastrulation continues as cells migrate from the epiblast, to form mesoderm. This lies between the ecto- and endoderm germ layers in all but two sites: buccopharyngeal and cloacal membranes. These membranes signify the beginning and end of the gastro-intestinal tract which will later develop. At this stage the notochord also forms, which is important in the embryonic folding and regulation of the mesoderm and ectodermal differentiation.

Stage 9: Prechordal splanchnic mesoderm begins to form the cardiogenic region.
The primordial heart develops from the cardiogenic region. Formation of the transverse septum, this structure is of importance owing to its relationship with the liver as an endodermal structure which also develops at this stage. The transverse septum, which later develops into the central tendon of the abdominal diaphragm is a key structure when assessing the mobility of the pericardium in relation to the liver, namely via its region of contact with the abdominal diaphragm, the area nuda. The pericardium itself is firmly anchored in the central tendinous region of the abdominal diaphragm.

Stage 12: **Segmentation of the mesoderm.**
Mesoderm: continued segmentation of paraxial mesoderm (21 - 29 somite pairs), heart prominence develops.

Stage 14: Further segmentation of the somite pairs, now 30 in number.
Prominence of the heart, liver, mesonephric ridge and umbilical cord. Presence of upper and lower limb buds, genesis of the endolymphatic canal. Within the teachings of Osteopathy College Sutherland, the importance of the relationship between the heart, liver and central nervous system during the embryological development are highlighted as supporting of each other.



UNSW Embryology image – Carnegie stage 14

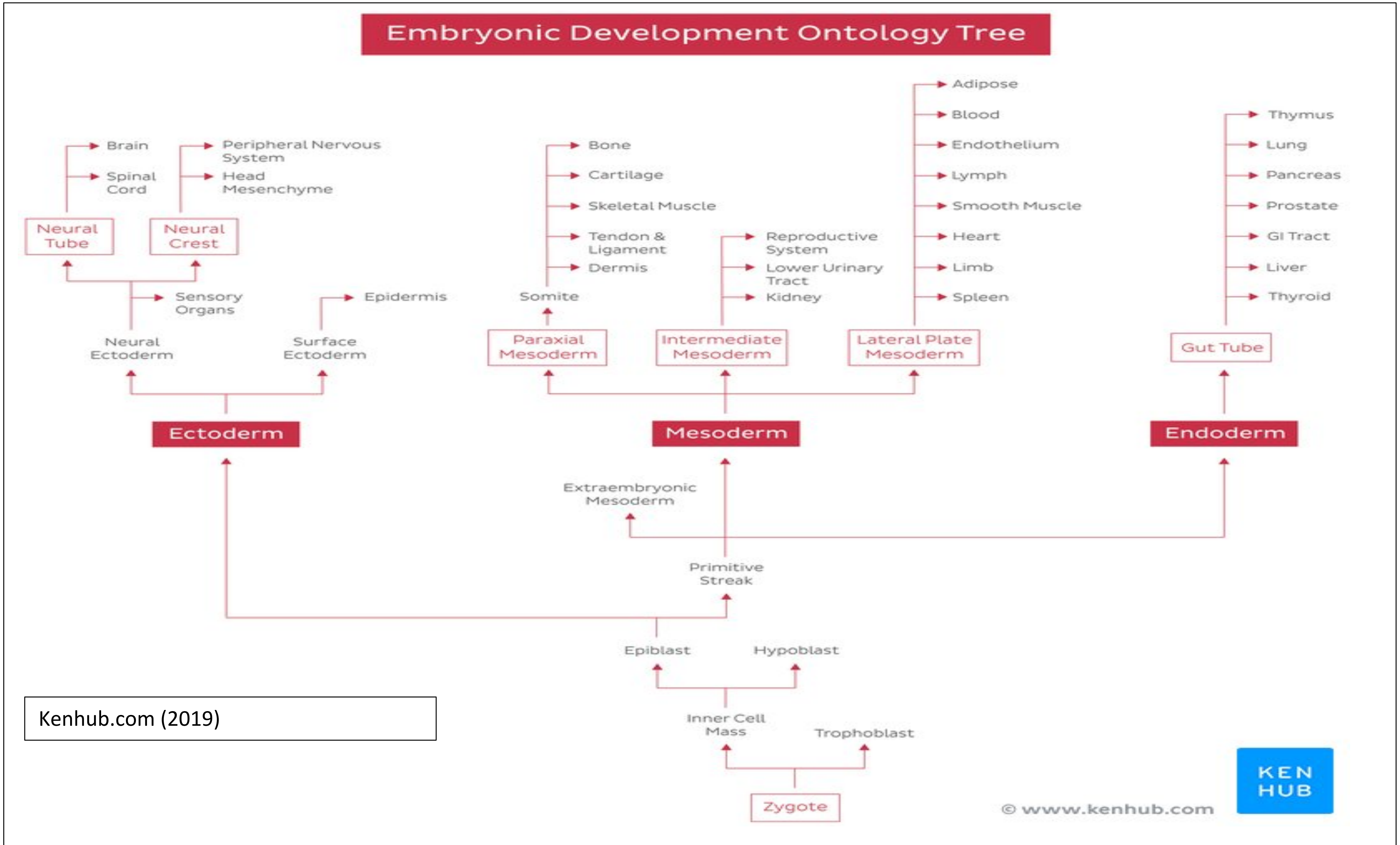
The developing brain requires constant nourishment to support its fast rate of growth, the liver and heart are important structures in the supply of nutrients to the central nervous system of the embryo. This development is further supported by the continuing development of the liver and heart. Structures formed in the neonate are a reflection of their embryological development, the metamorphosis from the neural tube into the fetal brain are a result of the expansional and rotational development during the embryological phase, which is in turn is dependent upon the interrelationships of these aforementioned structures. The heart also begins as a tube that subsequently undergoes rotational and expansional changes in relation to and in harmony with its surroundings to form the complex structure found in a neonate. (Hoste 2015). These relationships are a consideration when carrying out an osteopathic physical assessment from neonates to adults.

Stage 15: Coronary sinus and epicardial capillaries.
Connection of the coronary sinus with plexus of blind-ending epicardial capillaries in the coronary circulation.

"Atrioventricular bundle appears, atrioventricular cushions present, conotruncal ridges present, foramen secundum and semilunar cusps appear". (Arráez-Aybar, Turrero-Nogués & Marantos-Gamarra. 2008)

Stage 16: Cerebral arteries and para-aortic complex.
Middle cerebral artery development, proximal to the anterior cerebral artery on the division of the primitive carotid artery. Growth of the para-aortic complex: this is a plexiform complex derived from paravertebral sympathetic ganglia T6 – L1 including primordia of the suprarenal medulla, celiac, superior mesenteric and renal plexus.

11.2. Diagram Germ Layers and Their Corresponding Structures



Kenhub.com (2019)

12. Appraisal of Relevant Studies

The appraisals are set out in order of most relevance and value with regard to trial credibility and cohort size; statistical reliability is also taken into account.

12.1. Cerritelli et al (2011) Osteopathic Manipulation as a Complementary Treatment.

The aim of this study was to investigate the association between osteopathic treatment and hypertension. BP vascular alterations were measured with Intima media thickness measurements. For this study complete osteopathic treatment was chosen instead of one or more specific techniques. This has the advantage of being more representative of OT in a clinical setting. The great strength of this study was the 12-month follow-up of intima media thickness and BP.

A total of 31 out of 63 eligible subjects followed by a single cardiologist received OT every 15 days in addition to routine care. A control group of the other 32 subjects received routine care but did not receive OMT. Clinical measurements were recorded at baseline and after 12 months.
Univariate analysis found that osteopathic treatment was significantly associated with an improvement in all primary endpoints. Multivariate linear regression showed that, after adjusting for all potential confounders, osteopathic treatment was performing significantly better for intima-media thickness (delta between pre and post differences in treated and control groups: -0.517; 95% CI: -0.680, -0.353) and systolic blood pressure (-4.523; -6.291, -2.755), but not for diastolic blood pressure.

12.1.1. Summary

This study shows that, among patients affected by cardiovascular disorders who had peripheral vascular changes, osteopathic treatment is associated with an improvement in intima-media thickness and systolic blood pressure after one year. Multicentric randomized trials of adequate sample size are needed to evaluate the efficacy of OT in the treatment of hypertensive patient. This study is both very much in line with this literature study and shows promising results for positive outcomes of OT in patients with HTN. This supports the H1 hypothesis and disproves the $\mathbf{H_0}$ hypothesis.

Appraisal of Relevant Studies

12.2. Lombardini et al (2008) The Use of Osteopathic Manipulative Treatment as Adjuvant Therapy

This non-randomized trial enrolled patients with peripheral arterial disease. The study comes from the Department of Internal Medicine, Angiology and Atherosclerosis, University of Perugia, Italy.
35-55% of patients with peripheral arterial disease at presentation also have hypertension. (Makin, Lipgy, Silvermans & Beevers 2001) This study is included on the grounds of this common co-morbidity of peripheral arterial disease and hypertension. (Clement, De Buyzere & Duprez 2004)

Lombardini et al (2008), hypothesize that osteopathic manipulative treatment may represent a non-pharmacological therapeutic option in peripheral arterial disease. They examined endothelial function and lifestyle modifications in 15 intermittent claudication patients receiving osteopathic treatment and 15 intermittent claudication patients matched for age, sex and medical treatment as a control group.

12.2.1. Summary

Compared to the control group, the OT group had a significant increase in brachial flow-mediated vasodilation, ankle/brachial pressure index, treadmill testing and physical health component of life quality (all $p<0.05$) from the beginning to the end of the study. These results give some insight into the methods employed in this study, namely pressure indices between ankle and brachial, treadmill tests physical health and brachial flow-mediated vasodilation. (Raitakiri & Celermajer 2000).

These results are definitely promising. A criticism would be that the number of treatments and within which time frame are not stated. A larger subject group would improve the validity of these findings.

Appraisal of Relevant Studies

12.3. Henley, Ivins, Mills & Wen (2008) Osteopathic Manipulative Treatment and its Relationship to Autonomic Nervous System Activity

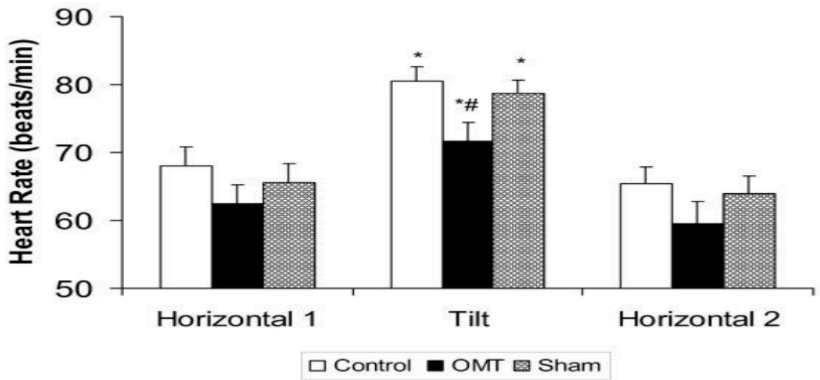
The aim of this study was to define the relationship between OT and the autonomic nervous system as demonstrated by heart rate variability: a repeated measures study. In an effort to define this relationship a cervical myofascial release technique was chosen to represent OT and the heart rate variability of the subjects as a substitute for autonomic activity. This study quantifies that relationship and demonstrates a cause and effect.

Inclusion criteria: normal healthy adults aged from19 to 50 years, normal ECG, and normal blood pressure
Exclusion criteria: chronic cardiovascular disease, diabetes, asthma, pregnancy, smoking etc.

Three experimental protocols were used in the study. The sessions were spaced at least 24 hours apart.
1) Control group where no intervention was performed.
2) OT group involving cervical myofascial release
3) Sham treatment group, hands were placed in the same position as the OT in the cervical region but no pressure was exerted.

All sessions lasted 30 minutes; changes in body position on a 50 degree head up tilt table were used to interpret measures of autonomic tone. The variance of the spectral components of heart rate variability, expressed as frequencies, measured the response to change in position of the subjects. Normalized low frequency and high frequency values, including low frequency/high frequency ratio, were calculated and used to determine the effect of position change on heart rate variability.

Figure Showing Effect of Body Position and Treatment on Heart Rate in the Three Positions: H I; T and H II



Values are mean ± Standard Error of the Mean (SEM). * indicates a significant difference ($p < 0.001$) within a condition between H1 and Tilt positions; # indicates a significant difference ($p < 0.001$) between control group and OT, sham and OMT groups at tilt position.

12.3.1. Summary

Predominantly parasympathetic responses were observed with subjects in the horizontal position, while a 50-degree tilt provided a significantly different measure of maximum sympathetic tone ($p<0.001$). Heart rate changed in all subjects with changes in position; respirations remained constant. When OT was performed in a sympathetic environment (tilt), a vagal response was produced that was strong enough to overcome the sympathetic tone.

The results of the study showed that the initiation of OT in a head-up tilt position resulted in a reversal, almost to baseline levels, to a more parasympathetic tone. This represented a shift from a sympathetic to a parasympathetic environment, demonstrating the effect of the OT treatment in overcoming the sympathetic tone. The results established a clear association between the effects of OT and changes in autonomic activity.

Results of this study demonstrate a quantitative relationship between OT and sympathovagal balance, cited as a shift in the balance of sympathetic to parasympathetic tone. Suggested, but not investigated, mechanisms are cited as neck afferents with projections to vestibular nuclei. The authors of this study conclude with suggestions for future studies to demonstrate the same autonomic nervous system effect through other OT techniques. For further understanding of the physiological mechanism, these should include High velocity/low amplitude OT and its effect on the autonomic nervous system when it is applied to patients in a diseased state.

12.4. Mannino (1979) The Application of Neurologic Reflexes to the Treatment of Hypertension

The author sets out to see if OT can inhibit the production of aldosterone and what effect this has on BP. The procedures used were Chapman's reflex techniques and were point specific. Men only, aged between 24 and 32 years, were used in the study. Accumulation of the subject population took 3 years with over 320 patients being screened.

12.4.1. Summary

A total of 45 subjects were included in the study, in no case was there a significant decrease in BP. However, in the hypertension subgroup there was a significant drop in serum aldosterone levels within 36 hours of OT ($p<0.01$). This shows that OT has an effect on part of the renin angiotensin aldosterone system (RAAS) which is clearly an important factor in hypertension, but does beg the question: if OT is responsible for a decrease in serum aldosterone levels why then is the blood pressure not significantly altered?

An insight can be seen when observing the pharmacodynamics of an aldosterone antagonist, spironolactone, whose effect on blood pressure is not observed for 5 to 7 days. It may be inadequate time was allowed for a decrease in blood pressure to show. Osteopathy performed in this study was limited to a single technique which is not consistent with the osteopathic concept of treating the individual as a whole, based upon the findings of a physical examination and not on the symptoms exhibited by the patient.

Appraisal of Relevant Studies

12.5. Plaugher et al (2002) Practice-based Randomized Controlled-comparison Clinical Trial of Chiropractic Adjustments

The authors describe three groups for this trial as:

1. A chiropractic care group received two months of full-spine chiropractic care. Frequency and duration per consultation are not stated.
2. A massage group that received a brief effleurage, the duration of which is also not stated.
3. A non-treatment group rested “alone” for 5 minutes in an adjustment room. It is not stated whether they were completely alone or accompanied in the room. If unaccompanied, it would already provide a bias due to less sensory stimulation.

In both the massage and chiropractic groups, all the subjects were classified as either overweight or obese. In the non-treatment group only 2 subjects were classified as such. SF-36 profiles for the groups were similar to that of the average population. This provides another bias in the subject groups.

Significant decreases in BP were shown in both the chiropractic care group and the non-treatment subjects who showed -4 and -4.9mmHg respectively, the massage group showed only 0.5mmHg reduction in diastolic BP. Despite the promising findings in the chiropractic care group the results of this trial are called into doubt due to the highlighted areas of bias mentioned above. (Kronmal & Rutan 1993.) Properties of the random zero sphygmomanometer

12.5.1. Summary

Group 1, chiropractic – mean change in diastolic BP was -4 (95% confidence interval [CI]: -8.6, 0.5) at the end of the study this was -6.3 (95% CI: 13.1, 0.4)
Group 2, massage – mean change in diastolic BP was 0.5 (95% CI: -3.5, 4.5) at the end of the study this was -1.0 (95% CI: -7.5, 15.6)
Group 3, non-treatment – mean change in diastolic BP was -4.9 (95% CI: -9.7, -0.1) at the end of the study this was -7.2 (95% CI: -13.3, -1.1)

The mean improvements in the chiropractic and non-treatment group remained consistent over the two-month follow-up period, this period is not stated in their paper.

Appraisal of Relevant Studies

12.6. Wong, Kassab, Mohr Med, & Abdul Quader (2018) Beyond conventional therapies: Complementary and Alternative Medicine in the Management of Hypertension

This study compares many disciplines within the complementary and alternative medicine spectrum in an evidence-based review. The osteopathic study cited in this review is by Cerretelli et al (2011). The study cites CV4 technique whereby the 4th cerebral ventricle of the brain is targeted using a two-handed hold of the occiput. The aim of this is to increase parasympathetic activity, supposedly resulting in a reduction in the systemic BP.

12.6.1. Summary

The main outcomes were "significant improvement in systolic blood pressure, but not in diastolic blood pressure". In their assessment of this CV4 technique study, Wong et al (2018) found the evidence to be weak in supporting the claim that OT has an effect of lowering BP in patients with HTN.
However, under scrutiny in this thesis, Cerritelli's paper can be seen to have demonstrated a reduction in systolic BP and improvement in vascular pathologies associated with hypertension, these improvements were present 12 months after the commencement of OT. Also, important to note is that in the Cerretelli et al paper, it is stated that full OT was carried out on the patients and not a singular osteopathy technique as stated in the paper by Wong et al. The evidence cited in the Ceretelli et al paper is hardly the 'weak evidence' as suggested by Wong et al. These changes are supported statistically, as follows:

1. Baseline body mass index to change in systolic BP ($p = 0.03$)
2. Heart rate to change in diastolic BP ($p = 0.03$)
3. Systolic BP to change in intima media thickness ($p = 0.04$)
4. Baseline systolic BP/diastolic BP to change in diastolic BP ($p < 0.01$; <0.001)
5. Baseline intima media thickness to change in diastolic BP ($p < 0.001$)

Osteopathic treatment to change in intima media thickness ($p<0.0001$), systolic BP ($p < 0.0001$) and diastolic BP ($p < 0.01$).

Appraisal of Relevant Studies

In the Wong et al paper complementary medicines that did show significant reduction in Systolic BP and Diastolic BP included:

1. Chiropractic
2. Qigong
3. Transcendental meditation
4. Various dietary supplementations including: Vitamin C; Coenzyme Q10; Melatonin; inorganic nitrate; beetroot juice and L-arginine.

These findings suggest a few things: that a multidisciplinary approach towards HTN will likely yield the best results, not a singular discipline treatment plan but also lifestyle changes including diet/dietary supplementation and physical activity. Another possibility is that a complete osteopathic approach could yield better results, as chiropractic and osteopathic medicine have many similarities in both assessment and treatment of biomechanical dysfunctions of the musculoskeletal system.

12.7. Jäkel, & von Hauenschild (2011) Therapeutic Effects of Cranial Osteopathic Manipulative Medicine

The aim of this study was to identify and critically evaluate the literature regarding the clinical efficacy of cranial OT, no criteria were set regarding type of disease. Studies were selected based on the following inclusion criteria: OT studies on humans only; study design of randomized controlled trials or observational studies that measured the effectiveness of cranial OT.

12.7.1. Summary

Eight studies met the inclusion criteria, seven were random controlled trials, controlled trials and the other was an observational study. A range of cranial OT used for the management of a variety of conditions were identified in the included studies. Positive clinical outcomes were reported for: pain reduction; change in autonomic nervous system function and improvement of sleeping patterns.

Downs and Black scores ranged from 14 to 23 points with a median score of 16. Downs and Black checklist is an assessment of the methodological quality of the trials, this checklist gives the trials a score ranging from 1 to 28. The scores are ranked as follows: excellent (26-28); good (20-25); fair (15-19); and poor (<14). The evidence currently available on the clinical efficacy of cranial OT is debatable and insufficient to draw concrete conclusions. Because of the moderate methodological quality of the studies and scarcity of available data, further research into this area is needed.

There were some promising results from this systemic review, unfortunately the trials included are not cited so as to enable further analysis of the data, also no “p” values are given in order to ascertain the statistical reliability of the findings

Appraisal of Relevant Studies

12.8. Cuoco, Fennie & Cheriyan (2016) Hypothetical Link Between Osteopathic Suboccipital Decompression and Neuroimmunomodulation

This study postulates that suboccipital decompression may stimulate the efferent branch of the vagal-mediated reflex. Cuoco (2016) stated that:

> the cholinergic anti-inflammatory pathway, thereby suppressing C-reactive protein and interleukin-6 levels post-ST-elevation myocardial infarction. Measured by increased high frequency spectral power of heart rate variability, in a statistically significant manner further supported by a significant decrease in the low-/high frequency spectral power ratio among healthy adults compared to sham treatment and time control.

12.8.1. Summary

The authors' suggested mechanism of action centers around relationships in muscle tonicity, and other tissue states likely to compromise the efferent or afferent activity of the vagus nerve. The authors quote an earlier study by Gilles, Hensel, Pacchia & Smith (2013) in which they wrote: "Suboccipital decompression enhances heart rate variability indices of cardiac control in healthy subjects".

It was demonstrated, in a statistically significant manner, that suboccipital decompression enhances vagal output to the heart as measured by increased high frequency spectral power of heart rate variability. This was further supported by a significant decrease in the low-/high frequency spectral power ratio amongst healthy adults compared to sham treatment and time control.

The specific OT used consisted of 5 minutes of kneading the cervical musculature, followed by 2-3 minutes of suboccipital decompression. For sham treatment, fingers were placed as near as possible to the occipital condyles, with no tension applied, for 8 minutes. In the time control, subjects had no physical contact for 15 minutes. Heart rate variability was not observed prior to each intervention, a weak point of this study. (Gilles et al 2013.)

12.9. Campón Chekroun. (2012). The Effects of Manual Compression of the Right Carotid Sinus on Blood Pressure and Heart Rate.

The study focusses on patients with hypertension who are receiving Treatment. The work was carried out at the Madrid school of osteopathy, the methods employed were a blinded, randomized, controlled trial (BRCT).

The aim was to identify the effects of stimulating the right carotid sinus on BP and heart rate in patients with HTN who were taking medication.
Sixty-four people were included in this study, of whom 33 were in the experimental group and the remainder (31) in a control group. The patients were aged between 20 and 56 with an average age of 39.84 +/- 8.74. Measurements of the BP and heart rate were taken and recorded at one, five and 60 minutes after intervention.

12.9.1. Summary

No statistically significant differences were found in the systolic BP in the control group or overall (F=0.773, p=0.48), nor between the two groups (p>0.05). However, there were differences observed in the experimental group (F=5.675, p=0.002). These differences were found between the measurements taken before and after the intervention, at one, five and 60 minutes.
There were no significant differences in diastolic BP either in the control group, or overall (F = 1.603; p = 0.206) or between the different time intervals. The clinical effect one hour after applying the compression technique on the right carotid sinus in patients with hypertension taking medication, was insignificant.

Analysis of the results revealed a significant difference between the measurements taken one minute and 60 minutes after the intervention. This study suggests a simple mechanism at work, namely, that of increased pressure in the region of the baroreceptors at the carotid sinus, via afferents of the glossopharyngeal nerve, inducing a carotid sinus reflex which results in a short-term reduction in heart rate and BP.

12.10. Morån & Calvente (2008) Changes in Blood Pressure and Heart Rate when Pressure is Applied to the Aortic Valve

The aim of this study was to determine, objectively, whether or not pressure maintained for 90 seconds on the estimated location of the aortic valve on the sternum produces changes in blood pressure and heart rate in patients with primary hypertension.

12.10.1. Summary

Seventy patients with primary hypertension were studied. An apparatus was specially designed for the study, named by the authors “Somial” (which is an abbreviation for the Spanish words for: support, microphone and pressure algometer). In the treatment group, pressure was applied toward the estimated location of the aortic valve via the sternum for 90 seconds. The control group was simply observed for a similar period.

A significant decrease in systolic arterial BP (7.4/9mmHg) was more likely to occur in patients in the treatment group than the control group, although this tendency was not deemed to be statistically significant. This statement is unclear as it mentions. firstly, a significant decrease, which is then deemed to be insignificant. Unfortunately, no “p” or “f” values are given to enable the reader to assess the validity of the data. “Patients with hypertension tend to experience a homogenous decrease in systolic arterial blood pressure as a result of pressure applied to the aortic valve for 90 seconds”. Again, this statement is the authors own assessment of the results without producing the original values for further scrutiny by the reader.

13. Discussion

Initially, reviewing all the papers detailed in this study, the theoretical based papers will be discussed briefly for possible insights into the workings of various forms of OT. Then, the studies seeking to determine whether changes in the autonomic nervous system via OT, will be highlighted. Following this, studies seeking to compare osteopathy with other forms of therapy for hypertensive patients will be explored. Finally, studies referring to complete osteopathic care are reviewed

Cuoco et al (2016) postulated in their study, reviewed in [12.8.] above, that an osteopathic technique, suboccipital compression, might stimulate the efferent branch of the vagal-mediated reflex. They supported this hypothesis quoting the 2013 work of Gilles et al who showed that suboccipital compression enhanced the vagal output to the heart. This may be a mechanism by which OT can reduce blood pressure.

Campón and Chekroun (2016) demonstrated that manual compression of the right carotid sinus reduced the blood pressure in hypertensive patients, supporting Cuoco's hypothesis. In 2008 Morån et al produced similar results by applying pressure to the assumed location of the aortic valve in patients with primary hypertension. Jäkel and Von Hauenschild (2011) described an improvement in autonomic nervous system function as part of their review of OT directed at the cranium.

A number of authors reported that osteopathic techniques can lead to positive effects on the cardiovascular system; Tamburella et al (2019), in the USA, describe an immediate, but reversible, change in cerebral blood perfusion. The changes followed a 45-minute complete OT and were measured immediately after, and again three days following treatment. Galindez-Ibarbengoetxea (2017) too describe a decrease in blood pressure following cervical HVLA manipulation, Moro (2014) showed that a muscle energy technique applied to C7/T1 spinal segment was safe to be carried out on patients with HTN.

Additional support for the H1 hypothesis was provided by Wong et al (2018) in their review of the literature relating to complementary and alternative medicine in the management of hypertension. They quoted the study from Cerritelli et al (2011) about treatment of HTN patients with OT, and concluded that the evidence that OT could be used to manage hypertension was weak. However, in the review of the paper by Cerritelli et al (2011) at [12.1], it was pointed out that the statistics indicated the opposite conclusion; OT was shown to be a strong influence in reducing BP.

Wong et al found that other forms of therapy, e.g. transcendental meditation and appropriate dietary supplementation, provided stronger evidence for a lowering of BP. This reinforces the view that a holistic approach to health is more likely to succeed than an isolated treatment method. In this thesis, a reduction of BP in hypertensive patients can be seen as a measure of improvement of general health.

In the study by Lombardini et al (2008), reviewed in section [12.2] above similar positive changes are listed. Namely an increase in blood flow in peripheral structures, which has the net effect of reducing BP as listed in section six referring to the relationship of peripheral resistance and systemic blood pressure. The patients in this study showed an increase in performance on treadmill testing and in physical health. An improvement was also seen in pressure indices between ankle and brachial arterial pressure.

An interesting study, seeking a decrease in BP, was performed by Mannino in 1979 using an endocrine route on hypertensive young men. Inhibiting the production of aldosterone using Chapman's reflex techniques, he showed a significant drop in aldosterone serum levels within 36 hours of OT ($p<0.01$). Surprisingly no drop in BP was recorded, but the study is worthy of replication and further development in the light of current knowledge. The proposed method of action was on the adrenal glands at paraspinal level T11 and T12 via a circular "make break" motion in a myofascial derived technique (Chapman's reflex points). Physiology of the facilitated spinal segment, as mentioned in paragraph [10.4.1], may be involved in this proposed mechanism of action.

In 2008 Lombardini studied the effect of OT on patients with peripheral arterial disease and concluded that OT significantly improved endothelial function and functional performance. In their study from 2010, Cerritelli et al went further than this and, with a cardiologist in the team, found that a year after starting OT on patients with hypertension and secondary vascular pathology, there had been a significant improvement in the pathological vascular changes and a reduction in the systolic blood pressure. This was a well-designed and recorded study with 31 patients benefitting from both osteopathic treatment and routine care. A control group of 32 patients received just routine care. The treatments were carried out at 15 day intervals for one year in total.

Discussion

It has not been possible to calculate the exact numbers of people in the various papers, because some state the total number in their study, but do not break this down into those who received physical therapy and those who were controls or received sham treatment. In order to establish an approximate idea of the figures, in studies with just a control, it is assumed one half of the total received osteopathic treatment. Where there was also a sham cohort, the total receiving osteopathy is assumed to be one third of the total.

Using these assumptions, approximately 190 adults with primary or secondary hypertension received physical therapy, seven by chiropractors and 183 from osteopaths. Most of the latter were single techniques, but the 31 patients of Cerritelli et al (2010) had complete osteopathic treatments. None of the papers studied reported a patient who became unwell, or whose blood pressure increased as a result of OT.

14. Conclusion

This thesis set out to find evidence that osteopathy could have a beneficial effect on adult patients with primary or secondary hypertension. And if it is safe to treat patients with hypertension using osteopathic treatment.
After a description and discussion of the normal anatomy, physiology and embryology of the vascular system, attention is directed to hypertension, its meaning and causation. Appropriate scientific sources were consulted and those more relevant to osteopathy described and discussed.

Several papers record work which found osteopathic treatments could influence the autonomic nervous system in a positive manner. One paper demonstrated an alteration to the endocrine system by lowering serum aldosterone levels. Strong evidence was found that osteopathic manipulation can trigger the autonomic nervous system to produce a reduction in the resting blood pressure of primary and secondary adult hypertensive patients. However, most of the osteopathic and chiropractic therapists found this benefit only transient. Therapists, using a complete OT regime, observed a reduction in blood pressure and secondary pathological changes which was maintained over a 12 month period. An important finding is that not only can OT stimulate autonomic nervous system activity, but it favors a shift towards parasympathetic tone which has the possibility of reducing heart activity and therefore BP. The conclusions were confirmed by statistical analysis.

Further studies are needed to confirm these findings. They should include a full osteopathic treatment plan, and not simply a collection of miscellaneous techniques as used in some of the scientific papers reviewed here. This holistic approach rings true to the osteopathic philosophy as taught in Amsterdam and the basic principle of osteopathy in treating the individual as a whole and not based solely upon the complaints or sickness with which a patient presents.
The work to prepare this thesis has uncovered a very important fact. From approximately 190 osteopathic treatments described in the various papers here, there is not a single record of an adverse effect upon a patient. Thus, osteopaths can treat patients who have primary or secondary hypertension, secure in the knowledge that it is safe to do so and that their treatment may have a beneficial effect of lowering the blood pressure and reducing the deleterious effects of hypertension. A holistic approach to hypertension, which should include the skills of physicians, osteopaths, other physical therapists and nutritionists will likely yield the best results. Changes in patient lifestyle, such as diet, exercise and cessation of smoking are also essential for improving the health of patients with elevated blood pressure.

15. Considerations for Future/Pilot Studies

This thesis draws upon a number of papers which suggest theoretical routes by which BP may be altered by osteopathic treatment. It goes on to discuss papers in which a transient reduction in BP was recorded in patients with primary hypertension. One source demonstrated a clinically significant change over a longer time frame.

The thesis concluded that further work needed to be done to establish whether OT could be included in a holistic approach to the treatment of the hypertensive patient. The following Pilot Study outlines a protocol designed to resolve this issue.

15.1. Selection of Pilot Study Patients

The study should not be restricted to patients known to have clinical HT, but applied to all patients over a particular age, say, 25 years. This is to avoid possible sources of error such as those people with undiagnosed HT. It could also determine whether OT can alter the BP of normotensive subjects which could benefit those patients with borderline hypertension.
The patient should be invited to take part in a survey into the effects of OT on BP without mentioning what that effect might be (in order to avoid a possible placebo effect). As the survey would be in a clinical environment it would not, of course, be possible to assign patients to a control group which would receive sham OT. All participating patients would be required to sign a simple consent form which would assure anonymity. Any patient unexpectedly found to have hypertension would be informed and advised to seek allopathic medical attention

15.2. Materials and Methods

One osteopath could make all the observations and perform OT to avoid errors owing to different techniques creeping in. Alternatively, several osteopaths could do the work to avoid the single osteopath’s preconceptions; although this would bring its own problems. Sphygmomanometers would be calibrated for accuracy.
During the initial anamnesis the patient would be asked about BP and the survey introduced. Blood pressure would be measured and recorded before and after the OT the details of which would also be written down.

15.3. Findings

The survey would endeavor to answer the following questions using statistical analysis:

- Could a change in BP be detected over a clinically significant period after osteopathic treatment?
- The patients should be subdivided into the following categories
  - In patients known to have hypertension
  - In patients not known to have hypertension, this group is further subdivided into:
    - Pre-hypertensive patients, 120-140 mm Hg systolic BP and/or 80-90 mm Hg diastolic BP.
    - Normotensive patients
    - Patients with hypotension, below 90/60 mm Hg, where a further reduction in pressure might be prejudicial to health. It would be interesting to note whether an increase in BP could be achieved in this patient group or a reduction in symptoms commonly associated with hypotension, such as syncope.

15.4. Results

If future studies produce significant findings they should be published in a peer-reviewed journal. Some papers quoted in the body of the thesis leave the reader asking questions – how many patients, over what period, what osteopathic technique was used and so on? Care should therefore be taken to record everything fully, thus posing the question ‘Can osteopathic manipulation alter blood pressure in a way that is clinically significant?’ To be answered, without ambiguity, in a manner which will benefit both patients and their osteopath.

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18. Glossary of Abbreviations

BRCT = Blinded randomized controlled trial
BP = Blood pressure
CCS = Clinical case study
HDL = High density lipoprotein
HTN = Hypertension
HVLA = High velocity low amplitude
LDL = Low density lipoprotein
LR = Literature Review
NCES = Non-controlled experimental study
OT = Osteopathic treatment
OS = Observational study
PS = Pilot study
PH = Primary hypertension
SH = Secondary hypertension