CHARLES UNIVERSITY

Faculty of Physical Education and Sport

Department of Physiotherapy

Etiology and interrelations in Migraine headache

Master Thesis

Author: Bc. Martine Skudal

Supervisor: Mgr. Agnieszka Kaczmarská, Ph. D.

Prague, April 2010

Abstract

Title: Etiology and interrelations in Migraine headache.

Etiologie a vzájemné vztahy u migrenózních bolestí hlavy.

Thesis Aim: In the thesis I discuss about migraine headache, with the aim of finding possible etiology and interrelations in Migraine headache.

Methods: I performed a literature research review on articles related to this topic.

Results: The etiology of migraine headache is quite comprehensive and can not for certain be explained. Migraineurs mostly experience the same symptoms, but there exists also some individual differences. On the other hand, several other studies can ascertain that psychological, physiological and kinesiological additional factors can provoke or worsen the Migraine headache.

Conclusion: Although it exist interesting findings concerned with the related topic, there still remains a lot of necessary research for the future.

Key words: Migraine, headache, vascular, cervical, psychological, hormonal, postural.

Declaration

I declare that this Master Thesis is based entirely on my own individual work, and on my own litterateur research. By the help of different books and journal databases on the internet, listed in the literature list in the end of this thesis, I managed to find all information needed for development of this Master Thesis.

Prague, April 2010 ……

Acknowledgement

First of all I want to thank my family for being supportive and for always standing by my side. During my childhood years I always received wise guiding and important advices in every serious decisions of my life. Also during my several mistakes, I was met by reasonable manners and with honest explanations that made sense to me. This gave me the basis for meeting challenges in a better way and to be aspiring when it comes to general factors in life.

I want to thank the professors at Charles University in Prague. Their passion for physiotherapy and the knowledge they bear has given me interest and will for learning more.

I would also like to thank Mgr. Agnieszka Kaczmarská, Ph. D., my supervisor for my Master thesis. She gave me knowledge, good advice and smart techniques on how to make a good thesis.

Martine Skudal

Prague, April 2010

Contents

Preface

Etiology and interrelations in Migraine headache, aim at performed researches and clinical findings for the establishment of influencing factors concerned in Migraine headache. It consists of two main sections. The first section is again divided into three head lines. The first involves a general overview of headache, the classifications, the clinical features, risk factors, clinical approach, anamnesis and examination. The second and third headline, include the two main subtypes of headache, vascular and cervical headache. And similarly to the first section they also comprise several under points concerning their own classification, the pathophysiology, risk factors, differential diagnosis, anamnesis, examination, etc.

The second section embraces specific interrelations concerned in the Migraine headache disorder, including psychological factors, hormonal changes and postural factors. The section also involves how they influence each other, and even more important how they influence migraine patients.

Chapter I: Literature review of vascular and cervical headache

1.1. Introduction

Headache is a very common health problem in today's society. 90 % of adults report having a headache at least once in their life [Porth, 2005]. 26 % of woman and 57 % of men report at least one headache a month [Saper, 1999]. Twenty – five percent of adults report having recurrent headaches and 4 % report having daily or nearly daily headaches [Kaniecki 2003]. Headache is now ranked by the world health organization (WHO) as number 19 among all diseases world-wide causing disability. Headache is high among causes of consulting medical practitioners. A survey of neurologists found that up to one-third of all their patients consulted because of headache – more than for any other complaint. But headache is also a common symptom, found in patients consulting physical therapy, for a whole different complaint. Headache has been and continues to be underestimated in scope and scale, and headache disorders remain under-recognized and under-treated throughout the world [WHO, 2004].

Today there exist a partnership between several societies and organization, which work together on the subject of headache. Some partners in action are the WHO, world health alliance (WHA), international headache society (IHS) and the European headache federation (EHF). They work on the global campaign to reduce the burden of headache worldwide. They stress the fact that headache disorders are real, and not just in our mind. The WHA is a global alliance of almost 40 national headache organizations from nearly 30 countries worldwide. They work with sharing information among headache organisations and by increasing the awareness and understanding of headache as a public health concern, with great economical and social impact. The IHS welcomes society members and everyone working or seeking information in the field of headache. Here you can find online journals, with the most recent news on the subject of headache. The EHF works for improving the life of those affected by headache in Europe.

Headache is caused by a number of conditions. Some headaches are primary disorders and other occur secondary to different disease conditions. The three most common types of primary chronic headaches are migraine headache, cluster headache, and tension – type headache

[Kaniecki, 2003]. Migraine and cluster headaches are classified as vascular headaches, whereas tension – type headache is considered a cervical headache. Headache is influence by disorders of neck or physical and emotional tension, along with psychological states [Lewit, 2007]. Emotional tension and anxiety can cause the muscles at the base of the head and jaw to become very tight, irritating the nerves and restricting blood flow, further producing a headache [Wolland, et al, 2002].

Migraine headache affects approximately 20 million people in the United States, 18 % affected woman and 6 % affected men [Mathew, 2001]. In Norway the results are some what similar, with 16 % affected woman and 8 % affected men [Hagen, Zwart, et al, 2000]. The result being considerable time lost from work and other activities [Mathew, 2001]. Migraine headaches are believed to be genetic, inherited as an autosomal dominant trait with incomplete penetrance [Saper, 1999]. But the genetic influence is stronger for migraine with aura than in migraine without aura [Mathew, 2001].

Tension – type headache is the most common headache type worldwide [Ailani, 2009] [Porth, 2005]. Luckily it is normally not sufficiently severe enough to interfere with daily activities [Forshaw, 2004]. There exists a close relation between increased muscle tension in the neck region, psychological problems and headache. Increased muscle tension is a physiological phenomenon, and should be treated by the most suitable physiological methods. Factor of reflex origin involves assuming that disturbed function plays the role of a nociceptive stimulus, and then a vasomotor reaction is part of the typical reaction, pain as a rule provokes vasoconstriction [Lewit, 1999].

It would be wrong not to mention that most causes of secondary headache are benign, but some can be an indication of serious disorders such as meningitis, brain tumour, or cerebral aneurysm [Porth, 2005].

The diagnosis and classification of headaches is often difficult. Comprehensive history and physical examination is needed to exclude secondary causes. This involves information about precipitating factors, such as foods and food additives, missed meals, and association with the menstrual period. Because certain medications and alcohol usage can provoke or aggravate

headaches, this information is essential. A headache diary may be helpful in identifying factors that contribute to headache onset [Porth, 2005].

A lot of studies have been published concerning the relations between hormonal changes, varying psychological states, with changes in soft tissue, leading to serious headaches. The relations seem comprehensive.

A large number of patients, suffering from migraine headache, are uncertain of the etiology and the treatment for it. How some influencing factors to migraine headache, relates to each other, is an extensive study. How due the hormonal changes and psychological states influence the soft tissue of cervical spine? Do the soft tissue of cervical spine provoke headache? And are there some direct influencing factors between hormonal changes and psychological states, and migraine?

The thesis is a systematic review of the relevant literature on the questionnaire of migraine headache, with regard to some possible influencing factors.

1.2. Definition

Headache itself is a painful and often disabling feature, which also occur secondarily to a considerable number of other conditions. Headaches are the most common disorders of the nervous system. They are pandemic and, in many cases, life – long conditions. The mechanism of tension type headache (TTH) is poorly understood, although it has long been regarded as a headache with muscular origins. It may be stress-related or associated with musculoskeletal problems in the neck [WHO, 2004].

Migraine is another form of headache; it is even referred to as a "migraine headache" [Forshaw, 2004]. Migraine is a common disabling primary headache disorder, with almost certainly, a genetic basis. It has a high prevalence and high socio-economic and personal impacts [WHO, 2004]. Migraine is a primary, episodic headache disturbance characterised with unequal combinations of neurological, gastrointestinal and autonomic changes [Silberstein, 2004]. Migraine headache is considered a multifactor and heterogeneous disorder. The pathophysiology involves neuronal and vascular phenomena. Despite a clear genetic component, the discovery of specific genes for common forms of migraine remains superficial. Age and sex, along with external factors are also believed to have a contributing effect [Schurks, 2009]. Some authors believe that migraine has its origin in the brains blood vessels. And that headache alone is attributed to conditions outside the cranium [Haug, et al, 1997] [Bjålie, et al, 2001]. Knowledge about the migraine is still limited, which hampers a definition [Schurks, 2009].

1.3. Etiology

Migraine has a heritable component [Hagen, 2003] and is believed to be a genetic heterogenic condition [Alstadhaug, et al, 2007]. 60% of patients with migraine have first degree relatives with migraine. With the usual migraine forms there are still not any precise gene discovery proven [Hagen, 2003]. A rare variant is the familiar hemiplegic migraine which has a dominant heritable factor. Migraine seems to be a disease in the brain and not primarily in blood vessels [Salvesen, 1999].

1.4. Headache

Headache is the most common complaint of civilized man affecting approximately 2/3 of the population [Brukner, Khan, et al, 2007]. Thus, it's not the main reason why patients seek a physiotherapist, but it appears commonly in the medical history of the patient [Goodman, Snyder, 2007]. The brain itself has no possibility to feel pain, due to the lack of pain receptors. The headaches are often due to "benign" extra cranial disorders, such as stimulation of receptors situated outside the brain [Snell, 2006]. Pathological pressure on blood vessels, cranial nerves, sinuses, and membrane surrounding the brain gives rise to the headache symptom. In 1 – 5 %, of total cases, serious causes have been reported. The cause is often due to tumours and infections of the central nervous system. Good headache classifications lead to development of many discrete entities among these disorders [Goodman, Snyder, 2007].

1.4.1. Classification

Headache may be classified into seven groups:

1. Headache associated with viral illness; respiratory infections, sinusitis, influenza
2. Vascular headaches; migraine, cluster headache
3. Cervical headache; referred from joints, muscles and fascia of the cervical region
4. Tension headache or muscle contraction headache
5. Intracranial causes: tumour, haemorrhage, subdural haematoma, meningitis, ischemia
6. Exercise – related headache; benign exertion headache, footballers migraine
7. Other causes; drugs, psychogenic, post – spinal procedure, post – traumatic.

The first four are seen frequently in the community, and headache of mixed type occur commonly [Brukner, Khan, et al, 2007].

The IHS has published a classification of headache disorders, which divide headache into three parts:

1. **Primary:** migraine, tension – type headache, and cluster headache
1. **Secondary:** cervicogenic headache; attributed to some other causative disorder specified in the diagnostic criteria attached to them. Treatment is often provided. This type of headache is defined as referred pain in any part of the head caused by musculoskeletal tissues innervated by cervical nerves (C1 – C4).
2. **Cranial neuralgias** [Goodman, Snyder, 2007].

Further, the IHS has in conjunction with WHO made an overall classification for current criteria for physical dysfunction in headache (table 1.1).

International Headache Society [IHS, 1988]	International Association for the Study of Pain [Jull, et al, 2004]	Sjaadstad et al. [Sjaastad, Fredriksen, et al, 1998]
Resistance to or limitation of passive neck movements	Reduced range of motion in the neck	Restriction of range of movements in the neck
Changes in neck contour, texture or tone or responses to active stretching or contraction	-	-
Abnormal tenderness in neck muscles	-	Pressure over the ipsilateral upper cervical or occipital region reproduces headache

Table 1.1 Current criteria for physical dysfunction in headache classification [Merskey, Bogduk, 1994].

1.4.2. Clinical features

As mentioned earlier, in the introduction, headache is caused by a number of conditions. Some headaches are considered to be primary disorders while others are secondary [Kaniecki, 2003]. The primary disorders can be divided into vascular or cervical headaches, according the nature of headache [Brukner, Khan, et al, 2007]. The vascular concept, involves the body's network of blood vessels. That includes the arteries, veins and capillaries that carry blood to and from the heart. The cervical concept, involves the neck region with structures like, bone tissue, intervertebral discs, ligaments, tendons, muscles, nervous tissues, and lymph nodes [Moore, Dalley, 2006]. Further, we divide each headache type, as either primary or secondary, according to their characteristic features (table 1.2).

Features	Vascular headache	Cervical headache
Age of onset	10 – 40 years	20 – 60 years
Onset	Fast	Slow
Site	Frontal or temporal	Occipital (usually), retro – orbital or temporal
Side	Unilateral/bilateral	Unilateral
Type of pain	Throbbing	Dull ache
Constancy	Episodic	Constant
Time course	Hours	Days
Neurological symptoms	Common (e.g. visual disturbances, nausea)	Occasionally (e.g. paresthesia)
History of trauma	Rare	Common (e.g. “whiplash”)
Triggers	Food, drugs, stress	Trauma, posture
Treatment	Avoid precipitating factors Drugs Stress reduction	Manual therapy Stress reduction Postural correction

Table 1.2 Clinical features of vascular and cervical headaches [Brukner, Khan, et al, 2007].

The table below indicate the characteristic features of the major headache types: migraine, tension and cervicogenic.

Migraine	Tension	Cervicogenic
Can be headache – free	Dull pressure	Pain starts in occipital region and spreads anterior toward the frontal area
With headache: throbbing or pulsating	Sensation of band around the head	Usually bilateral
Often unilateral; around or behind one eye.	Bilateral or global	Pain intensity fluctuates from mild to severe
Often with nausea, vomiting	Muscular tenderness or soreness in soft tissues of the upper cervical spine	Often worsen by neck movements or sustained postures
Common triggers: alcohol, food, hormonal changes, hunger, lack of sleep, perfume, stress, medications, environmental factors.	Not usually any associated signs and symptoms	Can resemble migraine with throbbing pain, nausea, phonophobia, photophobia
May precede by prodromal symptoms: visual changes (aura), motor weakness, dizziness, paresthesias	May get worse with loud sounds or bright lights	History of trauma; whiplash, disc disease, or arthritis
Facial pallor, cold hands and feet	Current diagnosis or history of anxiety, depression, or panic disorder	
History of headache in childhood or family		

Table 1.3 Clinical features of major headache types [Goodman, Snyder, 2007].

1.4.3. Risk factors

- Stress
- Inadequate coping
- Anxiety
- Depression
- Panic disorder
- Substance abuse
- Excessive caffeine consumption or withdrawal

Headaches are common in patients with post – traumatic brain injury, post – whiplash injury, or post – concussion injury [Goodman, Snyder, 2007].

1.4.4. Clinical Approach

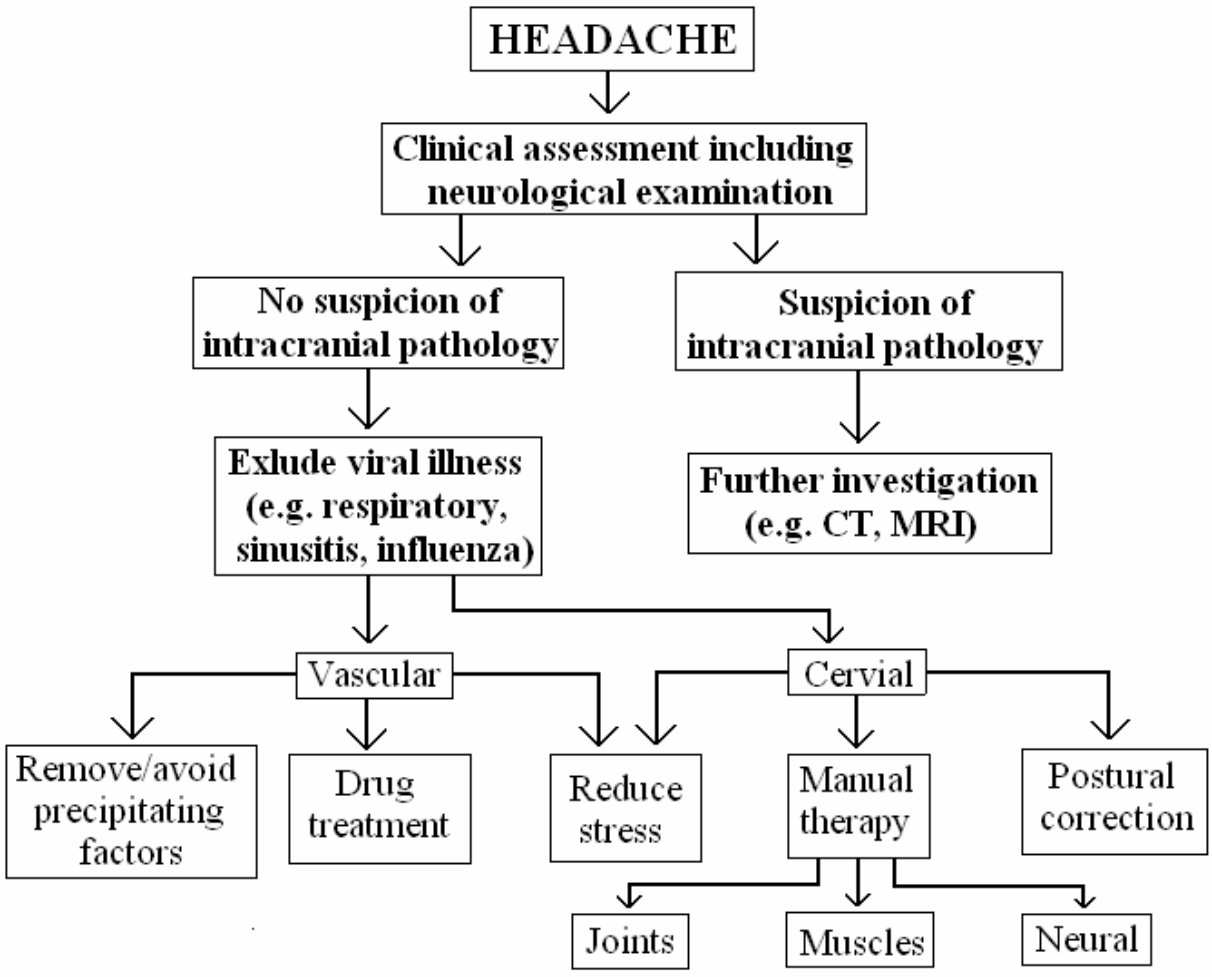


Figure 1.1 Clinical approaches to the patient with headache [Brukner, Khan, et al, 2007].

The practitioner should:

1. Exclude possible intracranial causes; including haemorrhage, tumour, infection and subdural haematoma.
2. Exclude viral illnesses, such as respiratory tract infection, sinusitis, and influenza.
3. Exclude drug – induced headaches; e.g. alcohol, analgesics (e.g. aspirin), antibiotics and antifungal, antihypertensive, caffeine, corticosteroids, cyclosporine, monoamine oxidase inhibitors, nicotine, nitrazepam, nitrous oxide, oral contraceptives, sympathomimetics, and vasodilators.
4. Exclude exercise – related headaches.
5. Differentiate between vascular, tension and cervical causes. If they are all excluded, the majority of headaches are then due to vascular causes, such as migraine, or referred from the joints and/or muscles of the neck [Brukner, Khan, et al, 2007].

1.4.5. Anamnesis

History is the most important component of the assessment of the headache. Certain points are essential for the diagnostic technique [Goodman, Snyder, 2007] [Den Norske Legehåndboken (DNL), 2009]. Underneath follows a setup on how to carry out the medical history.

1) Patient demographics
- Age
- Gender
- Race/Ethnicity
- Occupation

2) Personal history and family history is frequently positive
- Risk factors for disease
- Medical/surgical history
- Medications (current, recent past)

3) Psychosocial
- Education
- Family system
- Culture/religion

4) Risk factor assessment

5) Clinical presentation

6) Associated signs and symptoms of systemic diseases

7) Review of systems [Goodman, Snyder, 2007] [DNL, 2009].

A recent history of a blow to the head is relevant. If the pain is throbbing or more like a dull ache, and how the behaviour of a headache is in both short term and long term. A typical migraine attack last between 4 – 72 hours with or without aura. And 20 – 60 % of patient's receive a pre warning hours or days before the headache sets it [DNL, 2009]. A pre warning can be psychological, neurological, constitutional or autonomic – ex depression, cognitive dysfunction, and increased appetite [Silberstein, Young, 1995]. Most common symptoms are fatigue, difficulties in concentrating and stiff neck [Giffin, et al, 2003]. The frequency of attacks is also important. The presence of any neck and arm symptoms should also be noted. Whether the headache is easily irritated, this is relevant for manual therapy treatment. Are there any visual or sensory symptoms, nausea and vomiting, or any neurological symptoms or systemic symptoms, should be noted. Also the presence of neck pain or stiffness is also important. The pain can often change side, from time to time, during one attack. And it tends to prevent the ability to proceed with the daily activities. During the attacks the patient is normally pain free. A past history of head trauma is very relevant. Information about any medication or life stresses should be noted [Brukner, Khan, et al, 2007] [DNL, 2009]. During the regeneration the patient often feels tired, empty, irritable or dull. The concentration ability is often decreased, along with moody attitude. Tenderness in the scalp is often present [DNL, 2009].

1.4.6. Examination

A full neurological examination is required and the skull and cervical spine must always be particularly examined. Including the below mentioned points:

- General appearance
- Mental state
- Speech
- Skull examination
- Cervical spine examination
- Gait and stance

- Pupils and fundi
- Special senses (smell, vision, hearing)
- Other cranial nerves
- Motor system
- Sensory system
- General examination. [Goodman, Snyder, 2007] [DNL, 2009].

1.5. Vascular Headaches

Vascular headaches include migraine, cluster headache, toxic headache, exertional headache and some types of post – traumatic headache. Vascular headaches affect 20 % of the population at some point during their life [DNL, 2009]. Common to all these headaches is a tendency towards extra - cranial vascular dilatation manifested by the throbbing headache phase of a particular attack. Vasoconstriction may also be evident and responsible for the painless sensory phenomena prior to the onset of head pain. [Brukner, Khan, et al, 2007].

1.5.1. Classification

The classification of vascular headache is usually divided into migraine headache and cluster headache (table 1.4).

Characteristics	Migraine	Cluster
Family history	Yes	No
Sex	Females more than males	Males more often than females
Onset	Variable	During sleep
Location	Usually unilateral	Behind or around one eye
Character and severity	Pulsating, throbbing	Excruciating, sharp, steady
Duration	2 – 72 hours per episode	15 – 90 minutes per episode
Associated symptoms	Visual auras, sensitivity to light and sound, pale facial appearance, nausea and vomiting	Unilateral or bilateral sweating, facial flushing, nasal congestion, lacrimation, papillary changes

Table 1.4 Characteristics of migraine, cluster, and tension – type headaches [Harvey, Champe, 2009].

Vascular headaches usually begin early in life, often at puberty or in the second decade. The debut age may also be among little children. The headache itself usually begins early in the morning and reaches high intensity within 2 hours. It may also last for several hours. Usually resolves within a day, but can recur daily or several times a week, especially during spring season. Marked variations in headache frequency are seen within individuals. After the age of 60, headaches usually diminish. The use of medications, such as vasodilators, hormone replacement therapy or oral contraceptive pill, may exacerbate an underlying tendency towards vascular headaches [Brukner, Khan, et al, 2007] [DNL, 2009].

1.5.2. Cluster headache

Cluster headache is also known as histamine headache, migrainous neuralgia and Horton's headache. This form of headache may be distinguished from other vascular headaches by the typical nature of the history. The pain typically occurs in attacks and is an intense burning or boring sensation. The attacks frequently begin in middle age and may be precipitated by alcohol. On the affected side there may be associated rhinorrhea, nasal obstruction, perspiration and conjunctive injection. A partial Horner's syndrome is often seen. This condition is five times more common in males than in females. There is usually no family history. Patients are usually disabled during a cluster headache [Brukner, Khan, et al, 2007].

Patients with cluster headache are usually extremely sensitive to vasodilating agents. Oral glycerol trinitrate (nitroglycerin) has been used as a provocative test for this condition [Harvey, Champe, 2009].

Treatment depends on the age and health of the patient and the timing of attacks. Acute attacks may be aborted by inhalation of 100 % oxygen at 7 L per minute. The mechanism of this relief is unclear. Headache prophylaxis may be necessary. Methysergide may be used in younger patients and either prednisolone or lithium or both in older patients. Generally, the use of these medications requires specialist input due to the side – effect profile. Ergot preparations may also be used [Harvey, Champe, 2009] [DNL, 2009].

1.5.3. Migraine headache

It has been estimated that 18 % woman and 6 % men in the United States (U.S.) suffer from severe migraine headaches [Harvey, Champe, 2009]. The prevalence is highest among woman around the age of 40 [DNL, 2009]. Migraine is usually distinguished clinically from two other types of headaches, such as cluster headache and tension - type headache. People with severe migraine headache, complain of 1 – 5 attacks per month of moderate to severe pain, usually unilateral. Migraine plays a major role in the patient's life and result in big health costs [Harvey, Champe, 2009]. Highest incidence is among men at 10 – 12 years of age, and among woman at 14 – 17 years of age [DNL, 2009].

Migraines usually begin in childhood to early adulthood, and are often accompanied by nausea, vomiting, and visual disturbances. Migraines at the age of 50 are often present in peri – menopausal or menopausal woman. Advancing age makes other types of headaches more likely. Genetic predisposition is often present in a client. The examination results, beyond typical clinical presentation, are usually normal [Goodman, Snyder, 2007].

There are two types of migraine headaches. Migraine with (classic) and without (common) aura that is, vascular headache occurring with and without neurological symptoms. Most people think of migraine as headache alone, the true migraine sufferer usually notices a spectrum of symptoms, including nausea, vomiting, diarrhea, weight gain. They may notice periods with evidence of endocrine disturbance (e.g. fluid retention). In the typical migraine attack with aura, painless sensory neurological symptoms such as visual disturbances, paresthesia, vertigo, hemiplegia and ophthalmoplegia may precede the headache [Harvey, Champe, 2009]. Aura develops usually within 5 – 10 min and last less than 60 min. The aura phase usually arrives immediately before a migraine attack [DNL, 2009]. Approximately 85 % of patients with migraine do not experience aura. In the 15 % of migraine patients whose headache is preceded by an aura, the aura itself is sufficient for the diagnosis. Thus, with or without auras, the headache itself is similar in both. And for both types of migraine, women are three – fold more likely than men to experience either type of migraine [Harvey, Champe, 2009] [DNL, 2009]. In the table below you see IHS criteria for the diagnosis of migraine without aura.

A. At least five attacks fulfilling criteria B – D below.
B. Headache attacks lasting 4 – 72 hours.
C. Headache has at least two of the following characteristics: 1. Unilateral location 2. Pulsating quality 3. Moderate to severe intensity (inhibits or prohibits daily activities) 4. Aggravation by walking stairs or similar routine physical activity
D. During headache at least one of the following: 1. Nausea and/or vomiting 2. Photophobia and phonophobia

Table 1.5 The IHS criteria's for the diagnosis of migraine without aura [IHS, 1988]

1.5.4. Clinical features

Patients describe migraine headache pain as sharp and intense, unilateral or bilateral. It is often throbbing, beating or pulsing, and occasionally the pain is steady. Often it recurs at intervals. Commonly, it begins in the temple or forehead on both sides. When it starts on one side, it may spread to the other side. If the headache is intense, it may spread to the occipital region and even change to a muscle contraction type of headache. Occasionally, the vascular headache begins at the back of the head and moves forward [Snell, 2006].

Neurological symptoms vary depending on which part of the intracranial vascular tree is affected by the disturbance. In migraine with aura, occipital branches of the vascular tree may be affected and visual symptoms such as flashing lights, black spots or crossing lines in one or both visions are common visual symptoms. Field of view may become unclear or disappear. One can also experience visual and sensory symptoms, with hallucination. Also, patients may suffer the sensory phenomena without the headache developing, called headache equivalent [DNL, 2009]. In a rare form of migraine seen in children known as vertebrobasilar migraine, brain stem abnormalities such as behavioural disturbances and even death have been described [Brukner, Khan, et al, 2007].

Visual disturbances are believed to be due to sympathetic vasoconstriction of the cerebral arteries supplying the visual cortex. The headache is chiefly due to the dilation and stretching of other cerebral arteries and branches of the external carotid artery. Migraine seems to affect arteries both on the inside and outside of the skull. Its cause is unknown, but genetic, hormonal,

and biochemical factors may initiate an attack. It is thought that beta – blockers bring relief to some type of patients, due to the reduction in cerebral vasodilatation [Snell, 2006].

Sensory symptoms are usually described as tingling, numbness, pricking or pins and needles. These commonly start in the face or fingers and gradually spread up the limb over the same side of the body. Frequently appears a once sided numbness in face/tongue or hand/arm [Silberstein, Lipton, 1994]. Vertigo, dysphasia, diplopia, confusion and amnesia are less commonly reported. Nausea, vomiting and dizziness are common during or after the attack. After the headache, diuresis, diarrhea, euphoria or a wave of energy are commonly described.

Typical features are:

- Precipitating factors, such as tiredness, stress or release from stress (e.g. weekend migraine)
- Character and location of headache
- Periodicity
- Presence of migraine accompaniments (e.g. visual, gastrointestinal symptoms)
- Relief of anti – migraine therapy (e.g. sumatriptan) [Brukner, Khan, et al, 2007] [Silberstein, 1995].

1.5.5. Red Flags

- Headache that wakes the individual up or is present upon awakening (e.g. hypertension, tumour)
- Headache accompanied by documented elevated blood pressure changes
- Insidious or new onset of headache (less than 6 months)
- New onset of headache with associated neurological signs and symptoms (e.g. confusion, dizziness, gait or motor disturbances, fatigue, irritability or mood changes)
- New onset of headache accompanied by constitutional symptoms (e.g. fever, chills, sweats) or stiff neck (infection, arthritis)
- Episodes of “blacking out” during headache (seizures, haemorrhage, tumour)
- Sudden severe headache accompanied by flu like symptoms, aching muscles, jaw pain when eating, and visual disturbances (temporal arthritis)
- No previous personal or family history of migraine headaches [Goodman, Snyder, 2007].

1.5.6. Pathophysiology of migraine headache

Migraine without aura accounts for approximately 85 % of migraines, and migraine with aura accounts for most of the remaining migraines. Migraine without aura is a pulsating, throbbing, unilateral headache that typically lasts 1 to 2 days and is worsened by routine physical activity. The headache involves nausea and vomiting, and sensitivity to light and sound. Visual disturbances often occur and involve hallucinations such as stars, sparks, and flashes of light. Migraine with aura has similar symptoms, but with the addition of visual or neurological symptoms that precede the headache. It develops during 5 to 20 minutes and lasts less than an hour. There is only a small percentage which experiences the aura before an attack. Some people without the aura have prodromal symptoms, such as fatigue and irritability, which precede the attack by hours or even days [Porth, 2005].

Subtypes of migraine include ophthalmoplegic migraine, hemiplegic migraine, aphasic migraine, and retinal migraine. Ophthalmoplegic migraine with its localized pain around the eye, it is also characterized by diplopia, due to a transient paralysis of the muscles that control the eye movement. Transformed migraine is a mixed headache, with various symptoms associated with tension – type headache, sinus headache, or chronic daily headache, and is therefore difficult to classify [Headache Classification Subcommittee (HCS), 2004].

Migraine headache occur in children as well as adults. It is equally distributed between sexes, until puberty. Diagnostic criteria are made upon the presence of recurrent headaches separated by pain – free periods. Diagnosis is based on at least three of the following symptoms or associated findings: abdominal pain, nausea or vomiting, throbbing headache, unilateral location, associated aura (visual, sensory, motor), relief during sleep, and a positive family history [Annequin, Tourniare, Massoui, 2000] [Haslam, 2004]. Symptoms vary widely among children; some are in need of interrupting activity and seek relief in a dark room, to those detectable only by questioning. A common feature of migraine in children is intense nausea and vomiting, which can be associated with abdominal pain and fever; thus, migraine may be confused with other conditions such as appendicitis. After the 10^{th} birthday, it is common that children with migraine undergo spontaneous prolonged remission. Headache in children can be a symptom of other, more serious disorders, such as intracranial lesions. Therefore it is important that other causes of the headache, which require immediate treatment, are to be ruled out [Porth, 2005].

The pathophysiological mechanisms of the migraine pain are poorly understood. Although there are several theories, it is well established that during a migraine the trigeminal nerve becomes activated [Tepper, Rapoport, Sheftell, 2001] [Williamson, Hargreaves, 2001]. This activation may lead to the release of neuropeptides, causing painful neurogenic inflammation of the meningeal vasculature characterized by plasma protein extravasations, vasodilatation, and mast cell degranulation. Another possible mechanism implicates neurogenic vasodilatation of meningeal blood vessels as a key component of the inflammatory processes that occur during migraine. Activation of trigeminal sensory fibres evokes a neurogenic dural vasodilatation mediated by calcitonin gene – related peptide. The calcitonin gene – related peptide level is elevated during migraine and is normalized after successful treatment of sumatriptan [Williamson, Hargreaves, 2001]. The neurogenic basis for migraine is supported by the frequent presence of premonitory symptoms before the headache begins; focal neurological disturbances, which cannot be explained in terms of cerebral blood flow; and the numerous accompanying symptoms, including autonomic and constitutional dysfunction [Saper, 1999].

Also the hormonal variations are thought to play a role in the migraine attacks pattern, especially in the estrogen levels. A lot of woman experience the migraine headaches at the same time as their menstrual periods. Therefore the migraine headaches in woman are thought to be related to the aggravating effect of estrogen on the migraine mechanism [Mathew, 2001]. Dietary substances, such as monosodium glutamate, aged cheese, and chocolate, also may precipitate migraine headaches. The actual triggers for migraine are the chemicals in the food, not the allergens [Kunkel, 2000].

The treatment of migraine headaches includes preventative and abortive nonpharmacologic and pharmacological treatment. Nonpharmacologic treatment includes the avoidance of migraine triggers, such as foods, that precipitate an attack. Regular eating and sleeping habits give an advantage to the persons with migraine. Control the stress, which can precipitate an attack, is also important. A quiet, dark room seems to be the ideal treatment, when the attack first occurs [Snow, Weiss, Wall, et al, 2002].

Pharmacological treatment involves both abortive therapy for acute attacks and preventive therapy. A wide range of medications is used to treat the acute symptoms of migraine headache. First line agents include acetylsalicylic acid; combinations of acetaminophen, acetylsalicylic acid, and caffeine and non – steroidal anti – inflammatory drugs (NSAIDs) analgesics; serotonin (5 – HT_1) receptor agonists; ergotamine derivatives; and antiemetic medications. No oral routes of

administration are preferred in people who develop severe pain rapidly or upon awakening, or if severe nausea and vomiting usually occurs. For intranasal administration, sumatriptan and dihydroergotamine are both approved. Dihydroergotamine may be administered parenterally with an antiemetic or opioid analgesic for an intractable migraine headache [Schurks, 2009]. Frequent use of abortive headache medications may cause rebound headache [Harvey, Champe, 2009].

If migrainous headaches are disabling, if they occur more than two or three times a month, if abortive treatment is being used more than two times a week, or if the individual has hemiplegic migraine, migraine with prolonged aura, or migrainous infarction, preventative pharmacologic treatment may be necessary. And must be taken daily for months to years. First – line agents include b – adrenergic blocking medications, anti – depressants, and anti - seizure medications [Snow, Weiss, Wall, et al, 2002]. When a decision to discontinue preventive therapy is made, the medications should be withdrawn gradually. There exists other effective medications, but they also give serious side effects to some individuals. A person with coronary artery disease should not take 5 – HT_1 receptor agonists, due to risk of coronary vasospasm. Ergotamine preparations can cause uterine contractions and should not be given to pregnant woman. They can also cause vasospasm, and should be used with caution in persons with peripheral vascular disease [Harvey, Champe, 2009].

1.5.7. Biologic basis

Migraine with aura is a spreading depression of neuronal activity, including reduced blood flow in the most posterior part of the cerebral hemisphere. The hypo - perfusion spreads forward over the cortex surface to other contiguous areas of the brain. Functional changes are involved in the vascular alterations; for example, abnormal response to changes in arterial partial pressure of CO_2. Hypo - perfusion begins with the aura and continues into the headache phase, when hyper - perfusion occurs. Migraines without aura do not show any hypo - perfusion. Thus, the pain of both types of migraines may be due to extra cranial and intracranial arterial dilation. Stretching leads to release of neuroactive molecules, such as substance P [Harvey, Champe, 2009].

1.5.8. Precipitating factors

- Endocrine changes (e.g. premenstrual or menstrual, oral contraceptive pills, pregnancy, puberty, menopause, hyperthyroidism)
- Metabolic changes (e.g. fever, anaemia)
- Rhinitis
- Change in temperature or altitude
- Change in activity
- Alcohol, especially red wine
- Foods (e.g. chocolate, cheese, nuts, "hot dogs")
- Drugs (e.g. glycerol trinitrate [nitro-glycerine], nitrates, indomethacin)
- Blood pressure changes
- Sleep – too much or too little [DNL, 2009].

People with family history of migraine; have increased chances of receiving migraine by 50 % [Stewart, Staffa, 1997]. Mental disorders such as affective and anxiety disorders are often seen along with migraine [Fasmer, Oedegaard, 2004].

1.5.9. Differential Diagnosis

Associated signs and symptoms are the most important points for the diagnosis of headache. For example a throbbing headache with unexplained diaphoresis and elevated blood pressure may indicate a significant cardiovascular event. Daytime sleepiness, morning headache, and snoring may point to obstructive sleep apnoea. And headache with visual disturbances or facial numbness can be a sign of neurological origin of symptoms. Migraines can in fact mimic a stroke, due to its paralysis or weakness of one side of the body [Goodman, Snyder, 2007].

1.5.10. Examination

During a physical examination it's important to include measurement of vital signs, assessment of cardiac and vascular signs, and a detailed head and neck examination. A neurological examination should give results regarding mental status (pain behaviour), cranial nerves, motor function, reflexes, sensory systems, coordination, and gait [DNL, 2009] [Goodman, Snyder, 2007].

1.5.11. Treatment

Most patients choose to lie quietly in a dark room during a migraine attack. Sleep often terminates the attack. The primary method of active treatments is pharmacological. High-dose aspirin (ASA) (900 – 1200 mg) is the drug of choice for the acute treatment of migraine. Sumatriptan (intramuscular or intranasal) or ergot preparations may be used as second – line therapy [McCrory, et al, 2005].

Frequent sufferers of migraine may find preventive drug therapy necessary and reasonable effective. An important part of the management of the migraine sufferer is to identify and avoid precipitating factors [DNL, 2009]. Repeated doses of simple analgesia alone should be avoided. The consequence of the overuse of analgesic medication is the so-called "analgesic rebound headache", which becomes a self – generating headache requiring increasing doses of analgesia [Brukner, Khan, et al, 2007]. Simple analgesics (acetylsalicylic acid abbreviated (ASA), ibumetin, or paracetamol) is first choice medication, and combined with non – analgesic drugs it should be sufficient for most [Matchar, et al, 2000] [Duncan, et. al. 2008]. In cases where normal analgesics don't work to our satisfaction at attempts over 2 – 3 attacks, we increase to Triptans. Studies show that easy attacks can be treated with normal analgesics. Moderate to serious attacks need usually treatment with Triptans [Lipton, Cady, 1999] [Lipton, Stewart, 2000]. For long lasting attacks, or attacks after successful treatments with Triptans evaluate combination Triptans + Naproxen. Treatment of headache should be directed at the cause of the problem not simply pain management [DNL, 2009].

Acute treatments can be classified as non-specific (symptomatic) or migraine specific.
Non-specific treatments which involves;

- Analgesics: for example non - steroidal anti – inflammatory drugs.
- Anti - emetics: for example prochlorperazine to control vomiting.
- Opioids: considered as rescue medication when other treatments are non successful.

Specific therapy involves;

- Triptans and dihydroergotamine. Both of which are 5 – HT_{1D} receptor agonists. It has been proposed that activation of 5 – HT_{1D} receptors by these agents leads to vasoconstriction or to inhibition of the release of pro - inflammatory neuropeptides. Most patients prefer triptans over ergot derivatives, despite their high costs [Harvey, Champe, 2009].

1.5.12. Prophylaxis

When a patient experiences two migraine attacks or more during one month, and when the headaches are severe or complicated by serious neurological sign, therapy is indicated to prevent the migraine. Propranolol, but also β – blockers particularly nadolol, have been shown to be effective. [Harvey, Champe, 2009].

1.6. Cervical headache

Cervical or cervicogenic headache is the term used to describe pain believed to originate from the neck, due to abnormalities of the joints, muscles, fascia, and neural structures of the cervical region [Sjaastad, Salvesen, et al, 1998]. The estimated prevalence of the disorder varies considerably ranging from 0.7 % to 13.8 % [Martelletti, van Suijlekom, 2004]. A pathophysiology model for referred pain can be used to explain the pain in cervicogenic headache [Bovim, 1993] [Kerr, 1961] [Kerr, Olafson, 1961].

1.6.1. Pathophysiology of cervicogenic headache

The role of muscles in the pathophysiology of cervicogenic headache

The role of musculoskeletal system in the Pathophysiology of cervicogenic headache has been discussed in many studies [Andersen, et al, 2003] [Bansevicius, et al, 1999]. Electromyography (EMG) activity recorded over a trapezius with surface electrodes was significantly higher on the symptomatic side compared to the non – symptomatic side before and during a mental stress test in cervicogenic patients. Side differences in EMG activity could not be registered in the temporal muscles, although pain was significantly more severe on the symptomatic side. This can be explained by referred pain mechanisms in the temporal region and a more direct involvement of the shoulder and neck muscles in cervicogenic headache. It is not known whether the difference in trapezius EMG response between the symptomatic and non – symptomatic side in cervicogenic headache patients contribute to the pathogenesis of cervicogenic headache or if it is a secondary phenomena [Andersen, et al, 2003].

Skin and connective tissue changes in cervicogenic headache

Skin fold tenderness and thickness have also been measured in cervicogenic headache, tension type headache and migraine without aura. Significant asymmetry in skin – fold tenderness was found only in the cervicogenic group and side differences were limited to the trapezius region [Bansevicius, Pareja, 1998].

1.6.2. Clinical features

Common characteristics:

- Cervical headache is often associated with neck pain or stiffness and may be aggravated or occurring during neck or head movements.
- Pain may be of lower intensity when the patient lies down, but it tends to be present regardless of the position the patient assumes.
- Paroxysmal in character, with intervals of pain sequences [Brukner, Khan, et al, 2007].
- Unfavourable position during sleep and poor posture. This may be seen as a contributing factor or as an effect of headache. The abnormal posture typically seen with cervical headache is rounded shoulders, ante - flexion and extended neck position with protruded chin.
- Muscular imbalances such as; tightness of the upper cervical extensor muscles and weakness of the cervical flexor muscles [Kendall, et al, 2005].
- Restricted mobility of the scalp against skull is a typical soft tissue lesion, seen in headache disorders. It is linked to similar changes of the cervical fascia. It is rapidly palpated and easy to treat.
- Decreased range of head movement, except into extension.
- Asymmetry due to one side cervical origin.
- Ipsilateral shoulder or arm pain.
- Muscle spasms, faulty respiration and segmental abnormalities at cervico - cranial junction [Lewit, 1999].
- Feeling of light – headedness, dizziness and tinnitus.
- Nausea may be present but vomiting is rare.
- The patient often complains of impaired concentration, inability to function normally and depression.
- Psychological role
- Endocrinology factors
- Allergic factors [Sjaastad, Fredriksen, et al, 1998] [Hall, Robinson, 2004].

Headache is the first sign of disturbed cervical function, even, long before neck pain has been felt [Lewit, 1999]. A cervical headache is typically described as a constant, steady, dull ache, often unilaterally but sometimes bilateral. The patient describes a pulling or gripping feeling or,

alternatively, may describe a tight band around the head. The headache is usually in the sub occipital region and is commonly referred to the frontal, retro – orbital or temporal regions [Brukner, Khan, et al, 2007] [Sjaastad, Fredriksen, et al, 1998].

The referred pain to the face is commonly from trigger points in sternocleidomastoid muscle [Travell, 1981]. Typical sign of cervical headache is when the patient complains of pain radiating from the neck into the occipital and from there towards the eyes and temples, more to one side than the other [Lewit, 1999].

Cervical headache is usually of gradual onset. The patient often wakes with headache that may improve during the day. It may also be present for days, weeks or even months. There may be a history of acute trauma, such as whiplash injury sustained in a motor accident, or repetitive trauma associated with work or sporting activity [Brukner, Khan, et al, 2007].

Typical pain points:

- Lateral surface of spinous process of axis, more frequently on right
- Posterior arch of atlas, in the short extensors
- Transverse process of atlas and in sternocleidomastoid (SCM)
- Occipital pain points of atypical localization on the skull
- Temple in the temporal muscle
- Other masticator muscles
- Notch of the first division of the trigeminal nerve at the orbit [Lewit, 1999] [Aprill, et al, 2002].

Localization of hyperalgetic zones (HAZ):

- Medially below mastoid process
- At the temples and eyebrows
- Forehead above eyebrows
- Both sides of the nose [Lewit, 1999].

Stress is often associated with cervical headache. And it may be an important contributing factor to the development of the soft tissue abnormalities causing the headache or may aggravate abnormalities already present [Brukner, Khan, et al, 2007].

If pain is present as the person wakes up, we must think about the sleeping position [Lewit, 1999]. The patient should use a pillow that allows a comfortable position of the neck. It is not recommended to sleep without a pillow, because the head will drop back in extension of the neck. Then again, a too high pillow should be discouraged, because it can result in an increased forward – head position. A home – made pillow can provide the needed comfort and keep the neck in good position. A pillow that is flattened in the centre will provide support both posterior and lateral [Kendall, et al, 2005].

1.6.3. Neuroanatomy cervicogenic headache

The neuroanatomical basis for the cervicogenic headache is the "trigemino-cervical nucleus" in the spinal grey matter of the spinal cord at the $C_1 – C_3$ level. It exist a convergence on the nociceptive second order neurons receiving both trigeminal and cervical input. C_1 spinal nerve has some ectopic sensory ganglia and it innervates the short muscles of the suboccipital triangle [Bogduk, 1982]. The C_2 spinal nerve gives sensory supply to the median and lateral atlantoaxial joints; to several neck muscles (paravertebral, sternocleidomastoid, trapezius, semispinalis and splenius muscles); to the dura of the posterior cranial fossa and the upper spinal canal. Both the C_2 and C_3 spinal nerves supply the zygapophyseal joints and discs of the adjacent segments. The atlantoaxial ligaments and the dura mater of the spinal canal are innervated by the sinuvertebral nerves stemming from the $C_1 – C_3$ spinal nerves. The origin is sympathetic, the nerves contain nociceptive, proprioceptive, vasomotor and vaso – sensory fibres [Mendel, et al, 1992].

Inter - vertebral discs at the $C_2 – C_3$ and $C_3 – C_4$ levels have been the target of neurosurgical treatment of cervicogenic headache. Several cervical structures, such as cervical muscles and their attachments to the bone; as well as the capsule of the inter - vertebral joints and discs, ligaments, nerves and nerve roots are thought to be pain generating candidates in cervicogenic headache [Pøllman, et al,1997] [Jansen, et al, 1989]. Nociceptive stimuli from these structures are primarily mediated by the upper three spinal nerves. The greater occipital, the lesser or minor occipital, the third occipital and the greater auricular nerve have been implicated in the cervicogenic headache [Pøllman, 1997]. Nerve vessel compression on the C_2 root, where the ventral ramus cross the upper cervical segment of the vertebral artery, was hypothesized as a cause for cervicogenic headache [Lucas, 1994].

The morphological evidence for the compression of the upper cervical roots as a cause of cervicogenic headache is only indirect, but the applied methods are too crude to exclude its presence [Andersen, et al, 2003].

The trigeminocervical nucleus

There is a neurological link between the upper cervical nerves and the sensory fibres of the trigeminal nerve, which receives nociceptive information from the face and other pain sensitive structures in the head. As the upper three cervical nerves enter the dorsal columns, via the dorsal root ganglion, their fibres synapse with the descending fibres of the spinal trigeminal nucleus which descends within the spinal cord caudally to the level of C3 (table 1.2).

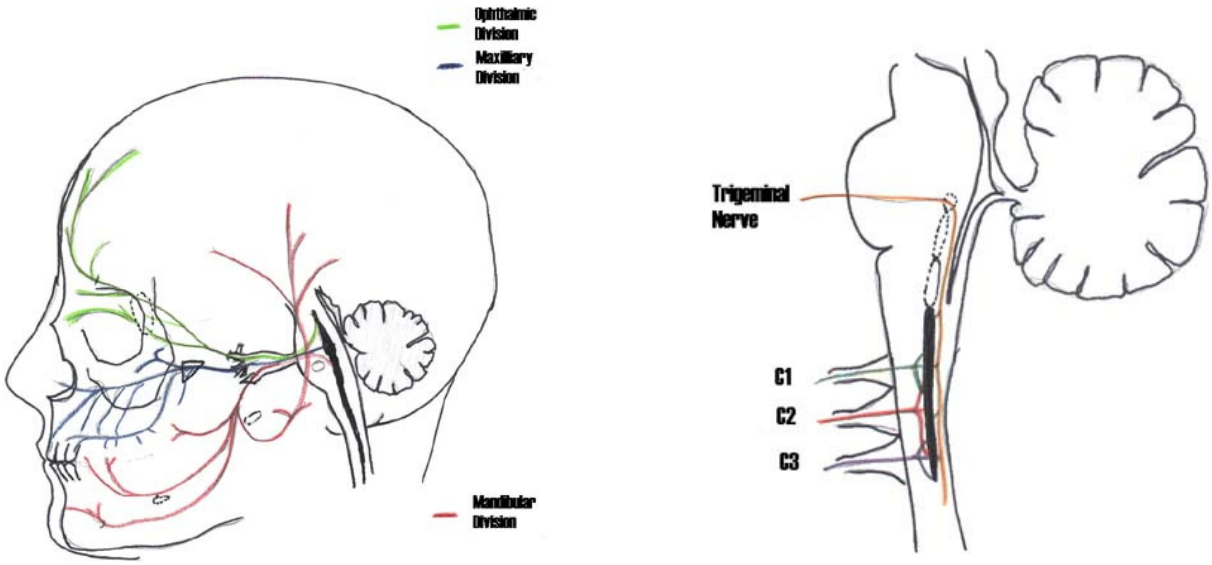


Figure 1.2 Trigeminocervical nucleuses [Bogduk, 1994]

The intermingled impulses then travel up to the cortex of the brain. The cortex is unable to distinguish the precise area from which the impulses arose, so information from the C1-C3 neck structures is indiscernible from trigeminal impulses. In other words there is the classic neurological condition of ‘referred pain’. The trigeminocervical nucleus incorporates the marginal zone, the substantia gelatinosa and the nucleus proprius of the grey matter of the

cervical spinal cord and the homologous divisions of the trigeminal nucleus. In both the cord and the trigeminal nucleus, these areas are the main centres involved in the transmission of nociceptive information, i.e. pain. Therefore the trigeminocervical nucleus can be viewed as the nociceptive nucleus for the entire head and neck [Bogduk, 1994].

Occipital nerve interactions

We find two occipital nerves, the greater and the lesser occipital nerve:

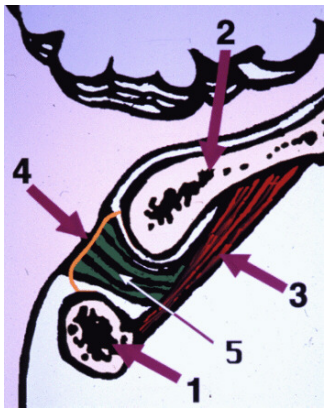
a) Greater occipital nerve: arises from the medial branch of the dorsal ramus between the first and second cervical nerve. It emerges from the suboccipital triangle, which is bounded by three muscles; rectus capitis posterior major, obluquus capitis superior and inferior. It then ascends obliquely between the inferior oblique and semispianlis capitis muscle. Passing through the trapezius muscle. The greater occipital nerve is mainly cutaneous and innervates the scalp at the top of the head, over the ears, and over the parotid glands.

b) Lesser occipital nerve: arises from the lateral branch of the ventral ramus of the second cervical nerve or from the loop between the second and third cervical nerves. It curves around and ascends along the posterior border of the SCM. It perforates the deep fascia near the cranium, and continues along the side of the head behind the auricle. Here it supplies the skin and communicates with the greater occipital, the great auricle, and the posterior auricular branch of the facial nerve. The smaller occipital varies in size, and is sometimes duplicated. Giving of an auricular branch that communicates with the mastoid branch of the great auricular. And this branch in sometimes derived from the great occipital nerve. Lesser occipital nerve innervates the scalp especially in the lateral area of the head behind the ears. [Moore, Dalley, 2006]

The location of pain is related to the areas supplied by the occipital nerve. The sensation of pain is caused by irritation or injury to the nerves. Irritation or injury of greater or lesser occipital nerve is considered to be one of the possible causes of cervicogenic headache, also referred to as occipital neuralgias. Irritation or injury by means of musculoskeletal involvement in particular has the ability of affecting vascular and nervous tissue. Musculoskeletal interactions are typical results from trauma to the back of the head or pinching of nerves by overly tight neck

muscles. Frequent lengthy periods of keeping the head in a downward and forward position are also associated with occipital neuralgia [Porth, 2005].

Rectus capitis posterior minor and dura mater



There exists an anatomical connection between a deep occipital-cervical muscle, the rectus capitis posterior minor and the dura mater. Rectus capitis posterior minor is a muscle located deep in the suboccipital region. It arises from the tubercle on the posterior arch of the atlas, widening as it ascends, it is inserted into the medial part of the inferior nuchal line of the occipital bone and the surface between it and the foramen magnum, and some to the spinal dura.

Picture 1.1 Illustration of atlas (1), occipital bone (2), rectus capitis posterior minor (3), spinal dura mater (4) and the muscle – dural bridge (5) [Hack, et al, 1995].

The image above shows a connective tissue bridge between the rectus capitis posterior minor muscle and the dorsal aspect of the spinal dura mater at the atlantio - occipital junction. The fibres of the muscle – dural bridge is oriented primarily perpendicular to the dura. This arrangement of fibres appears to resist movement of the dura toward the spinal cord. It has been speculated that the function of the muscle – dural bridge may be to prevent folding of the dura mater during hyperextension of the neck. Also, clinical evidence suggests that the muscle – dural bridge may play an important role in the pathogenesis of the cervicogenic headaches. Anatomic structures innervated by the cervical nerves C1 – C3 have the potential to cause headache pain. Included are the joint complexes of the upper 3 cervical segments, the dura mater, and the spinal cord. The dura-muscular, dura - ligamentous connections in the upper cervical spine and occipital areas may be the anatomic and physiologic reasons to the cause of the cervicogenic headache. [Hack, et al, 1995].

1.6.4. The cervicocranial syndrome

Professor Karel Lewit defines the syndrome as a lesion of the upper cervical spine [Lewit, 1999]. The term cervicocranial, involves the cervical region, specifically the atlantoaxial segment; the upper two segments of the cervical spine [Moore, Dalley, 2006]. The cervico - cranial

junction is often involved when lesions or abnormal tissue, is found on or in the upper cervical spine. The cervico - cranial syndrome covers headache of:

- Cervical origin
- Equilibrium origin
- Minor neurological disorders; cervical nystagmus

During abnormalities of lower cervical spine, the pain originates in upper extremities. Musculatures such as sternocleidomastoid, scalene, trapezius, and levator scapulae, may react to lesions at any segment of the c – spine. Reaction of the nervous system determines weather the patient will suffer only from pain in the neck, or in the shoulder or arm, or mainly from headache, although the same disturbances of function may underlie them all [Lewit, 1999] [Aprill, et al, 2002].

Headache of cervical origin is the most frequent and commonest single type of headache. Serious pathology must be ruled out, thus, headache of cervical origin have its own characteristic features [Lewit, 1999].

1.6.5. Faulty posture and muscle imbalance

Bad motor patterns and faulty posture is often the result of frequent headaches. Or headaches are the result of faulty posture. Either way, some people with headaches usually have a typical faulty position of head and neck [Kendall, et al, 2005]. The cervical spine is the most mobile section of the whole spine, therefore, also the most vulnerable. The C – spine is richest in proprioceptive nerves, which exercise an effect on the entire locomotors system [Lewit, 2007].

The result of muscle imbalance correlates with the upper cross syndrome. Janda emphasized the importance of muscle balance in function [Janda, et al, 1993]. Proper coordination and synergy is important at the agonist – antagonist – synergist relationship [Murphy, 1999] [Skaggs, 1999]. Alterations of these motor patterns occur in characteristic, predictable patterns (See table 1.6). Deficits in mobility of joints near the cervical spine can impact the function. For example, poor mobility in thoracic region causes compensatory reaction in the cervico – cranial region and/or in gleno – humeral joints [Bullock, et al, 2005] [Liebenson, 2002]. Associations have been shown between decreased thoracic extension mobility and both neck pain [Barton, et al, 1996] and shoulder pain [Lukasiewicz, et al, 1999]. And that thoracic

spine manipulation results in immediate analgesic effects in patients with mechanical neck pain [Cleland, et al, 2005].

Body Part	Postural Fault	Anatomical position of joints	Muscles in Shortened Position	Muscles in Lengthened and Inhibited Position
Head	Chin is too high and the head is protruded forward	Cervical spine hyperextension	Cervical spine extensors. Upper trapezius and levator scapulae	Deep cervical spine flexors.
Arms and shoulders	Protruded and rounded shoulders. Arms rotated inward so that palms face backward.	Scapula abducted and usually elevated	Serratus anterior Pectoralis minor Intercostalis	Middle trapezius Lower trapezius Subscapularis
Chest	Depressed chest and thoracic kyphosis	Thoracic spine flexion and intercostal spaces diminished.	Upper and lateral fibres of internal oblique. Shoulder adductors Pectorals minor Intercostals	Thoracic spine extensors Middle trapezius Lower trapezius Diaphragm (inhibited)

Table 1.6 Alterations of motor patterns occur in predictable patters [Kendall, et al, 2005] [Liebenson, 2006] [Janda, et al, 1993].

Muscle imbalances are not limited to the axial region. The pattern of over – and under – active muscles extends throughout the extremity [Lewit, 1999].

Tightness in the posterior neck muscles gives rise to neck pain and headaches. These symptoms are typically seen in people with a forward head and round upper back. This is a typical compensatory head position that results in an extension of the cervical spine. The faulty condition involves:

- Unnecessary compression posterior on the articulating facets and posterior surfaces of the vertebral bodies.
- Stretch weakness of the anterior vertebral neck flexors.
- Tightness of the neck extensors; upper trapezius, splenius capitis and semispinalis capitis.

We find two headaches which are typically associated with this kind of muscle tightness:

- Occipital headache
- Tension headache [Kendall, et al, 2005].

The greater occipital nerve, which is both sensory and motor, supplies the semispinalis and splenius capitis muscles. Near their attachment to the occipital bone, the nerve pierces the semispinalis capitis and the trapezius. Occipital nerve also innervates the scalp posterior up to the top of the head [Moore, Dalley, 2006].

- In the occipital headache the typical pain and tender areas are:
  - Where the nerve pierces the muscles.
  - In the scalp in the area supplied by the nerve.
- In a tension headache we find faulty postural position of head and neck. An element of stress is also involved, next to the tightness of posterior neck muscles. Therefore we observe intervals of headache, a result of periods with increased and decreased stress. Tight muscles usually respond to treatment that helps these muscles to relax [Kendall, et al, 2005].

Muscle contraction headaches involve symptoms like pain, nausea, vomiting, and blurred vision, but there is no pre - headache syndrome as seen in migraine [Margolis, Moses, 1992]. From another source comes the statement that this forward – head position has been found "to cause an alteration in the rest position of the mandible, upper thoracic respiration with subsequent hyperactivity of the respiratory accessory muscles, and mouth breathing with loss of the rest position of the tongue, and may lead to eventual osteoarthritis and remodelling of the temporomandibular joint" [Ayub, 1984].

1.6.6. Differential diagnosis:

Headache from abnormalities in the cervical region is variable:

- Irritation of the upper cervical nerve roots; due to damage to the atlantoaxial joint or compression of the nerves as they pass through the muscles. Leading to increased neuronal activity in both the cervical and trigeminal neuronal systems [Bartsch, Goadsby, 2002] [Goadsby, et al, 1997].
- Irritation of the lower cervical segments; irritation of the posterior primary rami, which transmits sensation of the spinal portion of the trigemino - cervical nucleus.
- Active trigger points.
- Frontal headaches: trigger points in sub occipital muscles
- Temporal headaches: trigger points in upper trapezius, splenius capitis and cervices, and sternocleidomastoid muscles.
- Poor posture: contributing factor or an effect.
- Stress
- Trauma [Lewit, 2007] [Goodman, Snyder, 2007].

1.6.7. Examination

Examination of the patient with suspected cervical headache involves systematic examination of the joints, muscles and neural structures of the cervical regions as well as assessment of cervical posture. One of the aims of the examination is to reproduce patient's symptoms. A number of abnormalities of different structures may contribute to the patient's pain [Liebenson, 2002]. Common joints abnormalities include stiffness and tenderness over the upper cervical (C 1–2, C 2-3) joints [Lewit, 2007]. Tenderness may be maximal centrally, especially where bilateral pain is present, or unilaterally over the apophyseal joints if unilateral pain is present. Abnormalities of the lower cervical joints are also normal to be present [Brukner, Khan, et al, 2007].

Of the muscles of cervical region, it is common to find tightness in the sub occipital and erector spinal muscles. This is often associated with weakness in the cervical flexors. Active trigger points are frequently present, particularly in the sub occipital, SCM and trapezius muscles [Lewit, 2007].

Deficits in cervical flexor and extensor muscle strength have been documented in patients with cervicogenic headache. The cranial - cervical flexion test (CCFT) assesses deficits in the endurance of the deep neck flexor muscles [Jull, Falla et al, 2004].

A neural component of the patient's headache is suspected if movements that increase neural tension increase the patient's pain [Brukner, Khan, et al, 2007].

1.6.8. Treatment

Physiotherapy has the enormous advantage of being "universally" available and the therapy is harmless. Therefore it is often the first choice of therapy in many headache forms including cervicogenic headache (Jay, et al, 1989). The treatment modalities will necessarily vary, and may also include traction and mobilization. Manual therapy is a matter of course in patients with a possible cervicogenic diagnosis [Inan, et al, 2003]. The same rules count as for any other disturbance of cervical origin. Movement restriction of cervico - cranial junction is so significant, and worth starting with first. Muscular imbalance can not be improved until movement restriction has been removed. Movement restriction between atlas and occipital must be examined in all directions [Lewit, 1999]. Treatments of cervical inter - vertebral joint abnormalities involves mobilization or manipulation of the C 1-2 and C 2-3 joints. Thus, a demand must be that magnetic resonance imaging (MRI) has been carried out prior to treatment and that particular cautiousness is exercised [Inan, et al, 2003].

A faulty head position is usually compensatory to a thoracic kyphosis, which may result from postural deviations of the low back or pelvis. There for must the treatment involve correction of the associated faults. Treatments of the neck involve exercises to strengthen the lower abdominal muscles. A good abdominal support gives the body the ability to assume a better upper back and chest position. [Kendall, et al, 2005]

Treatment requires correction of the abnormalities of joints, muscles and neural structures found on examination as well as correction of any possible precipitating factors such as postural abnormalities or emotional stress. [Brukner, Khan, et al, 2007].

Active treatment consists of heat, massage and stretching. Massage should be gentle and relaxing at first, then progress to deeper kneading. Stretching of the tight muscles must be very

gradual, using both active and assisted movements. Active exercises provided by the patient, involves stretching the posterior neck muscles by efforts to flatten the cervical spine. It may be done in lying, sitting, or standing position, but not in prone position. Contraindicated are exercises that hyperextend the cervical spine. [Kendall, et al, 2005]

Soft tissue therapy to the muscles and the fascia of the cervical region is aimed at releasing generally tight muscles and fascia (commonly the cervical extensors). Active trigger points should be treated with spray and stretch techniques or dry needling. [Brukner, Khan, et al, 2007]. Trigger points in muscles and at periostal points of attachment are best treated by post – isometric relaxation. Pain points on the skull are best treated by soft tissue technique or needling. HAZ respond very well to skin stretching. And restricted mobility of the scalp responds to soft – tissue techniques [Lewit, 1999].

Cervical muscle retraining has been shown to be beneficial by itself and in combination with manipulative therapy in reducing the incidence of cervicogenic headache. This includes retraining of the deep cervical flexors, extensors and scapular stabilizers [Jull, Trott, et al, 2002]. Postural retraining is an essential part of treatment. The patient must learn to reduce the amount of cervical extension by retracting the chin [McKenzie, 2006]. Identification and reduction of sources of stress to the patient should be incorporated in the treatment program [Brukner, Khan, et al, 2007].

Chapter II: Etiology and interrelations of migraine headache

2.1. Migraine with psychological and hormonal changes

Migraine is a common and often disabling neurovascular disorder [Bigal, et al, 2006] linked with various medical conditions and psychiatric disorders. Depression, anxiety, and stress related disorder [Peterlin, Ward, 2005] along with; hypertension, obesity and stroke are some of the conditions seen frequently [Peterlin, et al, 2009] [Scher, et al, 2003]. Of the stress related disorders; abuse and post – traumatic stress disorder (PTSD) are shown recently to be associated with migraine [Peterlin, Ward, Lidicker, et al, 2007] [Peterlin Tietjen, Brandes, et al, 2009] [De Leeuw, et al, 2005] [Tietjen, et al, 2007].

The burden of migraine seems to be increasing when psychiatric comorbidities are present, which makes the differential diagnosis more diffuse [Radat, Swendsen, 2004]. Identifying and describing the presence and interaction of psychiatric disorders in migraine patients may help to find the best treatment. For example, B – blockers would be less desirable in a migraineurs with depression, whereas in migraineurs with PTSD migraine [Peterlin, Ward, 2005] [Peterlin, Ward, Lidicker, et al, 2007] [Peterlin Tietjen, Brandes, et al, 2009] [De Leeuw, et al, 2005] [Tietjen, et al, 2007].

There exist many theories why psychiatric comorbidities occur with migraine. One possibility is that psychiatric factors are a rare cause of headaches. On the other hand, mental burden of continuous migraine can lead to various psychiatric dysfunctions. A third theory is that these disorders share the same pathophysiological abnormalities; genetic factors or abnormalities in serotonergic processing and response to estrogen, which can give rise to both conditions [Peterlin, Ward, 2005] [Soares, 2003].

2.1.1. Depression and migraine

Migraine and depression are commonly occurring disorders. Epidemiological studies report a high rate of both disorders in woman [Bigal, et al, 2006]. Depression has been estimated to occur in 12.6 % of woman and 6.3 % of men in the United States [Riolo, et al, 2005]. Numerous studies have demonstrated a higher occurrence of both disorders with each other than could occur just by a chance alone [Breslau, et al, 2000] [Camarda, et al, 2008].

The first general population study to demonstrate an association between migraine and depression was conducted by Merikangas, et al, [Merikangas, et al, 1990]. A group of 457 young Swiss adults between 27 and 28 years were assessed for migraine and various psychiatric conditions. Although neither a brief recurrent depression nor dysthymia had a significant association with migraine, migraineurs did have an increased odd for major depression. This finding was further supported by data from the midlife development in the U.S. survey (MIDUS). They evaluated the associations between several pain and psychiatric disorders, including migraine and depression. Over 3000 U.S. adults between 25 – 74 years old were evaluated. Close to 29 % of subjects with migraine were reported to be depressed compared with 12 % of subjects without migraine [McWilliams, et al, 2004].

The links between migraineurs and depression extend to those migraineurs missing one criteria to fulfil definitive migraine. Patel et al. performed a study on 8579 members of a health alliance plan. The patients with definite migraine had a higher prevalence of depression than controls. The members with a probable migraine also had a higher prevalence of depression [Patel et al, 2004].

Oedegaard et al. performed a study on the general Norwegian population, involving if depression with migraine is stronger in migraineurs with aura compared with those without. Over 49,000 participants were included. Both genders had an increased prevalence of depression compared with those without migraine. And woman migraineurs without aura had a lower likelihood to have depression. Whereas in men there was no particular difference [Oedegaard, et al, 2006]

The same study was further supported by a study performed by Samaan et al. and extended to include male migraineurs with aura. Over 1250 adult participants with recurrent depression were evaluated for probable migraine, a long with migraineurs with and without aura, and compared with 851 controls that had an absence or low liability to anxiety or depression. The participants with recurrent depression had a greater chance of having non - migrainous headache, which grew stronger for those with either probable migraine or migraine without aura, and was greatest in those with migraine with aura [Samaan, et al, 2009].

2.1.2. Anxiety and migraine

Anxiety is a common unipolar mood disorder that has been linked to migraine. In the U.S. the lifetime prevalence rate of anxiety is 28.8 %. The 12 - month prevalence is 18.1% [Kessler,

Berglund, et al, 2005] [Kessler, Chiu, et al, 2005]. Anxiety disorder has a predilection to female, occurring in twice as many women as men [Vesga – Lopez, et al, 2008]. There exist many studies which demonstrate that migraine and anxiety are associated.

Merikangas et al. performed a study, on a general Swiss population survey of 26 and 28 years old, to see if there was any association between migraine and anxiety. They found that in migraineurs, the chance of generalized anxiety disorders (GAD) was increased fivefold times [Merikangas, et al, 1990].

Recently, a similar study of the relationship between migraine and anxiety was performed in a Malaysian case – control study, where 70 participants fulfilled the criteria for migraine and age -, gender -, and race – matched controls were evaluated. A little above 34 % of migraineurs exhibited anxiety traits compared with 16 % of controls. Also, the study revealed that woman migraineurs were more anxious than men migraineurs [Tan, et al, 2007].

There exists a theory that GAD in migraineurs increase with increasing headache frequency. A study with 43, 478 participants from the general Norwegian population also support this relationship between migraine and anxiety [Zwart, et al, 2003].

People with anxiety and other comorbid psychiatric disorders have shown to respond poorer to treatment than those migraineurs without psychiatric comorbidities. People with both migraine and depression, underwent a study, which confirmed less pain relief 2 hours after acute migraine therapy, decreased treatment tolerability, less rapid resumption of activity, and decreased satisfaction with the treatment compared with migraine sufferers without anxiety or depression [Lanteri, et al, 2005].

2.1.3. Abuse, post – traumatic stress disorder and migraine

PTSD has a lifetime prevalence of 8 % in the general population, and has become an increasingly recognized disorder the past years [Peterlin Tietjen, Brandes, et al, 2009]. Also the lifetime prevalence of PTSD is twice as common in women as in men. Especially military combat, along with interpersonal traumas from physical and sexual abuse, is the most common cause of PTSD [Butterfield, et al, 2002].

Migraine can be influenced by different psychological factors; and stress is frequently considered to precipitate, exacerbate and maintain migraine. When a great variety of physical and/or psychological stimuli occurs, stress is a specific adaptive and defensive physiological reaction. The personal reaction depends on the intensity and nature of the stressor, the social

context, and on the subject's ability to appraise and cope with the events. This adds up to the person's threshold of vulnerability [Amery, et al, 1987] [Holm, et al, 1997].

Wacogne et al. performed a study which lasted from September 1997 to January 1999. The aim of the study was to evaluate the stress level in migraine patients attending a specialized centre, compared with a control group of healthy workers. The study involved 2 groups of adults, one of 141 migraineurs and one control group of 109 non – migraineurs. Healthy volunteers matched for age and sex. A stress questionnaire was received to measure level of stress in each patient. The perceived stress questionnaire is a self – assessment instrument of perceived stress [Wacogne, et al, 2003]. Consoli et al. elaborated it for the aim to evaluate daily stress routinely, its impact on health, and to understand the links between stress and disease, especially cardiovascular ones [Consoli, et al, 1997]. The study proved a statistical difference between the migraineurs and the control group. The global stress score was statistically higher in the migraine group than in the control group. The global stress score in migrainous women was higher than in migrainous men, and both are clinically significant. From the results it seems necessary to manage stress to improve the daily life of migraineurs [Wacogne, et al, 2003].

2.1.4. Estrogen and migraine

The hypothesis that the comorbidities of mood disorder (e.g., depression, anxiety) and migraine are linked to estrogen is supported by several lines of evidence (e.g., epidemiological, clinical, basic science studies). It's a fact that migraine and mood disorders occur more in women than in men [Bigal, et al, 2006] [Riolo, et al, 2005]. And during periods of marked hormonal fluctations, the vulnerability to migraine and mood disorders increases in women. During puberty the female predisposition is first shown. With stabilisation during pregnancy, followed by exacerbations 1 week after childbirth, and finally perimenopausal increases that persist to approximately 51 to 55 years of age [Grigoriadis, et al, 2002] [Mac Gregor, 2009]. The hypothesis that estrogens have a role in the pathophysiology of both disorders is a consequence of these associations.

The withdrawal of estrogens has been suggested to play a role in both disorders. Dalton showed in 1959 that at a psychiatric hospital, nearly half the women admitted for various symptoms were admitted immediately before or during menstruation [Dalton, 1959]. In 1972, Somerville suggested that estrogens withdrawal was associated with migraine. And that women are extremely at risk for estrogens withdrawal disorders such as premenstrual dysphoric disorder,

postpartum depression, menstrual related migraine, and postpartum exacerbation of migraine [Weissman, et al, 1996] [Thorpe, et al, 2001].

It exist a complex link between how estrogens is related to mood, stress related disorders and migraine [Denuelle, et al, 2007] [Solomon, et al, 2009]. The focus leans more towards women, but its important to note that estrogens and estrogens receptors are present in both men and women [Denuelle, et al, 2007] [Solomon, et al, 2009] [Walf, et al, 2006]. Estrogens play an important physiological role in both women and men (e.g. organisational effects on developing neurons, activation effects on mature neurons, and modulation of synapse formation). The modulation of neurotropic factors and neuropeptides implicated in both migraine and mood disorders, including neuropeptides Y, corticotrophin – releasing hormone, and the neurotransmitters (serotonin, dopamine and glutamate) is performed by estrogens [Grigoriadis, et al, 2002] [Martin, et al, 2006].

Estrogens and its receptors are highly localized in the hypothalamus. It's the activation of limbic system and hypothalamic – pituitary – adrenal (HPA) axis that is linked to the pathophysiology of mood disorders and migraine in humans [Grigoriadis, et al, 2002] [Martin, et al, 2006]. Animal studies show that high – estrogens females exhibit greater HPA axis responses to an acute stressor relative to males and low – estrogens females. Physiological dose of estradiol, with or without progesterone, gradually decreases the stress – induced activation of frontal cortex, hippocampal, and hypothalamic neurons in response to acute stressors. Estrogen treatment decreases the central stress responsivity, followed by antidepressant and anxiolytic effects and possibly pain modulation [Solomon, et al, 2009].

Migraine, stress – related disorders and unipolar mood disorders (e.g. depression, anxiety) are disproportional prevalent in woman. Several lines of evidence suggest a role for estrogen and its receptors in mood disorders and migraine [Solomon, et al, 2009].

2.1.5. Oral contraceptives and migraine headache

Aggravating a pre – existing headache, or trigger a new onset may be the result of combined oral contraceptives (COC). The most common adverse effect from COC is headache [Loder, et al, 2005]. Thus, it is not clear whether headache exists prior to, or is a consequence of, using COCs.

The international classification of headache disorders identifies two entities relating to the use of COCs. These two are exogenous hormone induced headache and estrogen – withdrawal

headache. From a clinical point of view it's clear that these two headache types are completely different from one another. Other published studies of migraine during COC administration are old fashion and lack a clear description and/or classification of the headaches observed [HCS, 2004].

The major diagnostic criteria for exogenous hormone – induced headache are shown in table 2.1

Exogenous harmonic – induced headache
A. Headache or migraine fulfilling criteria C and D
B. Regular use of exogenous hormones
C. Headache or migraine develops or markedly worsens within 3 months after starting on the exogenous hormones
D. Headache or migraine resolves to its previous pattern within 3 months after total discontinuation of exogenous hormones

Table 2.1 The major diagnostic criteria for exogenous hormone – induced headache [HCS, 2004].

A clinical trial analysis, involving active, untreated, or placebo control group, revealed only small and not all the time significant increase in the activity of headache during early treatment stages. Almost 25 % of woman with aura free migraine report an exacerbation of headache during the use of COC, thus most migrainous woman find that COC use does not change their headache [Mueller, 2000] [Granella, Sances, Pucci, et al, 2000] [MacGregor, Igarashi, et al, 1997]. In migraineurs with aura there is observed an aggravation of symptoms in at least 50 % of these cases [Cupini, et al, 1995] [Granella, et al, 1993].

Granella et al. reported a new onset of headaches in 1.2 % of migraineurs without aura and in 11.4 % of migraineurs with aura [Granella, et al, 1993]. While Cupini et al. reported much higher values, 16.2 % in migraineurs without aura and 22.2 % in migraineurs with aura [Cupini, et al, 1995]. Loder et al. found that a continuing use of COC led to an improvement of the headache state [Loder, et al, 2005]. In some cases there is immediate relief of headache, while in other cases there is a delay of 6 – 12 months where patients reported that migraine persists on a long – term basis [Massiou, et al, 2000].

The headache and COC relationship is complex. There exists a hypothesis that COCs containing lower ethinylestradiol (EE) doses are less likely to provoke headache, since they minimize the magnitude of estrogen withdrawal. A trial with woman on COCs switched to a

lower EE dose and reported no improvement [Grais, et al, 1985] or worsening of headache [Edelman, et al, 1983]. And Sulak et al. assumed that very low estrogen doses may fail to completely suppress ovarian function [Sulak, et al, 2000].

There was recently performed a large population – cross sectional study, where there was no report of any significant effect of estrogen content on migraine prevalence: irrespective of the EE dosage [Aegidius, et al, 2006].

Several studies have been preformed on the different clinical features that may be predictive of a worsening of migraine in COC users. Until now, there is no agreement among authors.

The major diagnostic criteria for estrogen – withdrawal headache are shown in table 2.2

Estrogen – withdrawal headache
A. Headache or migraine fulfilling criteria C and D
B. Daily use of exogenous estrogen for 3 of more weeks, which is interrupted
C. Headache or migraine develops within 5 days after last use of estrogen
D. Headache or migraine resolves within 3 days

Table 2.2 The major diagnostic criteria for estrogen – withdrawal headache [HCS, 2004]

COC users which experience headache may have been exposed to a withdrawal symptom. Cause the migraine headache is more likely to occur during the pill – free week, especially for the long – term users [Sulak, et al, 2000].

The characteristics of the oral contraceptive induced menstrual migraine (OCMM) were described by Allais, et al. to be certain of the clinical characteristics defined by the international classification of headache disorder - second edition (ICHD - II) [Allais, et al, 2008]. In the sample (20 woman suffering from OCMM, average age 32.2 plus minus 7 years, range 22 - 46), all attacks with typical migraine without aura features were of moderate to severe intensity at baseline. Within the first 5 days migraine appeared after cessation of estrogen use in 85 % of cases, which was the same report given by the ICHD - II [HCS, 2004]. In 15 % of cases the attacks were delayed to the sixth or seventh day after cessation of pill (figure 2.1)

Figure 2.1 Distribution of the first day of oral contraceptives – induced menstrual migraine attacks in a selected study population during 7 – day pill suspension [HCS, 2004].

Most of the patients experienced that the headache usually lasted minimum 48 hours in the presence of usual symptomatic drug treatment. Whereas in 3/20 patients the duration of the attack lasted for more than 72 hours. That was considered the upper limit, by the ICHD – II, for migraineurs without aura [HCS, 2004].

Existing criteria are extremely useful, but they do not cover all realities. The lack of epidemiological studies on large female cohorts makes it impossible to define the real incidence and clinical characteristics of this often disabling disease.

2.2 Migraine headache with postural relations

2.2.1. Neck pain in migraine headache

It is documented that migraine is most commonly perceived in the ophthalmic distribution of the trigeminal nerve, thus, there exists a percentage of migraineurs which revile to experience pain in the neck (39.7 %) and occipital region (39.8 %) with their migraine attacks [Kelman, 2005]. In a prospective cohort study they found muscle tension in neck as a secondary cause for increased risk of occurrence of both migraine and headache. The primary predictive value for onset of migraine was menstruation [Wober, et al, 2007].

It's important to differentiate migraine from cervicogenic headache, when discussing neck pain together with migraine. Cervicogenic headache is a disorder characterized as head and facial pain referred from somewhere in the neck region. Reported evidences are mechanical precipitations of an attack and the decreased range of motion in cervical spine [HCS, 2004] [Sjaastad, Bovim, 1991].

Migraineurs with neck pain can be reported either

1. As the initial site of pain that later radiates forward and reaches the point of migraine.
2. As a concomitant site of pain with the acute migraine.
3. Or as a site following the acute migraine phase.

If the neck pain is chronic, migraineurs often reported that it grows in intensity with the acute migraine. It is reported that the neck pain is actually related to the disorder itself, and not only as a co - occurring condition in migraine. Studies have shown that an increase width of neck muscles is present in adolescent migraineurs [Airi, et al, 2008] and that there also exists a difference in the neuromuscular function in the neck [Oksanen, et al, 2008]. Also, in the same age group the neck pain has been found to be associated with uncontrolled headaches that do not respond to analgesics [Laimi, et al, 2007]. Other studies reported that adults with transformed migraine were differentiated from those with episodic migraine by the differences in pain threshold in the neck [Kitaj, Klink, 2005]. Also, neck pain with migraine has been found to predict disability independent of headache characteristics [Ford, et al, 2008].

Nausea is a diagnostic criterion for the migraine disorder, by the International Classification of Headache Disorders [HCS, 2004]. Calhoun, et al. wanted to distinguish the rate

of neck pain compared to nausea in migraineurs. Since there is confirmed an increase of nausea with increasing pain of the attack, they decided to take both symptoms into consideration at the time of migraine treatment to avoid bias. The migraine participants were collected from both the academic headache clinic and from general community. The criteria's involved fibromyalgia, suspected cervicogenic headache, or history of cervical trauma or surgery. The study took place over 8 months in 2008. 234 people were confirmed eligible, and 113 of these completed their study diaries [Calhoun, et al, 2010]. Participant were interviewed and examined by headache medicine specialists, to confirm diagnosis, according with ICHD – II - criteria [HCS, 2004]. By the use of physical examination they wanted to exclude cervicogenic headache and fibromyalgia [Calhoun, et al, 2010].

Migraine details were written down over a period of 1 month and until 6 qualifying migraines had been treated. It's been reported that even a mild pain stage of migraine can be identified by migraineurs [NH – Mak, et al, 2007]. The participants were therefore aloud to treat any attack stage with acute agents, to obtain a balanced distribution. And for each migraine attack they recorded the absence or presence of nausea along with the intensity of headache and neck pain (on a 0 – 3 scale) [Calhoun, et al, 2010].

A statistical analysing system (SAS) was used to obtain all facts. McNemar`s test was use to distinguish the neck pain and nausea frequency. The analytic facts were written on demographic information. Statistically important were the *P* values of less than .05. 13 headaches were excluded from the study, due to poor data. The complete analysis was performed on 773 headaches [Calhoun, et al, 2010].

The average age of the participants was 37.4. In the group there were 94.7 % females and 84 % of them were non – Hispanic white. Average body mass index was 25.7. The frequency of the attacks changes from episodic to chronic migraine. Close to half of the subjects (47.8 %) received headaches on 15 or more days during each month [Calhoun, et al, 2010].

It was recorded 2411 headache days, with 786 of them being migraine days. Most of the migraine attacks were first treated in the moderate pain stage. And the neck pain was recorded more common than nausea, regardless of treatment stage [Calhoun, et al, 2010].

Indifferent of the headache pain intensity at the time of treatment, neck pain was more commonly occurring with migraine than was nausea ($P < .0001$) (table 2.3, figure 2.2)

Stage Treated	Number of migraines treated	Symptoms	Prevalence	Standard error of prevalence	Mc Nemar`s test *P* – value
Mild	212	Neck pain Nausea	0.428 0.175	0.034 0.026	N = 210 *P* < *.0001*
Moderate	395	Neck pain Nausea	0.611 0.357	0.025 0.024	N = 391 *P* < .0001
Severe	166	Neck pain Nausea	0.726 0.484	0.035 0.039	N = 165 *P* < .0001

Table 2.3 Regardless of the intensity of headache pain at time of treatment, neck pain was more prevalent than nausea at time of migraine treatment [Calhoun, et al, 2010].

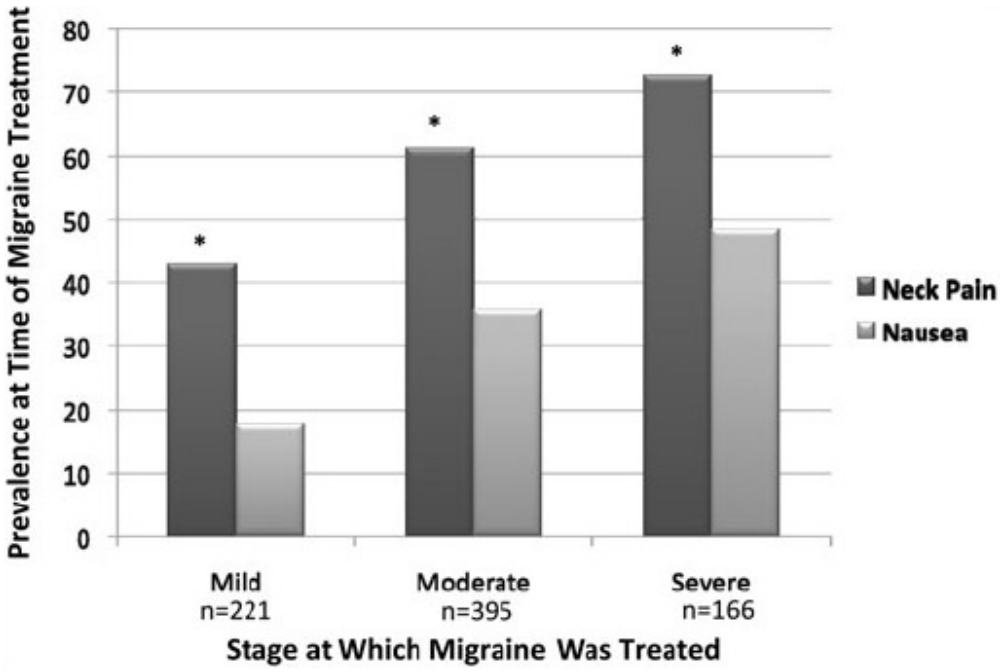


Figure 2.2 Prevalence at time of migraine (* *P* < .0001) [Calhoun, et al, 2010]

The occurrence of neck pain coincided with headache frequency (r = 0.32). Also the nausea coincided with headache frequency (r = 0.29), thus, that coincide was dependent on the participants with greatest headache frequency (Table 2). The correlation was weakened (r = 0.17) as those experiencing headache on 23 or more days a months were excluded from analysis [Calhoun, et al, 2010].

					By subject		By group	
HA Days/month	**No. of subjects**	**No. of migraines treated**	**Subject's average HA days/ month**	**Subject's average NP days/month**				
1 – 8	28	166	6.7	4.2	41.2	24.4	41.6	55.1
9 – 14	28	208	11.0	9.2	54.9	25.3	54.3	53.1
15 – 22	30	211	18.2	14.1	65.7	37.9	66.4	52.6
23 – 30	26	162	27.0	21.0	73.4	48.7	72.2	66.7

Table 2.4 Descriptors for the population, divided into quartiles based on recorded headache frequency [Calhoun, et al, 2010].

A fixed linear correlation with neck pain was constant during the full period of headache frequency (Table 2). Thus, the nausea remained quite consistent, affecting approximately half of all the attacks at the time of migraine treatment, until the frequency of headache was 23 or more days a month. At that point, nausea was present in approximately 2/3 of attacks. An explanation for this association might be that participants with chronic headaches treated at a higher mean level of headache pain (2.16 vs. 1.72) than those with episodic migraine [Calhoun, et al, 2010].

2.2.2. Pain referral patterns

Now and then clinicians meet diagnostic challenges, as the localization and time course of the disease are so diffuse and do not give a single and immediate diagnosis, in patients with headache pain. The topographical establishment is difficult as the pain may be diffuse with dull and burning quality, and the pain may move, radiate, or spread through different innervations territories. Migraine pain is restricted to the first ophthalmic division of the trigeminal nerve. The greater occipital nerve innervates the back head region, which has also been reported as a painful area in migraineurs. The migraine pain therefore extends beyond the trigeminal region and the primary localization of pain may therefore be at the occipital region. Muscle hypersensitivity and tenderness, decreased neck mobility and hyperalgesia are often present during the pain period [Anthony, et al, 1992] [Goadsby, Lipton, Ferrari, 2002].

The trigemino – cervical interaction can explain the clinical presentation, as the trigeminal and cervical afferents converge onto the same neurons in the brainstem. The convergence is a necessary component in the clinical phenomena of spread and pain originating from an affected

tissue is perceived as originating from another not directly innervated receptive field [Ruch, 1965].

Mechanical stimulation of large cranial vessels and of supratentorial dura mater leads to sensation of pain, which is mostly referred to the ophthalmic region [Wolff, 1963] [Penfield, et. al. 1940]. Thus, it may also be perceived in dermatomes supplied by the upper cervical roots [Wirth, et al, 1971]. It was further shown than, painful sensations occurred during stimulation of the trigeminal innervated supratentorial dura mater. Regardless of the stimuli applied [Penfield, et al, 1940]. Which leads to the conclusion that dura mater innervations and afferent input, or processing of dura mater input structures can be the neural substrate of many primary headaches. Structures innervated by the upper cervical roots, like posterior fossa and neck structures, which elicits occipital pain sensation, can also be perceived in trigeminal innervated areas. Although perceived as occipital pain, it may spread to trigeminal areas [Piovesan, et al, 2001] [Fukui, et al, 1996].

The upper three cervical spinal nerves innervate the posterior fossa, the occipital region, and the upper cervical spinal cord. C2 spinal nerve root is the considered to be the major afferent contributor, peripherally represented by the greater occipital nerve (GON) [Becser, et al, 1998] [Poletti, 1991]. Structures such as vessels and dura mater of the posterior fossa, deep paraspinal and suboccipital neck muscles, joints, ligament, and spinal discs are innervated by the upper cervical nerve roots. They are also the established source of pain and may be the sources of pain in cervicogenic headache [Anthony, et al, 1992] [Bogduk, 2001].

The first to suggest a convergence between trigeminal and cervical afferent, were Kerr and Olafson [Kerr, Olafson, 1961]. But only recently it was described in an animal model [Bartsch, Goadsby, 2002] [Bartsch, Goadsby, 2003] and further extended to human data [Piovesan, et al, 2003]. In the C2 dorsal horn there is a population of nociceptive second – order neurons which receives convergent synaptic input from the cervical afferents within the greater occipital nerve and from the trigeminal innervated supratentorial dura mater (Figure 2.3).

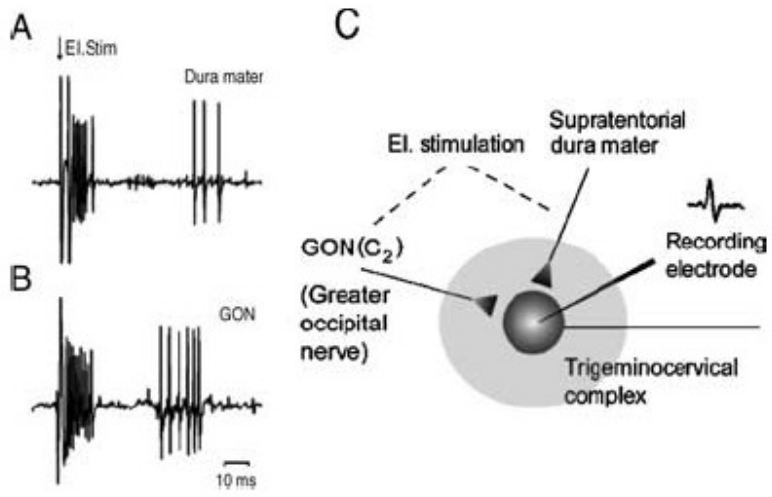


Figure 2.3 The convergence principle in the trigeminocervical complex (TNC) [Bartsch, Goadsby, 2002].

The figure presents the convergence principle in the (TNC). (A) Supratentorial dura mater and (B) GON was electrically stimulated and neural responses recorder in the second – order neurons in the dorsal horn of the TNC (C). A: showed that stimulation of the dura mater resulted in an early latency response in the A – fibre nerve and a late response within the C – fibre nerve range. B: stimulation of the greater occipital nerve showed a – fibre and c – fibre latency responses.

Not only do it exist a convergence on the ipsilateral second – order neuron, GON afferent often receive input from the contralateral GON [Bartsch, Goadsby, 2002]. This will facilitate a spread of pain to the contralateral side, which is commonly seen in headache patients. Dull and poorly localized quality of head and neck pain has alot to do with this anatomical arrangement (Figure 2.4) [Linderoth, et al, 1994].

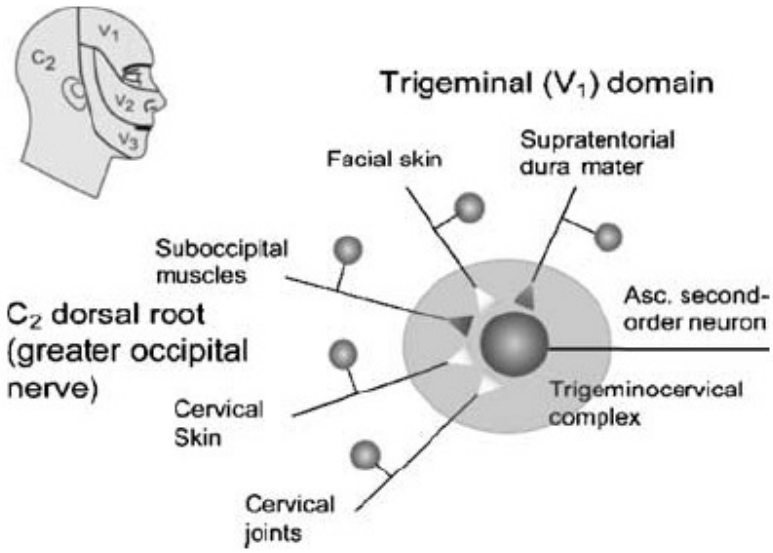


Figure 2.4 Possible sources of headache [Bartsch, et al, 2003]

The figure show possible sources of headache, as various afferent sources from trigeminal and cervical structures converge. Muscle and dural input, marked in grey, are effective in provoking changes in the neural excitability, which may result in spread and referred pain.

Nociceptive input to the central nervous system from the peripheral structures is subject to modulation of different levels of the central nervous system. Periaqueductal gray (PAG), nucleus raphe magnus (NRM,) and rostroventral medulla (RVM) are inhibitory brainstem structures, and they have a special antinociceptive effect [Behbehani, 1995]. Other structures are also involved, such as the hypothalamus, thalamus, and cortical regions. Recent study has had a great focus on the role of the ventrolateral division of the PAG (PAG) in trigeminal nociception. Activity of central trigeminal neurons, which receive nociceptive input from dural and trigeminovascular afferents, are modulated by the stimulation of the ventrolateral PAG [Bartsch, Knight, 2004] [Keay, et al, 1998] [Knight, et al, 2002]. The PAG involvement is confirmed from functional imaging studies in patients which experience sudden attacks of migraine without aura. This proves that the PAG has a specific role in the pathophysiology of migraine [Weiller, et al, 1995] [Bahra, et al, 2001].

2.2.3. Vascular changes related to migraine

The migraine attacks and the blood pressure changes are controversial. Studies have reported an association between migraine and hypertension, [Cooper, et al, 1989] [Pietrini, et al, 2005] while others have found no such association. The first study, using IHS criteria for classification of headache, found hypertension of 11 % in 974 subjects [Krogh – Rasmussen, et al, 1992]. Some studies report an association between migraine and elevated blood pressure, stroke, epilepsy, and psychiatric disorders [Breslau, Rasmussen, 2001]. During a migraine attack it's also been observed autonomic dysfunction accompanied by activation of contralateral locus cereleus, dorsal pontine area, and dorsal raphe nucleus [Leone, et al, 2007].

Hypertension and migraine are common diseases, and can be found together in 10 % to 20 % of the population. Secil, et al. underwent a study evaluating hypertensive and hypotensive changes in migraine patients. They found no statistically significant difference between systolic and diastolic values, which was obtained before, during the peak level, and one hour after the end of the attack. Even though there was no difference in diastolic hypotension values, diastolic hypotensive values were detected in a considerable number of patients. Also, there were no statistically significantly differences between systolic and diastolic blood pressure values, between males and females, when the absence or presence of aura was considered [Secil, et al, 2010].

2.2.4. Psychosomatic migraine headache

It has been documented that depression and musculoskeletal symptoms are closely related, even mutually predictive to each other [Magni, et al, 1994]. Also there has been reported that non-specific musculoskeletal symptoms are common in patients with depression [Fava, 2002]. Musculoskeletal symptoms and headache are closely related. And later studies have documented a positive association between headache and musculoskeletal discomfort in the upper body [Hagen, et al, 2002]. Migraine was long considered to be a type of vascular headache, whereas now it has also been found to be associated with several musculoskeletal symptoms, such as muscle tightness or soreness in the neck, shoulders, or back [Hagen, et al, 2002] [Maizels, Burchette, 2004].

The most commonly studied type of headache associated with depression is migraine [Breslau, Lipton, Stewart, et al, 2003], and it is not unusual in patients with major depressive disorders (MDD) [Hung, et al, 2006]. Previous studies of somatic symptoms in MDD patients

have rarely focused on the impact of migraine. Moreover, few studies have examined depression, anxiety, migraine, and musculoskeletal symptoms at once [Mongini, et al, 2004].

The diagnostic and statistical manual of mental disorders (DSM) list muscle tension as one criterion for the diagnosis of GAD, [American psychiatric association, 2000]. One reported study focused on self – reported muscle tension (SMT) in patients with MDD. Increased muscle tension is related to some painful symptoms [Merskey, 1999]. Von Knorring et al. reported that at least some of the pain in patients with MDD, have some relation to increased muscle tension [Von Knorring, et al, 1983]. An increase in muscle tension might therefore be one of the important factors related to general musculoskeletal discomfort or pain in MDD. And previous studies which have investigated somatic symptoms in patients with MDD have rarely focused on this symptom. Thus, one previous study demonstrated that migraine had negative impacts on physical dimensions of quality of life, especially on bodily pain [Hung, et al, 2006]. And increased muscle tension can have something to do with pain in patients with depression [Von Knorring, et al, 1983] [Merskey, 1999]. Further on, migraine and headache are associated with musculoskeletal symptoms such as muscle tightness [Hagen, et al, 2002] [Maizels, Burchette, 2004]. Hung et al. performed a study on the hypothesis that migraine and headache intensity might be important factors related to SMT in depression patients. Simultaneously they also investigated the impact of migraine, comorbid anxiety, and headache intensity on SMT in patients with MDD, due to the close relationship among depression, anxiety, migraine and musculoskeletal symptoms. There study proved that both migraine and increased headache intensity are two important independent predictors of increased self reported muscle tension in patients with depression [Hung, et al, 2008].

2.2.5. The importance of physiotherapy in migraine headache

Physical treatment along with manual therapy of the spine and soft tissue massages, are evaluated as recommended for the treatment of migraine as a prophylactic therapy. Both the experience provided in the practise and theoretical research support the importance of physical therapy. Thus, the existing data or facts on the different kind of therapies are quite poor. On behalf of the well known studies is it not easy to evaluate if these therapies are effective or not. The lack of well – designed prospective, randomized controlled trials with a sufficiently long follow – up to observe these therapies. There exists a great acceptance of physical therapy on one hand and a great opinion about drug treatment on the other. Due to this, these types of therapies

may be an alternative option for some patients if the effectiveness of the therapy is well clear. An analysis of the cost benefits of these therapies should evaluate the long amount of time required for them compared with drug intake [Gaul, Busch, 2009].

Chapter III: Discussion

From several studies performed by different researchers it is clear that psychological disorders (e.g. stress and anxiety) are higher in migraineurs than compared with non – migraineurs. Depression on the other hand is not so much associated with migraine. Depression is usually more present with tension – type headache [Stronks, Tulen, et al, 1999]. This may indicate that when depression occurs in migraineurs it is more likely to be a consequence than a cause [Breslau, 1998].

Migraineurs have a more intensive stress response compared with non – migraineurs. And for many patients, stress is underlined as one of the most common trigger factors with the menstrual cycle. Also, it's estimated that stress is an elementary factor in the triggering and duration of migraine attacks. Stress seems to influence the course of migraine disease, it leads to relapses, or reappearances of attacks so that an effective drug treatment becomes ineffective [Amery, et al, 1987]. Stress influences migraine negatively, and the recurrence of migraine attacks can lead to production of stress in the end and affect the quality of life. Thus, the impact of migraine on the quality of life will indeed depend on the severity of the disease, how the patient handles it and by the environment [Fanciulllacci, et al, 1998].

Migraine constitutes an important social handicap which has received a lot of attention from medical professional and health economics. Migraine patients seem to have a greater emotional stress response; where stress is considered a trigger factor of migraine attacks. It influences the quality of life and the general well – being of migraine patients. Therefore it's necessary to handle stress to improve the daily life of migraineurs. One should try to exclude situations of conflict or aggression, and also influence factors increasing anxiety. The goal is to achieve stability for the patient, and to avoid the anxious anticipation of the next attack [Wacogne, et al, 2003].

Neck muscle tenderness during migraine has been shown not to be reflective of generalized cranial tenderness, but rather, specifically related to muscle hyperesthesia, including sternocleidomastoid, suboccipital, and temporalis [Fernandez – De – Las – Penas, Cuadrado, et al, 2008]. This suggests spread and referral of pain via trigemino – cervical interaction, resulting in hyperalgesia and allodynia. Potential mechanisms include convergence of trigeminocervical afferents or central sensitizations [Calhoun, et al, 2010].

The high prevalence of neck pain in migraine and its reported associations with treatment resistance and disability, support the hypothesis that this neck pain may present hyperalgesia or allodynia [Calhoun, et al, 2010].

There exists an integration of input from neck structures and suboccipital neurostimulation in the modulation of migraine pain. Also, it found clear evidence of anatomical and functional coupling between nociceptive dural afferents and cervical afferents in the greater occipital nerve onto neurons in the trigeminocervical complex. These convergent neurons may be sensitized during headache and may be involved in clinical symptoms such as hypersensitivity, spread, and referred pain to trigeminal and cervical dermatomes. This may be the reason for common pain referral patterns in primary and cervicogenic headache disorders [Bartsch, Goadsby, 2005].

Some studies indicate that stimulation of peripheral neural structures, for example the greater occipital nerve, can elicit a pain modulation effect on migraine pain. In the spinal cord there exists a local circuit which may contribute to this modulatory effect. Thus, other studies point to a role of more central pain modulatory structures including the Periaqueductal gray and thalamus [Behbehani, 1995].

There were not found any correlation between hypotension or hypertension and migraine attack. Thus, there does exist conflicting results, the epidemiological evidence remains controversial. Although both hypertension and migraine are very strong occurring disorders in the general population, the relationship between migraine and hypertension is poorly characterized. There is a chance that the same person might have migraine and hypertension by coincidence [Mathew, 1999].

One hypothesis can be that the pathophysiological mechanisms which are involved during migraine, which are still largely unknown, could lead to a decrease in blood pressure. During a migraine attack there is a substance release of especially calcitonin gene – related peptide, which is a primary vasodilator. The peptide can contribute to diastolic and systolic hypotension during the entire attack. Also, the amygdale, hypothalamus and medullar cranial nerves nuclei are possible causes of autonomic manifestations. The physiological link between migraine and autonomic dysfunction has also been suggested to occur in the periaqueductal gray substance (ventrolateral region) and hypothalamus [Juhasz, Zsombok, Modos, et al, 2003].

Migraine comorbidities are associated with increased self reported muscle tension in different body parts in patients with depression. And this association is independent of age, gender, depression severity, and other anxiety comorbidities. Some studies have reported a link between migraine headache and musculoskeletal symptoms, but this association has never been reported in patients with major depressive disorders [Maizels, Burchette, 2004] [Terwindt, et al, 2000]. Thus, anxiety or combined anxiety and depression in patients with episodic migraine have an increased chance of receiving muscle tenderness in the head and neck region, which may develop into chronic migraine. Also, depression predicts fibromyalgia, which has symptoms of general muscle tension or soreness, in patients with transformed migraine [Peres, et al, 2001].

Chapter IV: Conclusion

As with migraine, unipolar mood disorders (e.g. depression, anxiety) and stress – related disorders are extremely prevalent in woman. Some data support that migraine and mood disorders are together as one disorder. Further on, several points of evidence report a role of estrogen and its receptors in mood disorders and migraine. This association is complex, thus, it has been linked to modulation of the hypothalamic – pituitary adrenal axis and serotonin. To truly increase our knowledge of the role of estrogen in mood disorders and migraine, basic and clinical researches evaluating these disorders needs to realize the effect of estrogen in both genders, as well as the life – cycle stage and hormonal cycle of woman.

Neck pain is a common and integral feature of migraine. Neck pain is also more commonly associated with migraine than nausea, which is one of the defining symptoms of migraine. A greater awareness of neck pain as an associated characteristic of migraine may improve the clinical diagnosis and have a beneficial impact on time of treatment.

Also, an understanding of the physiological mechanisms of the pain transmission and the trigeminocervical coupling has fundamental implications for the understanding of very common clinical phenomena and may provide a basis for the therapeutic modulation of pain processing.

The relationship between blood pressure and migraine has been controversial. Still of interest, is the increased number of diastolic hypotensive measurements in patients during the attacks of migraine. Thus, large – scale studies examining serial blood pressures during attacks are needed to address the relationship between migraine and hypotension. This can advance our understanding as to the vascular component of migraine attacks as well as systemic end points of migraine attacks.

The findings that concerned a relation between migraine and increased headache intensity as predictors of increased SMT in patient with depression, needs further research support due to the low number if studies concerned with this topic. And the further studies on musculoskeletal discomfort or painful symptoms in major depressive disorder patients should not neglect the impact of migraine.

5. Reference list

A

1. AEGIDIUS, K, SWART, J. A, HAGEN, K, SCHEI, B, STOVNER. L. J, *Oral contraceptives and increased headache prevalence,* (2006), the headache hunt study, Neurology 66: 349 – 353.
2. AILANI, J. J, *Current pain and headache reports: Chronic tension – type headache,* (2009), Vol. 13; page: 479 – 483.
3. AIRI, O, ERKINTALO, M, METSAHONKALA, L., et al, *Neck muscles cross – sectional area in adolescent with and without headache – MRI study,* (2008), Eur j pain. 12: 952 – 959.
4. ALLAIS, G, BUSSONE, G, AIROLA, G, BORGOGNO, P, CASTAGNOLI GABELLARI, I, DE LORENZO, C, et al, *Oral contraceptive – induced menstrual migraine. Clinical aspects and response to frovatriptan,* (2008), Neurol sci 29 (suppl 1): 186 – 190.
5. ALSTADHAUG, K. B, SALVESEN, R, *Migrenesmerte - mekanismer og konsekvenser for behandling,* (2007), Tidsskrift Norsk Lægeforening; 127: 3064-8.
6. AMERICAN PSYCHIATRIC ASSOCIATION, *Diagnostic and statistical manual of mental disorders,* (2000), 4th edition. Text revision. Washington, DC. American psychiatric publishing. Inc. ISBN: 0 – 89042 – 025 – 4.
7. AMERY, W. K, VANDENBERG H. V, *What can precipitate factors teach us about the pathogenesis of migraine?* (1987), Headache 27: 146 – 50.
8. ANDERSEN, N. B, VINGEN, J. V, WESTGARD, R, SAND, T, *Pathophysiology of cervicogenic headache: a review,* (2003), In (ed) Sjaastad, O, Fredriksen, T. A, Giorgio, B., Nappi, G, Cervicogenic Headache: Basic concepts, Smith – Gordon and Co Ltd. 19 – 30.
9. ANNEQUIN, D, TOURNIARE, B, MASSOUI, H, *Migraine and headache in childhood and adolescence,* (2000), Paediatric Clinics of North America 47, 617 – 631.
10. ANTHONY, M. *Headache and the greater occipital nerve,* (1992), Clinical neurol neurosurg, 94(4): 297 – 301.
11. APRILL, C, AXINN, M. J, BOGDUK, N, *Occipital headaches stemming from the lateral atlanto-axial (C1-2) joint,* (2002), Cephalalgia; 22: 15-22.

12. AYUB, E, GLASHEEN – WRAY, M, KRAUS, S, *Head posture*: *a case study of the effects on the rest position of the mandible,* (1984), J Orthopaedic Sports Phys Therapy; 6: 179 – 183.

B

13. BAHRA, A, MATHARU, M. S, BUCHEL, C, FRACKOWIAK, R. S, GOADSBY, P. J, *Brainstem activation specific to migraine headache,* (2001), Lancet; 357 (9261): 1016 – 1017.
14. BANSEVICIUS, D, PAREJA, J. A, *The skin roll test: a diagnostic tool for cervicogenic headache?* (1998), Functional Neurology; 13: 125 – 133.
15. BANSEVICIUS, D, WESTGAARD, R. H, SJAASTAD, O. M, *Tension type headache; pain, fatigue, tension and EMG responses to mental activation,* (1999), Headache; 39: 417 – 425.
16. BARTON, P. M, HAYES, K. C, *Neck flexor muscle strength, and relaxation times in normal subjects and subjects with unilateral neck pain and headache,* (1996) ,Arch Phys Med Rehabilitation, 77: 680 – 687.
17. BARTSCH, T, GOADSBY, P. J, *Anatomy and physiology pf pain referral in primary and cervicogenic headache disorders,* (2005), Headache. 2: 42 – 8.
18. BARTSCH, T, GOADSBY, P. J, *Increased responses in trigeminocervical nociceptive neurons to cervical input after stimulation of the dura mater,* (2003), Brain; 126 (Pt 8): 1801 – 1813.
19. BARTSCH, T, GOADSBY, P. J, *Stimulation of the greater occipital nerve induces increased central excitability of dural afferent input,* (2002) Brain; 125: 149 – 150.
20. BARTSCH, T, GOADSBY, P. J, *The trigeminocervical complex and migraine: Current concepts and synthesis,* (2003), Curr pain headache rep; 7 (5): 371 – 376.
21. BARTSCH, T, KNIGHT, Y. E, GOADSBY, P. J, *Activation of 5 – HT1B/1D receptors in the Periaqueductal grey inhibits meningeal nociception,* (2004), Ann neurol; 56 (3): 371 – 381.
22. BECSER, N, BOVIM, G, SJAASTAD, O, *Extra cranial nerves in the posterior part of the head. Anatomic variations and their possible clinical significance,* (1998), Spine; 23 (13): 1435 – 1441.

23. BEHBEHANI, M. M, *Functional characteristics of the midbrain Periaqueductal gray,* (1995), Prog Neurobiology; 46 (6): 575 – 605.
24. BIGAL, M, LIBERMAN, J. N, LIPTON, R. *Age – dependent prevalence and clinical features of migraine,* (2006), Neurology, 67: 246 – 251.
25. BJÅLIE, J. G, HAUG, E, SAND, O, *Menneske kroppen,* (2001), 4th ed. ISBN: 82 – 00 – 41831 – 6.
26. BOGDUK, N, *Cervicogenic headache: Anatomic basis and pathophysiological mechanisms,* (2001), Curr Pain Headache Rep; 5 (4): 382 – 386.
27. BOGDUK, N, MERSKEY, H, *Classification of chronic pain,* (1994), ISBN - 10: 0931092051
28. BOGDUK, N, *The clinical anatomy of the cervical dorsal rami*, (1982), Spine; 7: 319 – 330.
29. BOVIM, G, *Cervicogenic headache. Studies on clinical, anatomical and different diagnostic factors,* (1993), Thesis. Trondheim University, Norway.
30. BRESLAU, N, LIPTON, R. B, STEWART, W.F., et al, *Comorbidity of migraine and depression: investigating potential etiology and prognosis,* (2003), Neurology. 60: 1308 – 1312.
31. BRESLAU, N, *Psychiatric comorbidity in migraine,* (1998), Cephalalgia. 18: 56 – 61.
32. BRESLAU, N, RASMUSSEN, B. K, *The impact of migraine: epidemiology, risk factors, and co – morbidities,* (2001), Neurology. 56 (Suppl 1): 4 – 12.
33. BRESLAU, N, SCHULTZ, L. R, STEWART, W. F, et al, *Headache and major depression: is the association specific to migraine?* (2000), Neurology, 54: 308 – 314.
34. BRUKNER, P, KHAN, K. et al, *Clinical Sports Medicine,* (2007), (3rd edition). ISBN: 978 0 074715 20 8.
35. BULLOCK, M. P, FOSTER, N. E., WRIGHT, C. C, *Shoulder impingement: the effect of sitting posture on shoulder pain and range of motion.* (2005), Manual therapy, 10: 28 – 37.
36. BUTTERFIELD, M. I, BECKER, M, MARX, C. E, *Post – traumatic stress disorder in woman: current concepts and treatments,* (2002), Curr Psychiatry Rep, 4: 474 – 486.

C

37. CALHOUN, A. H, FORD, S, MILLEN, C, FINKEL, A.G, TRUONG, Y, NIE, Y, *The prevalence of neck pain in migraine,* (2010), Headache. Pmid: 20100298

38. CAMARDA, C, PIPIA, C, TAGLIALAVORI, A, et al, *Comorbidity between depressive symptoms and migraine: preliminary data from the Zabut Aging Project,* (2008), Neuro science, 29: 149 – 1451.
39. CHISHOLM, M. E, CAMPBELL, D. C, *Postpartum postural headache due to superior sagittal sinus thrombosis mistaken for spontaneous intracranial hypotension,* (2001), Can J Anaesthesia; 48: 302 – 4.
40. CLELAND, J. A, CHILDS, J. D, McRAE, M, PALMER, J. A, STOWELL, T. *Immediate effects of thoracic manipulation in patients with neck pain: A randomized clinical trial,* (2005), Manual Therapy, 10: 127 – 35.
41. CONSOLI, S. M, TAINE, P, SZABASON, F, LACOUR, C, METRA P. C, *Development and validation of a perceived stress questionnaire recommended as a follow – up indicator in occupational medicine,* (1997), Encephale, 23: 184 – 193.
42. COOPER, W. D, GLOVER, D. R, HORMBREY, J. M, KIMBER, G. R, *Headache and blood pressure: evidence of a close relationship,* (1989), J hum hypertonus. 3:41 – 44.
43. CUPINI, L. M, MATTEIS, M, TROISI, E, CALABRESI, P, BEMARDI, G, SILVESTRINI, M, *Sex – hormone – related events in migrainous females. A clinical comparative study between migraine with aura and migraine without aura,* (1995), Cephalalgia 15: 140 – 144.

D

44. DALTON, K. *Menstruation and acute psychiatric illnesses,* (1959), BMJ, 34: 148 – 149.
45. DE LEEUW, R, SCHMIDT, J. E, CARLSON, C. R, *Traumatic stressor and post – traumatic stress disorder symptoms in headache patient,* (2005), Headache, 45: 1365 – 1374.
46. DEN NORSKE LEGEHÅNDBOKEN, 2009. ISBN: 978-82-92002-25-4
47. DENUELLE, M, FABRE, N, PAYOUX, P, et al, *Hypothalamic activation in spontaneous migraine attacks,* (2007), Headache, 47: 1418 – 1426.
48. DUNCAN, C. W, WATSON, D. P. B, STEIN, A, et al*, Diagnosis and management of headache in adults; summary of SIGN guideline,* (2008), BMJ; 337: a2329.

E

49. EDELMAN, D. A, KOTHENBEUTEL, R, LEVINSKI, M. J, KELLY, S. E, *Comparative trials of low – dose combined oral contraceptives,* (1983), J reprod med: 28: 195 – 200.

F

50. FANCIULLLACCI, C, ALESSANDRI, M, FANCIULLACCI, M, *The relationship between stress and migraine,* (1998), Funct Neurol. 3: 215 – 23.
51. FASMER, O. B, OEDEGAARD, K. J, *Migrene og psykiske lidelser,* (2004), Tidsskrift Norsk Lægeforening; 124: 2350-3.
52. FAVA, M, *Somatic symptoms, depression, and antidepressant treatment,* (2002), J clinic psychiatry. 63: 305 – 307.
53. FERNANDEZ – DE – LAS – PENAS, C, CUADRADO, M. L, et al, *Side – to side differences in pressure pain thresholds and pericranial muscle tenderness in strictly unilateral migraine,* (2008), Eur J Neruol. 15: 162 – 168.
54. FORD, S, CALHOUN, A, KAHN, K, MANN, J, FINKEL, A, *Predictors of disability in migraineurs referred to a tertiary clinic: Neck pain, headache characteristics, and coping behaviours,* (2008), Headache. 48: 523 – 528.
55. FORSHAW, M, *Understanding Headaches and Migraines,* (2004), ISBN: 978 – 0 – 470 – 84760 – 2.
56. FREDRIKSEN, T. A, FOUGNER, R, TANGERUD, A, SJAASTAD, O, *Cervicogenic headache: radiological investigations concerning head/neck,* (1989), Cephalalgia; 9:139 - 146.
57. FUKUI, S, OHSETO, K, SHIOTANI, M, OHNO, K, KARASAWA, H, NAGANUMA, Y, YUDA, Y, *Referred pain distribution of the cervical zygapophysial joints and cervical dorsal ramie,* (2006), Pain; 68 (1): 79 – 83.

G

58. GAUL, C, BUSCH, V, *Impact of physiotherapy, massages and lymphatic drainage in migraine therapy,* (2009), Schmerz, 23 (4): 347 – 354.
59. GRAIS, A. S, RUSHWAN, H, *A crossover pill study among Sudanese woman,* (1985), Int j gynaecol obsetet 23: 229 – 233.

60. GIFFIN, N. J, RUGGIERO, L, LIPTON, R. B, et al, *A novel approach to the study of premonitory symptoms in migraine using an electronic diary,* (2003), Neurology; 60: 935-40.
61. GOADSBY, P. J, KNIGHT, Y, HOSKIN, K, *Stimulation of the greater occipital nerve increases metabolic activity in the trigeminal nucleus caudalis and cervical dorsal horn of the cat,* (1997), Pain; 73(1): 23 – 28.
62. GOADSBY, P. J, LIPTON, R. B, FERRARI, M. D, *Migraine – current understanding and treatment,* (2002), N Engl J Med, 346: 257 - 270.
63. GOODMAN, C. C, SNYDER, T. E. K, *Differential Diagnosis for Physical Therapists,* (2007), ISBN: 13 – 978 – 0 – 7216 – 0619 – 4.
64. GRANELLA, F, SANCES, G, PUCCI, E, NAPPI, R. E, GHIOTTO, N, NAPPI, G, *Migraine with aura and reproductive life events: a case control study,* (2000), Cephalalgia 20 (8): 701 – 707.
65. GRANELLA, F, SANCES, G, ZANFERRARI, C, COSTA, A, MARTIGNONI, G. C, *Migraines without aura and reproductive life events: a clinical epidemiological study in 1300 woman,* (1993), Headache 33: 385 – 389.
66. GRIGORIADIS, S, KENNEDY, S. H, *Role of estrogen in the treatment of depression,* (2002), Am J Therapeutics, 9: 503 – 509.

H

67. HACK, G. D, KORITZER, R. T, ROBINSON, W. L, HALLGREN, R. C, GREENMAN, P. E, *Anatomic Relation Between the Rectus Capitis Posterior Minor Muscle and the Dura Mater,* (1995), Spine, 20, 23, 2484-2486.
68. HAGEN, K, EINARSEN, C, ZWART, J. A, et al, *The co – occurrence of headache and musculoskeletal symptoms amongst 51,050 adults in Norway,* (2002), Eur J Neurol. 9: 527 – 533.
69. HAGEN, K, *Genetiske aspekter ved migrene,* (2003), Tidsskrift Norsk Lægeforening, 123: 2727-30.
70. HAGEN, K, ZWART, J. A, VATTEN, L, STOVNER, L. J, BOVIM, G, *Prevalence of migraine and non-migrainous headache,* (2000), Head - HUNT - a large population based study. Cephalalgia, 20:900-6.

71. HALL, T, ROBINSON, K, *The flexion-rotation test and active cervical mobility — a comparative measurement study in cervicogenic headache*, (2004), Man Ther, 9:197 -202.
72. HARVEY, R. A, CHAMPE, P. C, *Pharmacology,* (2009), ISBN - 10: 1 – 6054 – 7200 – X
73. HASLAM, R. H. A, *Headaches,* (2004), in BEHRMAN, R. E, KLIEGMAN, R. M, JENSON, H. B, (Eds.), *Nelson textbook of paediatrics* (17th ed., pp. 2012 - 2015). Philadelphia: Elsevier Saunders.
74. HAUG, E, SAND, O, SJAASTAD, Ø. V, *Menneskets fysiologi,* (1997), 4th ed., ISBN: 82 – 00 – 03608 – 1.
75. HEADACHE CLASSIFICATION SUBCOMMITTEE of the HIS, *The international classification of headache disorders,* (2004) ed. 2. *Cephalalgia* 24 (Suppl. 1), 1 – 152.
76. HOLM, J. E, LOKKEN, C, COOK MYERS, T, *Migraine and stress; a daily examination of temporal relationship in woman migraineurs,* (1997), Headache, 37: 553 – 558.
77. HUNG, C. I, et al, *Migraine predicts self - reported muscle tension in patients with major depressive disorders,* (2008), Psychosomatics. 49: 502 – 510.
78. HUNG, C. I, LIU, C. Y, FUH, J. L, et al, *Comorbid migraine is associated with a negative impact on quality of life in patients with major depression,* (2006), Cephalalgia. 26: 26 – 32.

I

79. INAN, L. E, INAN, N, *Conservative treatment in cervicogenic headache,* (2003), In (ed) Sjaastad, O., Fredriksen, T. A., Giorgio, B., Nappi, G. Cervicogenic Headache: Basic concepts, Smith – Gordon and Co Ltd. 101 – 103.
80. INTERNATIONAL HEADACHE SOCIETY, Headache Classification Committee. *Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain,* (1988), *Cephalalgia,* 8 (7S): 1 – 96.

J

81. JANDA, V, *Muscle strength in relation to muscle length, pain and muscle imbalance,* (1993), In Harms – Rindahl K (ed): Muscle strength. New York, Churchill Livingstone.

82. JANSEN, J, BARDOSI, A, HILDEBRANDT, J, LUCKE, A, *Cervicogenic, hemicranial attacks associated with vascular irritation or compression of the cervical nerve root C_2,* (1989), Clinical manifestations and morphological findings. Pain; 9: 203 – 212.
83. JAY, G. W, BRUNSON, J, BRANSON, S. J, *The effectiveness of physical therapy in the treatment of chronic daily headaches,* (1989), Headache; 29: 156 – 162.
84. JUHASZ, G, ZSOMBOK, T, MODOS, E. A, et al, *No – induced migraine attack: strong increase in plasma calcitonin gene – related peptide (CGRP) concentration and negative correlation with platelet serotonin release,* (2003), Pain. 106: 461 – 470.
85. JULL, G. A, FALLA, D, TRELEAVEN, J, et al, *A therapeutic exercise approach for cervical disorders,* In: BOYLING, J. D, JULL, G. A., eds. *Grieves Modern Manual Therapy,* (2004), 3rd ed. edn. Edinburgh: Churchill Livingstone, 451 – 70.
86. JULL, G. A, NIERE, K. R, *The cervical spine and headache.* In: BOYLING, J. D, JULL, G. A, eds. *Grieves Modern Manual Therapy,* (2004) 3rd edn. Edinburgh: Churchill Livingstone, 291 – 310.
87. JULL, G. A, TROTT, P, POTTER, H, et al, *A randomized controlled trial of exercise and manipulative therapy for cervicogenic headache,* (2002), Spine, 27 (17): 1835 – 43.

K

88. KANIECKI, R, *Headache assessment and management,* (2003), Journal of the American Medical Association, 289, 1430 – 1433.
89. KEAY, K. A, BANDLER, R, *Vascular head pain selectively activates ventrolateral periaqueductal grey in the cat,* (1998), Neurosci lett; 245 (1): 58 – 60.
90. KELMAN, L, *Migraine pain location: A tertiary care study of 1283 migraineurs,* (2005), Headache; 45: 1038 – 1047.
91. KENDALL, F. P, MCCREARY, E. K, et al, *Muscles testing and function with posture and pain,* (2005), 5th ed. ISBN: 0 – 7817 – 4780 – 5.
92. KERR, F. W. L, OLAFSON, R. A, *Trigeminal and cervical volleys,* (1961), Arch Neurol; 5: 69 – 76
93. KERR, F. W. L, *Structural relation of the trigeminal spinal tract to upper cervical roots and solitary nucleus in the cat,* (1961), Exp Neurol; 4: 134 – 148.

94. KESSLER, R. C, BERGLUND, P, DEMLER, O, et al, *Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication,* (2005), Arch Gen Psychiatry, 62: 593 – 602.
95. KESSLER, R. C, CHIU, W. T, DEMLER, O, WALTERS, E. E, *Prevalence, severity, and comorbidity of a 12 - month DSM-IV disorders in the National Comorbidity Survey Replication,* (2005), Arch Gen Psychiatry, 62: 617 – 627.
96. KITAJ, M. B, KLINK, M, *Pain thresholds in daily transformed migraine versus episodic migraine headache patients,* (2005), Headache. 45: 992 – 998.
97. KNIGHT, Y. E, BARTSCH, T, KAUBET, T, GOADSBY, P. J, *P/Q – type calcium – channel blockage in the periaqueductal gray facilitates trigeminal nociception: a functional genetic link for migraine?* (2002), J neurosci; 22 (5): RC213.
98. KROGH – RASMUSSEN, B, OLESEN, J, *Symptomatic and non – symptomatic headaches in a general population,* (1992), Neurology. 42: 1225 – 1231.
99. KUNKEL, R. S, *Managing primary headache syndromes,* (2002), Patient Care January 30. [On - line]. Available: www.patient-careonline.com

L

100. LAIMI, K, SALMINEN, J. J, METSAHONKALA, L, et al, *Characteristics of neck pain associated with adolescent headache,* (2007), Cephalalgia. 27: 1244 – 1254.
101. LANTERI – MINET, M, RADAT, F, CHATUARD, M, LUCAS, C, *Anxiety and depression associated with migraine: influence on migraine subjects` disability and quality of life and acute migraine management,* (2005), Pain, 319 – 326.
102. LEONE, M, PROIETTI CECCEHINI, A, MEA, E, CURONE, M, TULLO, V, CASUCCI, G, BONAVITA, V, BUSSONE, G, *Functional neuroimaging and headache pathophysiology: new findings and new prospects,* (2007), Neurol sci. 28 (suppl 2): 108 – 113.
103. LEWIT, K, *Manipulative therapy in rehabilitation of the locomotor system,* (1999), 3rd ed. ISBN: 0 – 7506 – 2964 – 9.
104. LEWIT, K, *Manipulative therapy, Musculoskeletal Medicine,* (2007) 8th ed. ISBN: 9 – 780 – 7020 – 3056 – 7.
105. LIEBENSON, C. S, *Advice for the clinician and patient: Functional reactivation for neck pain patients,* (2002), Journal of bodywork and movement therapies, 6; 1: 59 – 68.

106. LIEBENSON, C, *Rehabilitation of the Spine, A practitioner's Manual,* (2006), 2nd ed. ISBN: 0 – 7817 – 2997 – 1.

107. LINDEROTH, B, BRODIN, E, *"Mirror pain" and indications of bilateral dorsal horn activation in response to unilateral nociception,* (1994), Pain; 58 (2): 277 – 278.

108. LIPTON, R. B, BIGAL, M. E, STEINER, T. J, SILBERSTEIN, S. D, OLESEN, J, *Classification of primary headache,* (2004), Neurology. 63: 427 – 435.

109. LIPTON, R. B, CADY, R. K, O'QUINN, S, HALL, C. B, STEWART, W. F, *Sumatriptan treats the full spectrum of headache in individuals with disabling IHS migraine,* (1999), Headache; 40: 783-91.

110. LIPTON, R. B, STEWART, W. F, STONE, A. M, LAINEZ, M. J. A, SAWYER, J. P. C, *Stratified care vs. step care strategies for migraine,* (2000), the disability in strategies of care (DISC) study: a randomized trial. JAMA; 284: 2599-605.

111. LODER, E. W, BUSE, D. C, GOLUB, J. R, *Headache as a side effect of combination estrogen – progestin oral contraceptives: a systematic review,* (2005), Am J obstet gynecol 193: 636 – 649.

112. LUCAS, G. D. A, LAUDANNA, A, CHOPARD, R. P, RAFAELLI, Jr. E, *Anatomy of the lesser occipital nerve in relation to cervicogenic headache,* (1994), Clinical Anatomy; 7: 90 – 96.

113. LUKASIEWICZ, A. C, McCLURE, P, MICHENER, L, et al, *Comparison of 3 – dimensional scapular position and orientation between subjects with and without shoulder impingement,* (1999), J Orthop Sports Phys Ther, 29: 574 – 586.

114. LU, K. C, CHAO, C. C, WANG, T. L, CHONG, C. F, CHEN, C. C, *A differential diagnosis in postural headache: herniation of a giant posterior fossa arachnoid cyst,* (Feb. 2008), American journal emergency medicine. 26 (2): 247: 1 – 3.

M

115. MACGREGOR, E. A, IGARASHI, H, WILKINSON, M, *Headache and hormones: subjective versus objective assessment,* (1997), Headache Q 8: 126 – 136.

116. MACGREGOR E. A, *Headache and hormonal replacement therapy in the postmenopausal woman,* (2009), Curr Treat Options Neurol, 11: 10 – 17.

117. MAGNI, G, MORESCHI, C, RIGATTI – LUCHINI, S, et al, *Prospective study on the relationship between depressive symptoms and chronic musculoskeletal pain,* (1994), Pain. 56: 289 – 297.
118. MAIZELS, M, BURCHETTE, R, *Somatic symptoms in headache patients: the influence of headache diagnosis, frequency, and comorbidity,* (2004), Headache. 44: 983 – 993.
119. MARGOLIS, S, MOSES, S, eds. *Johns Hopkins Medical Handbook,* (1992), New York: Rebus.
120. MARTELLETTI, P, VAN SUIJLEKOM, H, *Cervicogenic headache: practical approaches to therapy,* (2004), CNS Drugs; 18: 12: 793 – 805.
121. MARTIN, V. T, BEHBEHANI, M, *Ovarian hormones and migraine headache: understanding mechanisms and pathogenesis: part I,* (2006), Headache, 46: 3 – 23.
122. MASSIOU, H, MACGREGOR, E. A, *Evolution and treatment of migraine with oral contraceptives,* (2000), Cephalalgia 20: 170 – 174.
123. MATCHAR, D. B, YOUNG, W. B, ROSENBERG, J. A, et al, *Evidence-based guidelines for migraine headache in the primary care setting: pharmacological management of acute attacks,* (April 25, 2000), http://www.aan.com.
124. MATHEW, N. T, *Migraine and hypertension,* (1999), Cephalalgia. 19 (suppl 25): 17 – 19.
125. MATHEW, N. T, *Pathophysiology, epidemiology, and impact of migraine,* (2001), Clinical Cornerstone 4, 1 – 17.
126. MCCRORY, P, HEYWOOD, J, UGONI, A, *Open label study of intranasal sumatriptan (Imigran) for footballer's headache,* (2005), Br J Sports Med; 39: 552 – 4.
127. MCKENZIE, R. A, *Treat your own neck,* (2006), ISBN: 9780958269216
128. MCWILLIAMS, L. A, GOODWIN, R. D, COX, B. J, *Depression and anxiety associated with three pain conditions: results from a nationally representative sample,* (2004), Pain, 111: 77 – 83
129. MENDEL, T, WINK, C. S, ZIMNY, M. L, *Neural elements in human cervical intervertebral discs,* (1992), Spine; 17: 130 – 135.
130. MERIKANGAS, K. R, ANGST, J, ISLER, H, *Migraine and psychopathology: results of the Zurich Cohort Study of Young Adults,* (1990), Arch Gen Psychiatry, 47: 849 – 853.
131. MERSKEY, H, BOGDUK, N, *Classification of Chronic Pain,* (1994), Seattle, WA: IASP Press: 94 – 5.

132. MERSKEY, H, *Pain and psychological medicine*, (1999), In textbook of pain. 4th edition. Edited by Wall PD. Melzack R. London, UK, Harcourt, 929 – 949.

133. MILLEA, P. J, BRODIE, J. J, *Tension – type headache*, (2002), American Family Physician 66, 797 – 804.

134. MONGINI, F, CICCONE, G, DEREGIBUS, A, et al, *Muscle tenderness in different headache types and its relation to anxiety and depression,* (2004), Pain. 112: 59 – 64.

135. MOORE, K. L, DALLEY, A. F, *Clinically Oriented Anatomy,* (2006), 5th ed. ISBN: 0 – 7817 – 3639 – 0.

136. MUELLER, L, *Predictable of exogenous hormone effect in subgroups of migraineurs,* (2000), Headache 40: 189 – 193.

137. MURPHY, D, *Conservative care of Cervical Spine Disorders,* (1999), McGraw Hill, New York.

N

138. NH – MAK. D. S, CADY, R, CHEN, Y. T, MA, L, BELL, C. F, HU, X. N, *Can migraineurs accurately identify their headaches as "migraine" at attack onset?* (2007), Headache. 47: 645 – 653.

O

139. OEDEGAARD, K. J, NECKELMANN, D, MYKLETUN, A, et al, *Migraine with and without aura: association with depression and anxiety disorder in a population – based study,* (2006), The HUNT study. Cephalalgia, 26: 1 – 6.

140. OKSANEN, A, POYHONEN, T, YLINEN, J. J, et al, *Force production and EMG activity of neck muscles in adolescent headache,* (2008), Disable Rehabil. 30: 231 – 239.

P

141. PATEL, N. V, BIGAL, M. E, KOLODNER, K. B, et al, *Prevalence and impact of migraine and probable migraine in a health plan,* (2004), Neurology, 63: 1432 – 1438.

142. PENFIELD, W, MCNAUGHTON, F, *Dural headache and innervation of the dura mater,* (1940), Arch Neurol Psychiatry; 44: 43 – 75.

143. PERES, M. F. P, YOUNG, W. B, KAUP, A.O, et al, *Fibromyalgia common in patients with transformed migraine,* (2001), Neurology. 57: 1326 – 1328.

144. PETERLIN, B. L, ROSSO, A. L, RAPOPORT, A. M, SCHER, A. I, *Obesity and migraine: the effect of age, gender and adipose tissue distribution,* (2009), Headache in press.
145. PETERLIN, B. L, TIETJEN, G. E, BRANDES, J. L, et al, *Posttraumatic stress disorder i migraine,* (2009), Headache, 49; 541 – 551.
146. PETERLIN, B. L, WARD, T. N, *Neuropsychiatry aspects of migraine,* (2005), Curr Psychiatry Rep, 7: 371 – 375.
147. PETERLIN, B. L, WARD T, LIDICKER, J, et al, *A retrospective, comparative study on the frequency of abuse in migraine and chronic daily headache,* (2007), Headache, 47: 397 – 401.
148. PIETRINI, U, DE LUCA, M, DE SANTIS, G, *Hypertension in hedache patients? A clinical study,* (2005), Acta neurol scand. 112: 259 – 264.
149. PIOVESAN, E. J, KOWACS, P. A, OSHINSKY, M. L, *Convergence of cervical and trigeminal sensory afferents,* (2003), Curr pain headache rep; 7 (5): 377 – 383.
150. PIOVESAN, E. J, KOWACS, P. A, TATSUi, C. E, LANGE, M. C, RIBAS, L.C., WERNECK, L. C, *Referred pain after painful stimulation of the greater occipital nerve in humans,* (2001), Evidence of convergence of cervical afferences on trigeminal nuclei. Cephalalgia; 21 (2): 107 – 109.
151. POLETTI, C. E, *C2 and C3 pain dermatomes in man,* (1991), Cephalalgia; 11 (3): 155 – 159.
152. PORTH, C. M, *Essentials of Pathophysiology,* (2005)**.** ISBN - 10: 0 – 7817 – 7087 – 4
153. PØLLMANN, W, KEIDEL, M, PFAFFENRATH, V, *Headache and the cervical spine. A critical review,* (1997), Cephalalgia; 17: 801 – 816.

R

154. RADAT, F, SWENDSEN, J, *Psychiatric comorbidity in migraine: a review,* (2004), Cephalalgia, 25: 165 – 178.
155. RIOLO, S. A, NGUYEN, T. A, GREDEN, J. F, et al, *Prevelance of depression by race/ethnicity: findings from the National Health and Nutrition Examination Survey III,* (2005), Am J Public health, 95: 998 – 1000.
156. RUCH, T. C, *Pathophysiology of pain,* (1965), In: Ruch TC, Patton, H.D., eds. Physiology and biophysics. Philadelphia. Saunders, 345 – 363.

S

157. SALVESEN, R, *Nyere synspunkter på etiologi og patofysiologi ved migrene,* (1999), Tidsskrift Norsk Lægeforening, 119: 1437-43

158. SAMAAN, Z, FARMER, A. E, CRADDOCK, N, et al, *A case – control study of migraine in recurrent depression,* (2009), Br J Psychiatry in press.

159. SAPER, J. R, *Headache disorders,* (1999). Medical clinics of North America 83, 663 – 670.

160. SCHER, A. I, STEWART, W. F, RICCI, J. A, LITPON, R. B, *Factors associated with the onset and remission of chronic daily headache in a population – based study,* (2003), Pain, 106: 81 – 89

161. SCHURKS, M, *Der Nervenarzt,* (2009), journal, Springer Berlin/Heidelberg, 1433 – 0407 [on-line].

162. SEAMAN, D, *Joint complex dysfunction, a novel term to replace subluxation subluxation complex: etiological and treatment considerations,* (1997), J manipulative phys ther. 20: 634 – 44.

163. SECIL, Y, UNDE, C, BECKMANN, Y. Y, BOZKAYA, Y. T, OZERKAN, F, BASOGLU, M, *Blood pressure changes in migraine patients before, during and after migraine attacks,* (2010), Pmid: 20158621

164. SILBERSTEIN, S. D, *Migraine,* (2004), Lancet; 363: 381-91.

165. SILBERSTEIN, S. D, *Practice parameter: Evidence – based guidelines for migraine headache,* (2000), Neurology 55, 754 – 763.

166. SILBERSTEIN, S. D, YOUNG, W. B, *Migraine aura and prodrome*, (1995), Semin Neurol; 45: 175-82.

167. SILBERSTEIN, S. D, *Migraine symptoms: results of a survey of self-reported migraineurs.* (1995), Headache; 35: 387-96.

168. SILBERSTEIN, S. D, LIPTON, R. B, *Overview of diagnosis and treatment of migraine,* (1994), Neurology; 44: 6-16.

169. SJAASTAD, O, BOVIM, G, *Cervicogenic headache. The differentiation from common migraine. An overview,* (1991), Funct neurol; 6: 93 – 100.

170. SJAASTAD, O, FREDRIKSEN, T, PFAFFENRATH, V, *Cervicogenic headache; diagnostic criteria,* (1998), the cervicogenic Headache International Study Group. Headache; 38(6): 442 – 445.

171. SJAASTAD, O, SALVESEN, R, JANSEN, J, FREDRIKSEN, T. A, *Cervicogenic headache a critical view on pathogenesis,* (1998), Funct Neurol; 1: 7 - 14.

172. SKAGGS, C, *Diagnosis and treatment of Temporomandibular Disorders*, in Murphy D, *Conservative Care of Cervical Spine Disorders,* (1999), McGraw Hill, New York.

173. SNELL, R. S, *Clinical neuroanatomy,* (2006), (6^{th} ed.). ISBN: 0 – 7817 – 5993 – 5.

174. SNOW, V, WEISS, K, WALL, E. M, et al, *Pharmacologic management of acute attacks of migraine and prevention of migraine headache,* (2002), Annals of Internal Medicine 137, 840 – 849.

175. SOARES, C. N, POITRAS, J. R, PROUTY, J, *Effect of reproductive hormones and selective estrogen receptor modulators on mood during menopause,* (2003), Drugs aging, 20: 85 – 100.

176. SOLOMON, M. B, HERMAN, J. P, *Sex differences in psychopathology: of gonads, adrenals and mental illness,* (2009), Physiol Behav, 97: 250 – 258.

177. STEWART, W, STAFFA, J, LIPTON, R, OTTMANN, R, *Familial risk of migraine: a population based study,* (1997), Ann Neurol; 41: 166-72.

178. STRONKS, D. L, TULEN, J. H, et al, *Personality traits and psychological reactions to mental stress of female migraine ptitents,* (1999), Cephalalgia. 19: 566 – 74.

179. SULAK, P. J, SCOW, R. D, PREECE, C, RIGGS, M. W, KUEHL, T. J, *Hormone withdrawal symptoms in oral contraceptive users,* (2000), Obstet gynecol 95: 261 – 266.

T

180. TAN, H. J, SUGANTHI, C, DHACHAYANI, S, et al, *The coexistence of anxiety and depressive personality traits in migraine,* (2007), Singapore Med J, 48: 307 – 310.

181. TEPPER, S. J, RAPOPORT, A, SHEFTELL, F, *The pathophysiology of migraine,* (2001), Neurologist, 7, 279 – 786.

182. TERWINDT, G. M, FERRARI, M. D, TIJHUIS, M, et al, *The impact of migraine on quality of life in the general population,* (2000), The GEM study. Neurology. 55: 624 – 629.

183. THORPE, L, WHITNEY, D. K, KUTCHER, S. P, et al, *Clinical guideline for the treatment of depressive disorders VI. Special population,* (2001), Can J Psychiatry, 46: 63 – 67.

184. TIETJEN, G. E, HERIAL, N. A, HARDGROVE, J, et al, *Migraine comorbidity constellations,* (2007), Headache, 47: 857 – 865.

185. TRAVELL, J, *Identification of myofascial trigger point syndromes: a case of atypical facial neuralgia.* (1981), Archives of Physical Medicine and Rehabilitation.

V

186. VESGA-LOPEZ, O, SCHNEIER, F. R, WANG, S, et al, *Gender differences in generalized anxiety disorder: result from the National Epidemiological Survey on Alcohol and Related Conditions (NESARC),* (2008), J Clin Psychiatry, 69: 1606 – 1616.

187. VON KNORRING, L, PERRIS, C, EISMANN, M, et al, *Pain as a symptom in depressive disorders, I: relationship to diagnostic subgroup and depressive symptomatology,* (1983), Pain. 15: 19 – 26.

W

188. WACOGNE, C, LACOSTE, J. P, GUILLIBERT, E, HUGUES, F. C, LE JEUNNE, C, *Stress, anxiety, depression and migraine,* (2003), Cephalalgia, 23: 451 – 455. London ISSN 0333 – 1024.

189. WALF, A. A, FRYE, C. A, *A review and update of mechanisms of estrogens in the hippocampus and amygdale for anxiety and depression behaviour,* (2006). Neuropsychopharmacology, 31: 1097 – 1111.

190. WEILLER, C, MAY, A, LIMMROTH, V, JUPTNER, M, KAUBE, H, SCHAYCK, R. V, COENEN, H. H, DIENER, H. C, *Brain stem activation in spontaneous human migraine attacks,* (1995), Nat med; 1 (7): 658 – 660.

191. WEISSMAN, M. M, BLAND, R. C, CANINO, G. J, et al, *Cross – national epidemiology of depression and bipolar disorder,* (1996), Jama, 276: 293 - 299.

192. WILLIAMS, B, *Foramen magnum impaction in a case of acro – osteolysis,* (1977*),* Br j surg; 64: 70 – 73.

193. WILLIAMSON, D. H, HARGREAVES, *R. J, Neurogenic inflammation in the context on migraine,* (2001), Microscopy Research and Technique 53, 167 – 178.

194. WIRTH, F. P, JR., VAN BUREN, J. M, *Referral of pain from dural stimulation in man,* (1971), J Neurosurg; 34: (5): 630 – 642.

195. WOBER, C, BRANNATH, W, SCHMIDT, K, et al, *Prospective analysis of factors related to migraine attacks: The pamina study,* (2007), Cephalalgia; 27: 304 – 314.

196. WOLFF, H. G, *Headache and other head pain,* (1948), New York: University Press

197. WOLFF, H, G, *Headache and other head pain,* (1963), New York: Oxford University Press.

198. WOLLAND, A. M, PEDERSEN, B. S, *Migrene og annen hodepine,* (2002), 1st ed. ISBN: 97 8 82 02 21 25 82

199. WORLD HEALTH ORGANIZATION, *The International Classification of Headache Disorders,* (2004), 2nd edition Cephalalgia; 24 suppl 1: 1-160). ISBN: 92 4 15 46 54 9

Y

200. YOUNG, W. B, SILBERSTEIN, S. D, *Paroxysmal headache caused by colloid cyst of the third ventricle: case report and review of the literature,* (1997), Headache; 37: 15 – 20.

Z

201. ZWART, J. A, DYB, G, HAGEN, K, et al, *Depression and anxiety disorders associated with headache frequency,* (2003), The Nord-Trøndelag Study. Eur J Neurol, 10: 147 – 152.

6. Supplements

6.1. Abbreviations

ASA – Acetylsalicylic acid abbreviated

C – Cervical

CCFT – cervicocranial flexion test

COC – Combined oral contraceptives

DNL – Den Norske Legehåndboken

DSM – Diagnostic and statistical manual of mental disorders

EE – Ethinylestradiol

EHF – European headache federation

EMG – Electromyography

GAD – Generalized anxiety disorder

GON – Greater occipital nerve

HAZ – Hyperalgetic zone

HCS – Headache classification subcommittee

HPA – Hypothalamic pituitary adrenal

ICHD – II – International headache classification of headache disorders – second edition

IHS – International headache society

MDD – Major depressive disorders

MIDUS – Midlife development in the U.S. survey

MRI – Magnetic resonance imaging

NRM – Nucleus raphe magnus

NSAID – Non – steroidal anti – inflammatory drugs

OCMM – Oral contraceptive induced menstrual migraine

PAG – Periaqueductal gray

PTSD – Post – traumatic stress disorder

RVM – Rostroventral medulla

SAS – Statistical analysing scale

SCM – Sternocleidomastoid

SMT – Self - reported muscle tension

TNC – Trigeminocervical complex

TTH – Tension type headache

U.S. – United States

WHA – World health alliance

WHO – World health organization