Neuromuscular problems (neck, back, and head pain) are the second most common pain next to viral- and bacterial-induced pain. Pain in the cervical masticatory muscles (head pain) is one of the most common problems for females. In double-blind, randomized studies, the female-to-male ratio is 3-to-1 for chronic pain in most of the major head and neck pathologies. However, the actual number of women seeking care is closer to 10-to-1, or even as high as 15-to-1 for some chronic pain clinics. In 2001, the ratio of females-to-males requesting examination at Raleigh Facial Pain Services was 84% and in 2002 it was 80%. The exact reasons for this predisposition are difficult to research due to its multiple causes—hormonal influences, central sensitization (rewiring), and sympathetic system changes.

Increasingly, research is linking chronic pain to gender. The study of chronic muscle syndromes, such as myofascial pain, jaw joint pathologies,\(^1\) dysfunction,\(^2\) atypical odontalgia,\(^3\) Meniere’s disease,\(^4\) Lupus,\(^5\) burning mouth,\(^6\) and cervical dysfunction,\(^7\) all reveal a strong female predisposition. Some 86% of female chronic pain sufferers in a Swedish study were found to clench or grind their teeth.\(^8\) Tension headache also has a female predominance with 46% of females having frequent tension headache compared to males at 38%.\(^9\) Nearly all the chronic pain syndromes, such as chronic fatigue syndrome, fibromyalgia,\(^10\) and certain malignancies, have a female predominance.\(^11\) Migraines affect 18% of females while only 6% of males.\(^12\) Menstrual migraine is reportedly associated with estrogen fluxes with many of these migraines but typically resolves at menopause.\(^13\)

There are currently three theories for women’s predisposition to pain:

1. Hormonal differences,
2. Rewiring of the nervous system,

**Hormonal Reasons for Pain**

For many years, it has been found that hormone replacement therapy exacerbates migraines.\(^14\) Oral contraceptives change the character and frequency of migraines.\(^15\) In the presence of estrogen, there is a heightened response to neural injury.\(^16\) Mechanical sensitivity of masticatory muscles increases with ovarian hormone fluctuations.\(^17\) In 60% of migraine sufferers, the headache worsens around the premenstrual phase of the menstrual cycle.\(^18\) Fourteen percent of women with migraine experience headache only with the menses.\(^19\) Most women see changes in their headache frequency at puberty and menopause.\(^20\) These numbers provide an obvious relationship between estrogen and chronic pain. Only recently have these pieces of the puzzle about the pathophysiology of women’s hormones and headache relationship begun to make sense.

One of the most fascinating research findings in recent years is the estrogen receptor on the female’s mast cell. This receptor — genetically coded to provide the female with an inflammation enhancement — is absent in men. The mast cell is a storage tanker for many neurogenic chemicals and is the predominant cell in the inflammation process. When the estrogen levels flux and blood levels of estrogen increase, estrogen couples with the mast cell receptor making it more sensitive to an inflammation stimulus and the dumping of its load of neurogenic chemicals.\(^21\) As it does so, neurogenic chemicals are released more quickly, and with greater numbers of mast cells responding. One of the substances released by the
migraines more prevalent in this popula-

tion but the ensuing pain is felt more in-
tensely.

Estrogen and progesterone also induce
increased secretion of prostaglandin,
which inhibits central norepinephrine re-
lease (a nerve messenger in the pain in-
hibitory system), antagonizes morphine
analgesia (rendering pain pills not as ef-
effective), sensitizes pain receptors (more
pain receptors react to same stimulus),
and increases neurogenic inflammation.23

This increase in inflammation and pain in
the female sets the stage for central
nervous system involvement in chronic

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The migraine headache is now thought
to be a neurogenic chemical overload
that reaches toxic levels in the blood stream
going to the brain. The neurogenic chem-
cicals come from a variety of head and neck
structures such as muscle and joint over
use, sinus infections, ear infections, eye
contact with environment, mouth bacter-
ial invasion, and allergies. The main
source of this inflammation stimulus is the
use of jaw and neck muscles for bad pos-
ture, clenching, chewing gum, damaged
joints, bad bite, or tension in the muscles.

When blood levels of neurogenic inflam-
mation chemicals reach a level that the
brain perceives as toxic and threatening
to brain safety, the migraine receptor is
stimulated to cause vasodilation of blood
vessels. This serves to flush toxins away
from the brain. The pain from a migraine
is mostly from the receptors in the blood
vessels that are aggravated due to the
stretching caused by this sudden enlarge-
ment of the blood vessel. Each person’s
migraine generator threshold is set at dif-
f erent levels by genetics. It is believed that
certain females have a lower setting than
others. The neurotransmitter, serotonin,
which has long been associated with the
migraine headache, varies with the plas-
ma levels of estrogen.22 The number of
serotonin receptors available, its binding
capacities, and its functional status are all
associated with estrogen levels.22 Imitrex
is a serotonin mimicking drug used to
abort (stop) migraines once they are in
full swing.

Further complicating the migraine ex-
perience of women is that females exhib-
it greater sensitivity to laboratory pain as
compared to males. Gender differences in
pain sensitivity are not site specific, and
they seem more noticeable in deep sus-
tained pain sensations similar to the pain
of back, neck, and head.24 Not only are
migraines more prevalent in this popula-
pain. An increase in stimulus causes an
increase in reactivity of the pain system oc-
curring each month. PMS is thought to
be nothing more than the side effects of
neurogenic chemicals in blood stream.

Rewiring the Nervous System

Chronic pain has lasting effects on the
pain sensing systems. Constant or recur-
rent pain induces a lowering of the thresh-
old for pain by the pain receptors.26 The
pain system also activates the so-called
’silent nociceptor’ in the dorsal horn. One
of the mechanisms of wind up is by A-beta
fiber glutamate, binding to the AMPA re-
ceptor, activating protein kinase, remov-
ing Magesium plug, allowing C-fiber glu-
mate to bind to NMDA receptors, allow-
ing inflow Calcium, and thereby turning
on these dorsal horn cells for activity.27

These receptors do not normally react to
the environment but, when activated by
pain, are brought into action. The pain
system then reacts to increasingly smaller
and less intense stimuli.

It has been known for years that any in-
crease in stress has no effect on acute pain,
but does increase levels of discomfort for
those with chronic pain. One may stress a
patient that has a toothache or a broken
leg and there is no increase in perceived
pain levels. If one stresses a patient that
has a chronic head or neck pain then there
is a sharp increase in perceived pain levels.
Normal pain fibers (C-fibers) do not react to stress molecules (adrenalin).

Pain causes alpha-1 receptors to be pro-
duced and transported to C-fiber termi-

nals.29 These receptors are sensitive to
adrenalin produced by the sympathetic
system when the body is under stress and
the pain fibers (that usually respond only
to pain stimulus) will now respond to
stress stimulus. This is thought to be a pro-
tective mechanism to help the body avoid
more painful stimulus in order to heal.

The stress system thus gets a direct wiring
on these dorsal horn cells for activity.27

Unfortunately, chronic pain also makes the
muscle pain receptors more sensitive to stress,
anxiety, and depression.29

One enhancement is the sprouting of
nerve fibers which is necessary for heal-
ing, but it also stimulates nerve growth
that is part of enhanced pain reporting.

One enhancement is the sprouting of
sympathetic fibers in the dorsal horn to
connect to pain system nerves (C-fibers).29

The stress system thus gets a direct wiring
to the pain system. This is another reason
why stress has a relationship to chronic
pain but not to acute pain and why touch
and pressure can create pain in chronic
pain patients.

The purpose of the adaptive response
to pain is to limit activity to allow healing,
but when it is over-stimulated; this pain
adaptation becomes part of the pain syn-
drome. It is also hard to limit activity in
the head region due to its importance to
life. The central pain system is affected by
the peripheral adaptive system of the
nervous system. The longer pain is pres-
ent, the more sensitive the pain reporting

**Sympathetic (Stress) Reasons for Pain**
Muscle pathologies such as neck aches,
backaches, and headaches are definitely
more predominant in females. Each of
these muscle-based pathologies shows a
relationship between pain and an increase
in stress. The stress (perceived danger) ac-
tivates the sympathetic system which caus-
es a nerve impulse to travel down the sym-
pathetic pathway (called the gamma ef-
ferent nerve fiber) to muscle.29,31 These
nerve fibers activate muscle spindles to
prepare the muscle to move in response
to perceived danger. Unfortunately, most
stress situations — such as a reckless driv-
er pulling out in front of you and causing
a near collision — do not resolve in a
“fight or flight” muscle movement. Over
prolonged and frequent stimulation, the
muscle spindle becomes damaged and
enlarged and subsequently causes a sus-
tained contraction of the smooth muscle
of the muscle spindle. The over-stimu-
lation of the sympathetic system (protection
system) creates the onus for these dam-
aged smooth muscle fibers and is referred
to as a trigger point. Recent research re-
veals evidence that damaged muscle tis-
sues (trigger points) are muscle spindles
under the control of the sympathetic sys-
tem.32 In one study, sympathetic blocking
agents (phentolyamine) injected into the
trigger point blocked the pain, but the
skeletal blocking agents (curare or botox)
did not block the pain.33

The amount of neurogenic chemicals
in the muscle and the extra workload due
to painful muscle splinting creates the en-
vIRONMENT for damaged muscle fibers.
Muscle pathology is set off by increased
inflammation in muscles during estrogen
fluxes. The pain from increased swelling
and muscle pain causes more muscle con-
traction and an increase in muscle tone.
Trigger points develop which become the
sources of neurogenic stimulation of the
pain system. The inflammation, swelling,
and pain gradually induce less exercise,
poor sleep, and additional pain.

Chronic muscle pathologies such as fi-
bromyalgia, chronic fatigue syndrome,
myofascial pain syndrome, and tension
headache all have trigger points associat-
ed with them. The muscle-based patholo-
gies are difficult to diagnose because they
can refer pain to distant areas. A good ex-
ample of this is a heart attack that feels
like indigestion. These trigger point re-
ferral patterns, outlined by Travell &
Simon,34 are now used in chronic pain di-
agnosis as a way to identify the correct site
of the pain source. Travell & Simon also
make the critical observation that deep
muscle pain is not location-specific in the
brain. In other words, the perceived site
of pain may be different from the actual
source of pain. Travell and Simon’s book
outlines trigger points’ distinct patterns
of referral. For example, the atypical ear-
ache may have referred pain from other
locations and the atypical toothache may
be referred pain from muscles. This is im-
portant in diagnosing women since mus-
cle-based pathologies are more promi-
nent and prevalent in this group.

During over-stimulation of the muscles
in females, it is observed that the sympa-
thetic system is enhanced, more reactive,
and more sustained. The female sympa-
thetic system is enlarged (amygdyla) and more responsive to stimuli. The “lower highway” — the primitive protective system — is enhanced in females that have been subjected to verbal, physical, or sexual abuse. This phenomenon is summed up in the term “emotional hijacking” used by Daniel Goleman in his book *Emotional Intelligence.* The female species seems more prone to taking on the cares of the world, family, society, church, community, and world — especially after they become mothers.

The over-stimulation of the sympatheticic system begins to set the stage for autonomic system imbalance. When one side of the system is dominant, the other is recessive. The parasympathetic system is in charge of life support systems and the sympathetic is in charge of protection. Conservation of resources allows for use of one system more than another. When we over-stimulate the sympatheticic system, the parasympathetic system is suppressed. The longer the perceived danger or stress, the less the life support systems work correctly and eventually sleep and digestive systems begin to malfunction. Slowly, progressively, and insidiously, sleep quality goes down with increase awakening, slower sleep onset, and awakening unrestful. A key goal must be to improve the balance of the autonomic system.

**Summary**

The longer a pain continues, the greater the increase in maladaptation of the nervous system, including sympathetic sprouting, α-Beta fibers connecting to C-fibers, activation of silent pain receptors, Apha-1 receptor production, trigger point development, increased inflammatory chemicals, emotional hijacking, and autonomic system imbalance. The resulting pain precipitates a cascade of less exercise, poor sleep, malabsorption of nutrients, stress, depression, and pain. In this vicious cycle, pain becomes even more stubborn, refractory, and multifaceted — especially given the physiologic predisposition of women. Pain must be treated early and aggressively — especially in women — to avoid deviation into a chronic pain state.

**References**