

Elevated [11C]-D-Deprenyl Uptake in Chronic Whiplash Associated Disorder Suggests Persistent Musculoskeletal Inflammation

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BACKGROUND FROM DAN MURPHY (from prior Article Reviews)

- All pain has an inflammatory component.
- Post-traumatic inflammation is often the consequence of the membrane release of arachidonic acid fat cascading into pro-inflammatory hormone prostaglandin E2 (PGE2). [Therefore omega-6/-3 balancing is an important clinical strategy].
- Inflammation alters the pain threshold and increases pain perception.
- The resolution of inflammation is fibrosis or scar tissue.
- Fibrotic granulation tissue is capable of maintaining an inflammatory response long after the completion of the healing process, a component of chronic pain.
- Tension within the scar granulation tissue initiates remodeling, reducing inflammation. [Supports the need for early persistent mobilization and chiropractic adjustments].

FROM ABSTRACT

There are few diagnostic tools for chronic musculoskeletal pain as structural imaging methods seldom reveal pathological alterations. This is especially true for Whiplash Associated Disorder, for which physical signs of persistent injuries to the neck have yet to be established.

We sought to visualize inflammatory processes in the neck region by means of Positron Emission Tomography (PET) using the tracer 11C-D-deprenyl, a potential marker for inflammation.

Twenty-two patients with enduring pain after a rear impact car accident (Whiplash Associated Disorder grade II [pain and reduced motion but no neurological signs]) and 14 healthy controls were investigated.

Patients displayed significantly elevated tracer uptake in the neck, particularly in regions around the spinous process of the second cervical vertebra. This suggests that whiplash patients have signs of local persistent peripheral tissue inflammation, which may potentially serve as a diagnostic biomarker.

The present investigation demonstrates that painful processes in the periphery can be objectively visualized and quantified with PET and that 11C-D-deprenyl is a promising tracer for these purposes.

KEY POINTS FROM THIS STUDY:

This study used 18 women and 4 men 24-48 years of age with chronic neck pain (between 6 and 24 months) after a car accident involving whiplash trauma.

“All patients reported neck pain, limited range of neck movement and frequent headaches.”

Fourteen matched healthy female control subjects were also investigated. Also, six patients with acute musculoskeletal pain from a sprained ankle were evaluated; they had no current or prior neck pain.

Prior to the PET scan, all participants rated their pain intensity on a visual analogue pain scale (VAS), filled out a pain drawing, and completed the Neck Disability Index (NDI). All participants refrained from analgesics and anti-inflammatory drugs one to three days, and from tobacco, alcohol and caffeine for 12 hours. The DDE was administered intravenously in the arm of each subject.

- 1) “Chronic musculoskeletal pain syndromes are common, cause extensive individual suffering and place a large burden on health care in society. Yet, pain remains notoriously difficult to visualize and diagnose objectively.”
- 2) “The pathophysiology of persistent pain is elusive and there is a great need for ways to visualize and quantify pain mechanisms.”
- 3) A common chronic pain syndrome is Whiplash Associated Disorder (WAD), triggered by a soft tissue injury to the neck caused by a rear end motor vehicle collision or similar trauma.
- 4) In a sub-portion of the population, “whiplash injuries proceed to chronic debilitating pain.” **[Important]**
- 5) The etiology of chronic whiplash pain is not known, and “there is a lack of an objective biomarker for chronic WAD.”
- 6) “Magnetic resonance imaging (MRI) studies of the neck in WAD have indicated structural abnormalities in the deep cervical muscles and ligaments, typically around the uppermost vertebrae.” [references to the alar ligaments].
- 7) “Structural imaging does not capture on-going biological processes; whereas molecular imaging with positron emission tomography (PET) has the potential to visualize such mechanisms.”
- 8) The authors present evidence that a candidate to capture on-going biological processes is a PET tracer for musculoskeletal injuries and inflammation is DDE ([¹¹C]-D-Deprenyl Uptake). Evidence shows that “DDE can be used to visualize chronic inflammatory processes.”

9) "The present study explores if DDE retention is elevated in the neck region in chronic WAD patients as compared to pain free controls. We hypothesized that WAD patients would have an elevated DDE retention in deep neck muscle regions."

10) Chronic whiplash patients had significantly elevated VAS neck pain ratings than subjects in both control groups.

11) "The location of the peak DDE retention was in the fat tissue surrounding the muscle." **[Important]** The site of inflammation "appeared to be localized to adipose tissue surrounding deep cervical muscles." **[Important]** "The tracer retention observed in fatty regions surrounding deep cervical muscle may indicate that adipose tissue is actively involved in the inflammatory process."

12) Peak inflammation was located around the spinous process of C2 in most chronic whiplash patients, and also at the "insertion of rectus capitis posterior major in the occipital bone." Chronic whiplash patients also showed inflammation in these muscles:

- Semispinalis cervicis muscle at C2 [3, UC]
- Oblicus capitis inferior muscle [3, UC]
- Rectus capitis posterior major at occiput [3, UC]
- Rectus capitis posterior major muscle [3, UC]
- Spinous process C2 [2, UC]
- Fat between sternocleidomastoid and levator scapulae [1, UC]
- Nuchal ligament at C2 [1, UC]
- Multifidus muscle at C2 [1, UC]
- Sternocleidomastoid muscle at C1 [1, UC]
- Semispinalis at occipital insertion [1, UC]
- Insertion of sternocleidomastoideus in occipital bone [1, UC]

- Fat between semispinalis capitis and C3 [1, LC]
- Semispinalis cervicis muscle at C7 [1, LC]
- Levator scapulae at C4 [1, LC]
- Semispinalis at C6 [1, LC]
- Splenius capitis muscle at C5 [1, LC]
- Splenius capitis muscle at C5 [1, LC]
- Sternocleidomastoid muscle [1, LC]

[NOTE: Upper cervical (occiput-C2) inflammation findings = 20/27 = 74%]
 [Below C2 inflammation findings = 7/27 = 26%]

13) Moderate inflammation was noted in the cerebellum.
[Important, suggests traumatic brain injury]

14) Patients displayed elevated DDE retention in cervical soft tissue, suggesting that localized chronic inflammation is apparent in many grade II whiplash associated disorder patients.

- 15) "The trend towards a positive correlation between tracer retention and subjective pain ratings also suggests that DDE has may indicate the presence of painful inflammatory processes."
- 16) "Structural MRI studies indicate that WAD patients have high fatty infiltration in the cervical muscles." **[Important]**
- 17) These authors attribute the pro-inflammation findings in chronic whiplash patients to 3 mechanisms:
- A)) Fatty infiltration in the cervical muscles.
 - B)) A change in the type of muscle fibers following injury.
 - C)) Impairments in intramuscular microcirculation.
- 18) These authors also suggest 2 other possible mechanisms for post-traumatic chronic pain syndrome:
- A)) Increased sympathetic noradrenergic outflow. **[Important: there is evidence that the subluxation causes increased sympathetic tone].**
 - B)) An adaptive increase in superoxide dismutase activity (SOD). [Increased because trauma drives inflammation (and pain), inflammation drives increased free radicals, and the body protects itself from free radicals by increasing SOD].
- 19) "Along with inflammation, these alterations in the microstructure and tissue composition of cervical tissue in WAD patients are possible mechanisms which could lead to elevated [11C] D deprenyl retention."
- 20) "Chronic Pain Imaging Using DDE PET and that DDE can be regarded as a promising tracer for these purposes."
- 21) "A large subset of patients with chronic pain after a whiplash injury displayed elevated DDE retention, suggestive of persistent peripheral tissue inflammation."
- 22) "The possibility to visualize and quantify sites of inflammation in chronic pain may be very useful in diagnosis and treatment monitoring."

COMMENTS FROM DAN MURPHY

Clearly, inflammation in the tissues of the upper cervical spine was most prevalent in these chronic patients, indicating the importance of the upper cervical spine in post-traumatic whiplash pain syndrome and the importance of upper cervical spine management for these chronic patients. Also, I believe that anti-inflammatory omega-6/omega-3 balancing is critical in chronic pain management.