

BRAIN ATROPHY WITH CHRONIC PAIN

Call for Enhanced Treatment

By

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Recent studies clearly show that chronic pain unto itself causes brain atrophy and altered neurochemistry and sensory function of the central nervous system.

Introduction

The evidence is in, as unpleasant as it may be.

Chronic pain may produce a loss or atrophy of brain tissue.¹⁻⁸ All practicing physicians and their surrogates and allies must immediately begin understanding the ramifications of this finding. All parties must be educated about this fact and aggressively attempt to prevent brain atrophy in chronic pain patients. While our knowledge about this dire complication and what tools we should employ to prevent and treat it are admittedly meager, we have to begin a new chapter in Practical Pain Management.

The Evidence

In 2004 Apkarian and colleagues at Northwestern University published their initial findings on patients with chronic back pain.¹ By use of brain scans they determined that chronic pain caused brain shrinkage by as much as 11% - equivalent to the amount of gray matter that is lost in 10-20 years of normal aging. The decrease in volume in the prefrontal cortex and the thalamus of the brain was related to the duration of time. Every year of pain appeared to decrease gray matter by 1.3 cubic centimeters. The good news about this study is that the shrinkage was without much neuronal loss suggesting that proper treatment might reverse this portion of the decreased brain matter.

Since this seminal report, a number of investigators from a variety of institutions using a variety of techniques have documented loss of brain tissue in chronic pain patients including those with chronic headaches, fibromyalgia, back pain and irritable bowel syndrome.²⁻⁶ Most of the major studies

involving chronic pain and brain tissue loss are referenced here for readers who wish to explore these findings in greater detail.²⁻⁸

In any discussion or study of chronic pain complications, the question about drugs, particularly opioids, as a causative factor is naturally asked. All the studies noted above had at least some subjects who did not take opioids. To determine whether brain structural changes occur independent of opioids, Buckalew and colleagues at the Universities of Pittsburgh and West Virginia carefully studied a group of older adults with chronic pain who did not take opioids and who had none of these confounding conditions: hypertension, diabetes, major depression disorder, post-traumatic stress disorder, or a previous stroke.⁸ They found essentially the same altered and reduced brain matter as all of the other studies.¹⁻⁷ It is also cogent to point out that long term opioid therapy has not been found to produce significant decreases in neuro-cognitive abilities.^{9,10} In fact, pain relief may improve them.⁹

Not only have scans and magnetic imagery documented the loss of gray matter, a number of other studies complement these studies in that the brains of chronic pain patients have altered neurochemistry and central nervous system processing of input signals such as odors, taste, heat, emotions, and touch.¹¹⁻¹⁶ Studies show that chronic pain patients do not process external stimuli in normal fashion.¹¹ Patients with chronic back pain have altered dopamine and opioid availability in the forebrain.^{17,18} Fibromyalgia patients appear to have a reduction in the receptor availability of dopamine and opioid mu-receptors in parts of the forebrain.^{19,20} In summary it appears that brain neurochemicals important for pain modulation are not responding as they do in healthy individuals.¹¹⁻²⁰

Implications of These Findings

The findings in chronic pain patients of brain tissue loss and altered central nervous system physiology and neurochemistry is a profound discovery that should be known to all physicians. Implications of this discovery are clear. Recently, in an educational document published by the American Academy of Pain Management, Dr. Catherine Bushnell of McGill University in Montreal, who is a principal investigator in many of the studies referenced here stated, "The data suggest that patients should receive treatment as early and as aggressively as possible. The old adage "no pain, no gain" appears to be diametrically opposed to current findings about the impact of pain." She, and possibly some previous fence-sitters, now want to call chronic pain a disease unto itself.

It is now clear that the risk-benefit ratio of aggressive treatment versus moderate treatment which leaves the patient with some degree of constant pain need to be altered. Brain atrophy, and altered brain physiology and neurochemistry now join the risk profile of undertreated chronic pain which currently consists of hypertension, tachycardia, altered adrenal hormone levels, suppression of the immune system, depression, and interference with physical function and activities of daily life. (Table One) It is now abundantly clear that chronic pain, particularly the severe intractable form, is a disease unto itself whose risks, per se, appear to far outweigh those of essentially all medical treatments including high dose opioid therapy.^{9,10}

Clinical Ramifications

A review of the anatomic, physiologic, and neurochemistry studies of chronic pain on the brain clearly suggests that some chronic pain patients will develop clinical syndromes of poor attention span,

cognitive abilities, and possibly dementia.^{1-8,11-18} Is this happening? This author believes this to be the case based on long-term observations of chronic pain patients. Although chronic pain patients, in my experience, seldom admit to a loss of cognitive or mental abilities, they often complain of a poor memory. Is it time that chronic pain patients in treatment be sequentially monitored over time with mental scales such as the "Mini-Mental Exam?" Should we be trying to provide better diets, nutritional supplements, and dementia preventing mental exercises such as crossword puzzles? Perhaps the pain patient who claimed her B-12 shot really helped knew what she was talking about. Can psychologists who specialize in dementia prevention help us? Shown in Table Two are four cases from my personal practice which were undertreated for years before referral to me and who I believe developed mental deterioration. At this point I have a poor understanding of how to diagnose, prevent, or treat mental deterioration in chronic pain patients, but these studies on brain atrophy provide insight into clinical observations.

Mechanism of Brain Atrophy

There should be no better subject to discuss in the hallways of medical practice than the possible causes of brain atrophy and neurochemical abnormalities that occur in chronic pain. Considering that some studies also show a loss of nerve density of peripheral nerves and spinal cord of pain patients, an electrical phenomenon must be considered as a cause. Is electricity being retained by damaged peripheral nerves that cause a "hot wire" affect that fundamentally inflames, dissolves, and scars tissue? Does pain cause a hormonal or immune dysfunction that can literally dissolve gray matter? Hypercortisolemia has been observed in chronic pain patients and it is known to cause a demented state.²¹⁻²³ Severe pain is also well-known to cause hypertension and tachycardia, particularly during pain flares. Both are known to affect cerebral blood flow. Whatever future research points to as

causation, physicians should take their best shot now at preventing the disappearance of gray matter. In addition to better pain control, it is obvious that we need better strategies to normalize electrical conduction, hormone metabolism, and restoration of tissue.

Start Education Immediately

The number one thing physicians should immediately do with this new research information is educate all concerned parties including patients, families, psychologists, pharmacists, surrogates, insurance carriers, and medical boards. (Table Three) In particular, any party such as a family member who is critical of opioid treatment needs to be bluntly told that withholding treatment, including opioid therapy, may subject the patient to brain atrophy and the loss of intelligence, memory, and possible development of dementia. Simply, the risks of delayed or undertreatment appear too great. On the other hand, we do not know whether opioids or any other treatment can prevent or restore brain atrophy or altered brain physiology and neurochemicals.

Clinical Recommendations

It must be recognized that we may not be able to either prevent or restore brain tissue in chronic pain states. Nevertheless, these new research findings suggest some intuitive and logical measures. Education of ourselves and patients is naturally, first on our list. Second is sooner and more aggressive treatment with all methods that are currently available. For example, alcoholic and some other forms of dementia respond to nutritional therapies. Since excess electricity produced in chronic pain states may be a causative factor, techniques to reduce and control electrical flow may be in order. Certainly the encouragement of mental exercise, increased physical activity, and social interaction should help

keep brains active. Above all, doctors who treat severe chronic pain patients should focus on this complication and eagerly share any hints and tips they uncover. It's also my recommendation that we attempt to identify psychologists who have interest and skills in working with dementia.

Conclusion

The finding that chronic pain, per se, causes brain atrophy and altered physiology and neurochemistry is a profound discovery. Chronic pain, particularly the severe intractable forms, should be considered a disease unto itself. These risks along with cardiovascular, hormone, immune and physiologic function risks clearly outweigh the risk of undertreatment. At this time there is no guarantee that we can prevent or restore brain atrophy with any known treatment or measures. Now that we are aware that this complication may occur, it is time to experiment, observe, and develop strategies to prevent and ameliorate it.

<p style="text-align:center"><u>TABLE ONE</u></p> <p style="text-align:center"><u>RISKS OF CHRONIC PAIN</u></p> <p style="text-align:center"><i>BRAIN ATROPHY</i></p> <p style="text-align:center"><i>ALTERED BRAIN NEUROCHEMISTRY</i></p> <p style="text-align:center"><i>ALTERED BRAIN SENSORY PROCESSING</i></p> <p style="text-align:center"><i>HYPERTENSION</i></p> <p style="text-align:center"><i>TACHYCARDIA</i></p> <p style="text-align:center"><i>IMMUNE SUPPRESSION</i></p> <p style="text-align:center"><i>ELEVATED ADRENAL CORTICOIDS</i></p> <p style="text-align:center"><i>ADRENAL EXHAUSTION</i></p> <p style="text-align:center"><i>DEPRESSION</i></p> <p style="text-align:center"><i>PHYSICAL IMMOBILITY</i></p> <p style="text-align:center"><i>DERANGED ACTIVITIES OF DAILY LIVING</i></p> <p style="text-align:center"><i>INSOMNIA</i></p> <p style="text-align:center"><i>ANOREXIA AND MALNUTRITION</i></p> <p style="text-align:center"><i>SUICIDE</i></p>
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TABLE TWO

FOUR CLINICAL CASES WHO MENTALLY DETERIORATED

1. A 25 year old female was referred with severe chronic pain due to fibromyalgia. She claimed undertreatment for at least three years which interfered with her promising career. Morning serum cortisol levels were over 30ug/dl and she had a resting heart rate over 110 beats per minute. Despite aggressive opioid and other treatment, within 10 years she became so mentally incapacitated that she could not work, was home-bound, and had to be cared for by family.
2. A 55 year old male executive has severe back pain with radiculopathy in both legs. For about five years he had interrupted pain care consisting of standard interventions, opioid dosages, and a variety of neuropathic, anti-inflammatory, and anti-depression agents. By age 60 he had to retire and was unable to adequately concentrate, read, or do calculations to retain employment. He remains at home and cared for by his wife.
3. A 40 year old male television camera technician developed a severe back injury requiring multiple back surgeries, fusion, and implanted rods. Despite an implanted intrathecal morphine pump and numerous medical treatments including opioids, he developed such memory loss and cognitive abilities that he could not work or do such activities as balance a check book.
4. A 40 year old registered nurse was referred with severe pain due to fibromyalgia. Her resting morning cortisol was under 1ug/dl, and she had tachycardia over 100 beats per minute. Despite multiple treatments including opioids, she mentally deteriorated over a 5 year period to the point that she could not work and had to live at home with parents.

The above cases are examples of clinical observations of severe chronic pain patients. They are presented here with little knowledge of underlying causes of their mental deterioration or whether they have brain atrophy.

TABLE THREE

WHO NEEDS TO BE EDUCATED ABOUT BRAIN ATROPHY

<i>PATIENTS</i>	<i>FAMILIES</i>	<i>NP's/PA</i>
<i>PSYCHOLOGISTS</i>	<i>SOCIAL WORKERS</i>	<i>PHARMACISTS</i>
<i>CLERGY</i>	<i>INSURANCE CARRIERS</i>	<i>MEDICAL BOARDS</i>

TABLE FOUR

SOME CLINICAL RECOMMENDATIONS AND APPROACHES

- EDUCATE ALL PARTIES
- INCLUDE BRAIN ATROPHY RISK IN CONSENT FORM AND AGREEMENTS
- EARLY AND AGGRESSIVE TREATMENT
- NUTRITION
- ELECTRICAL CONTROL MEASURES
- MENTAL, INTELLIGENCE, AND MEMORY SCREENING AND EXERCISES

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