

# ON THE SURFACE:

## Understanding Fibromyalgia in Your Patients

Do you have patients who complain of chronic widespread pain and tenderness along with these symptoms?

- Fatigue
- Reduced functioning
- Sleep disturbance
- Morning stiffness

Could it be *Fibromyalgia*?

- Fibromyalgia is the most common chronic widespread pain condition in the US<sup>1</sup>
- According to national epidemiological studies, millions of Americans suffer from Fibromyalgia<sup>2</sup>
- The American College of Rheumatology (ACR) has developed specific criteria to diagnose Fibromyalgia\*

Is *Fibromyalgia* “all in their heads”?

Yes, it is in their heads—but emerging science suggests it is not psychosomatic

- Fibromyalgia is thought to be a neurologic condition  
– Central sensitization is a leading theory—a dysfunctional hyperexcitability in pain processing<sup>3</sup>

Emerging evidence suggests:

- Pain processing that is dysfunctional, possibly leading to a lower pain threshold<sup>4</sup>
- Elevated levels of substance P and its role in the transmission of pain to the central nervous system<sup>5-8</sup>
- Anatomical gray matter changes in the brain, possibly associated with Fibromyalgia<sup>9-12</sup>

\* See last page for ACR criteria.

# A STEP FORWARD:

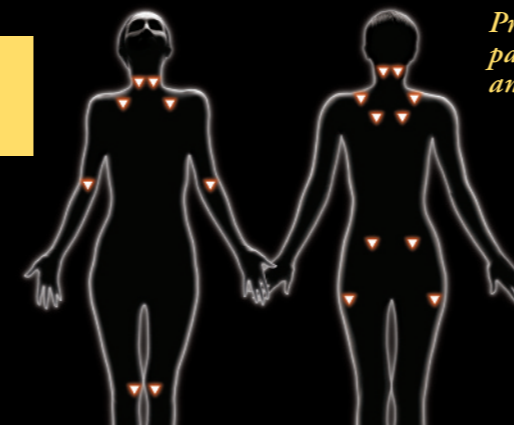
## Diagnosing and Managing Fibromyalgia

### Identifying Fibromyalgia Patients

Fibromyalgia symptoms include<sup>13</sup>:

- Chronic widespread pain and tenderness
- Fatigue
- Morning stiffness
- Reduced functioning
- Sleep disturbance

American College of Rheumatology  
Criteria for Diagnosing Fibromyalgia



Presence of widespread pain for at least 3 months, and all of the following<sup>13</sup>:

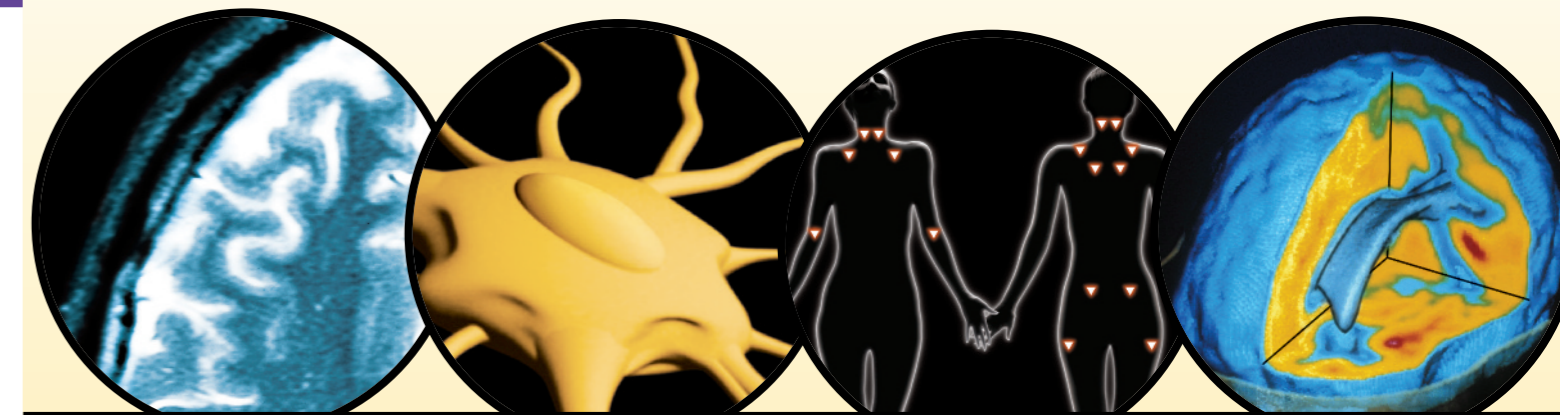
1. Pain on the right and left sides of the body
2. Pain above and below the waist
3. Pain in the axial skeleton
4. Pain on palpation in at least 11 of 18 tender points

A debilitating condition that affects daily functioning

- Widespread pain is reported by more than 97% of patients with Fibromyalgia<sup>13</sup>
- Over 60% of Fibromyalgia sufferers reported difficulty in a recent quantitative survey (N=1735)<sup>14</sup>:
  - Doing light household tasks
  - Walking (½ mile)
  - Going up and down a flight of stairs
  - Lifting or carrying 10 lbs

Recognizing the symptoms and diagnosing patients with *Fibromyalgia* can help you provide them with meaningful pain relief and improvements in function

**References:** 1. Burckhardt CS, Goldenberg D, Crofford L, et al. *Guideline for the Management of Fibromyalgia Syndrome Pain in Adults and Children*. APS Clinical Practice Guidelines Series, No. 4. Glenview, Ill: American Pain Society; 2005. 2. Data on file. Decision Resources, Fibromyalgia, August 28, 2008. Pfizer Inc, New York, NY. 3. Staud R. Biology and therapy of fibromyalgia: pain in fibromyalgia syndrome. *Arthritis Res Ther*. 2006;8(3):208-214. 4. Gracely RH, Petzke F, Wolf JM, Clauw DJ. Functional magnetic resonance imaging evidence of augmented pain processing in fibromyalgia. *Arthritis Rheum*. 2002;46:1333-1343. 5. Russell IJ, Orr MD, Littman B, et al. Elevated cerebrospinal fluid levels of substance P in patients with the fibromyalgia syndrome. *Arthritis Rheum*. 1994;37:1593-1601. 6. Russell IJ, Orr MD, Michalek JE. Substance P [SP], SP endopeptidase activity [SPE] and SP N-terminal peptide [SP1-7] in fibromyalgia syndrome [FS] cerebrospinal fluid [CSF]. In: Russell IJ, ed. *Myopain '95: Abstracts from the 3rd World Congress on Myofascial Pain and Fibromyalgia*; July 30–August 3, 1995; San Antonio, Tex. 7. Bradley LA, Alberts KR, Alarcón GS, et al. Abnormal brain regional cerebral blood flow (rCBF) and cerebrospinal fluid (CSF) levels of substance P (SP) in patients and non-patients with fibromyalgia (FM). *Arthritis Rheum*. 1996;(suppl 9):212. Abst 1109. 8. Burke A, Smyth EM, FitzGerald GA. Analgesic-antipyretic agents. In: Brunton LL, Lazo JS, Parker KL, eds. *Goodman & Gilman's The Pharmacological Basis of Therapeutics*. 11th ed. New York: McGraw-Hill; 2006:681. 9. Kuchinad A, Schweinhardt P, Seminowicz DA, Wood PB, Chizh BA, Bushnell MC. Accelerated brain gray matter loss in fibromyalgia patients: premature aging of the brain? *J Neurosci*. 2007;27(15):4004-4007. 10. Schmidt-Wilcke T, Luedering R, Weigand T, et al. Striatal grey matter increase in patients suffering from fibromyalgia—a voxel-based morphometry study. *Pain*. 2007;132(suppl 1):S109-S116. 11. Lutz J, Jäger L, de Quervain D, et al. White and gray matter abnormalities in the brain of patients with fibromyalgia: a diffusion-tensor and volumetric imaging study. *Arthritis Rheum*. 2008;50(12):3960-3969. 12. Luedering R, Weigand T, Bogdahn U, Schmidt-Wilcke T. Working memory performance is correlated with local brain morphology in the medial frontal and anterior cingulate cortex in fibromyalgia patients: structural correlates of pain–cognition interaction. *Brain*. 2008;131:3222-3231. 13. Wolfe F, Smythe HA, Yunus MB, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia: report of the Multicenter Criteria Committee. *Arthritis Rheum*. 1990;33:160-172. 14. Jones J, Rutledge DN, Jones KD, Matalana L, Rooks DS. Self-assessed physical function levels of women with fibromyalgia: a national survey. *Women's Health Issues*. 2008;18:406-412.



FIBROMYALGIA:  
*Exploring the Science Behind the Pain*

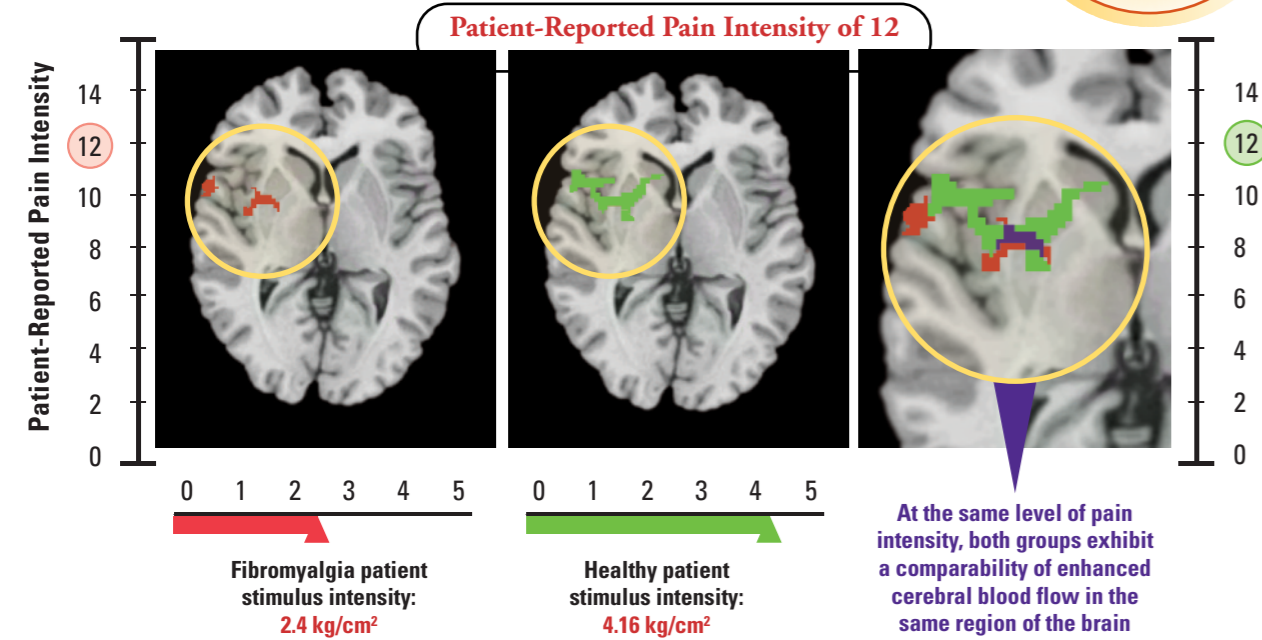
# A CLOSER LOOK:

## Dysfunctional Pain Processing

Patients with Fibromyalgia have a significantly lower pain threshold, as shown in an fMRI study<sup>4</sup>

Patient-reported pain measures correlated with fMRI scans<sup>4</sup>

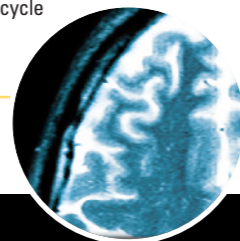
As patients experience pain, enhanced cerebral blood flow can be observed in brain regions through fMRI



For healthy control patients to experience the same high level of pain as Fibromyalgia patients, nearly double the stimulus intensity was required (4.16 kg/cm<sup>2</sup>)<sup>4</sup>

<b>Objective:</b>	To evaluate patterns of cerebral activation during application of painful pressure in Fibromyalgia patients versus controls. <sup>4</sup>
<b>Patients:</b>	Sixteen Fibromyalgia patients, mean age 52.6 years (range 19-69), and 16 healthy controls, mean 45.8 years (range 22-61), were analyzed for cerebral blood flow in response to painful and non-painful stimuli. None of the subjects were clinically depressed. Patients taking opioid analgesics were excluded; other analgesics were discontinued 12 hours before procedures. <sup>4</sup>
<b>Method:</b>	After establishment of the study subjects' pain sensitivity, fMRI scans were made during a series of test cycles. During each cycle, stimulus that caused mild pressure was applied for 30 seconds, then was increased to a painful level and applied for 30 seconds. All stimuli were decreased for 0.3 second at 3-second intervals. Functional images of the entire brain were obtained at 5-second intervals, resulting in 6 functional volumes for each 30-second stimulus. This cycle was repeated 10 times. <sup>4</sup>
<b>Results:</b>	Patients with Fibromyalgia had a significantly lower pain threshold. <sup>4</sup>

Adapted from Gracely et al. *Arthritis Rheum.* 2002.<sup>4</sup>  
fMRI = functional magnetic resonance imaging.

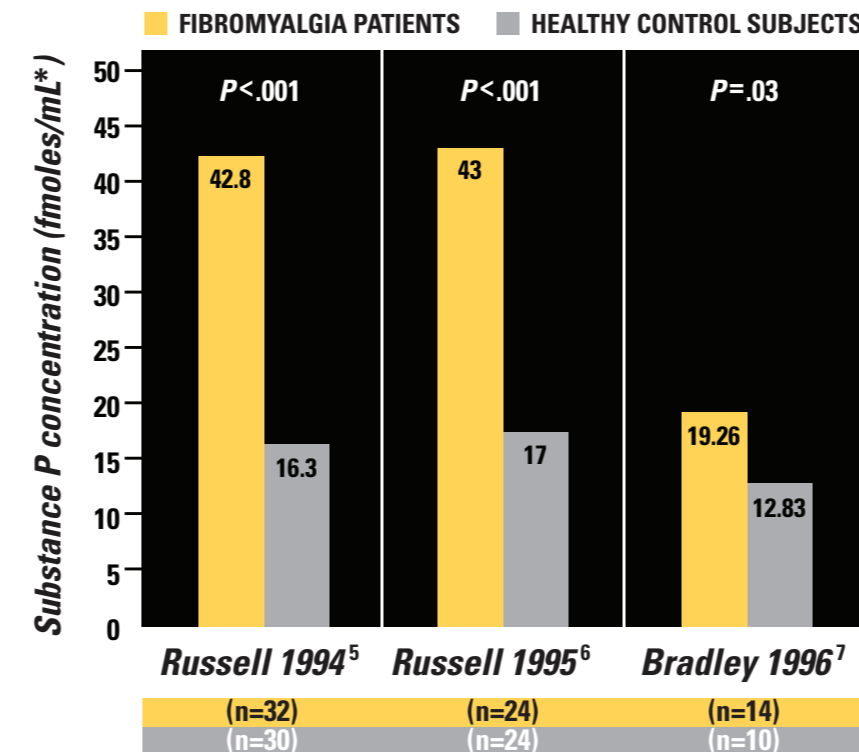


# WITHIN THE CSF:

## Elevated Levels of Substance P

In multiple studies, levels of substance P have been shown to be significantly higher in the cerebrospinal fluid (CSF) of Fibromyalgia patients than in normal controls<sup>5-7</sup>

- Substance P, a neurotransmitter, may play a key role in the transmission of pain to the central nervous system<sup>8</sup>



<b>Objective:</b>	To measure levels of substance P (SP) in patients with Fibromyalgia. <sup>5-7</sup>
<b>Method:</b>	The CSF level of immunoreactive SP was investigated in patients diagnosed with Fibromyalgia and in healthy control subjects. CSF samples were collected by lumbar puncture and SP levels were measured by radioimmunoassay. <sup>5-7</sup>
<b>Results:</b>	All 3 studies show that SP levels were significantly elevated in Fibromyalgia patients compared to normal values in healthy control subjects. <sup>5-7</sup>

\* fmol/mL = fraction of molecular weight in grams per milliliter.



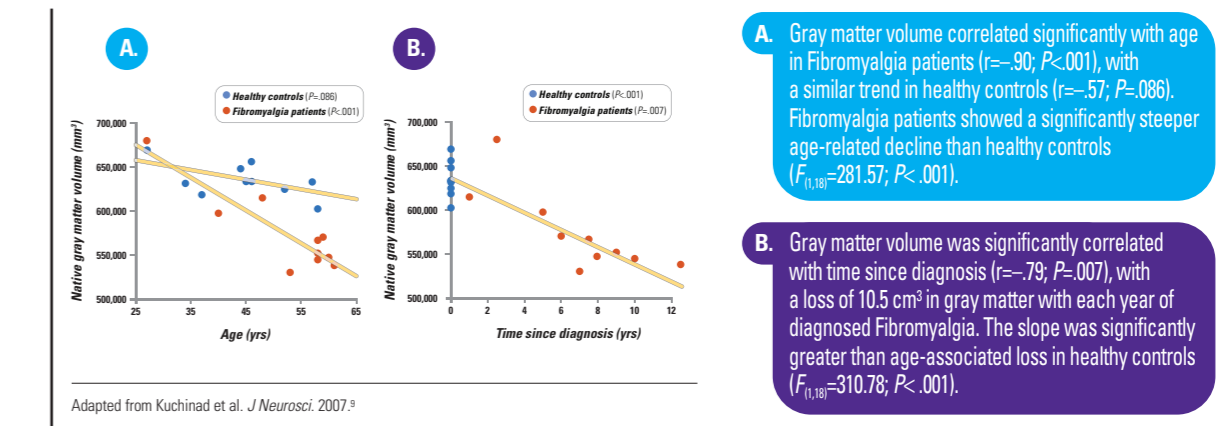
# INSIDE THE BRAIN:

## Anatomical Changes

Accumulating evidence now suggests that Fibromyalgia may be associated with anatomical changes in the brain<sup>9-12</sup>

- In the Kuchinad et al study, patients with Fibromyalgia appeared to have significantly less gray matter volume and total brain volume than healthy controls<sup>9</sup>
  - Gray matter loss occurred in regions of the brain related to pain processing
  - Gray matter loss was related to age and to disease duration vs healthy controls
  - It is undetermined whether the structural changes observed in these patients cause or are caused by their Fibromyalgia

Age-related gray matter loss was accelerated in Fibromyalgia patients and was correlated with disease duration<sup>9</sup>



These neuroanatomical changes suggest that Fibromyalgia may be associated with central nervous system dysfunction<sup>9</sup>

<b>Objective:</b>	To investigate anatomical changes in the brains, observed through gray matter loss, of Fibromyalgia patients compared to controls. <sup>9</sup>
<b>Patients:</b>	The level of gray matter loss was measured in 10 patients diagnosed with Fibromyalgia and in 10 healthy control subjects. <sup>9</sup>
<b>Method:</b>	The brains of these patients were examined using voxel-based morphometric analysis of magnetic resonance brain images. Statistical maps of differences in gray matter density between patients and healthy controls at every voxel were obtained using a general linear model, and using age as a covariate. <sup>9</sup>
<b>Results:</b>	Patients with Fibromyalgia had accelerated gray matter loss related to age and to disease duration vs healthy controls. <sup>9</sup>

