Journal of Pain & Relief
ISSN: 2167-0846

Case Report Open Access

Neurobiological Indicators of Altered Centralized Pain Processing in Fibromyalgia

Tanaka P*

Department of Medicine and Health Sciences, Universiti Sultan Zainal Abidin, Malaysia

Abstract

Identifying a common language and classification to diagnose and treat fibromyalgia has been challenging, because patients may first seek care from different disciplines with unique perspectives and terminologies.

Keywords: Pain syndrome; Diagnostic criteria; Psychiatric conditions; Fibromyalgia patients; Psychological dimensions; Increased sensitivity

Introduction

Fibromyalgia, similar to other medically unexplained pain syndromes, may be classified in numerous ways. There remains an ongoing debate as to whether fibromyalgia should be considered a distinct disorder or grouped with other disorders that have over lapping symptomology into a chronic wide spread pain syndrome spectrum. Two international workgroups have recently released new classification criteria for chronic pain conditions. The International Association for the Study of Pain developed new ICD-11 codes that separate chronic pain conditions by whether or not the pain is secondary to another condition [1]. The new designation of chronic primary pain syndromes includes fibromyalgia in the chronic widespread pain category. The American Pain Society led the efforts to improve diagnostic classification criteria for chronic pain conditions. The work group determined that the core diagnostic criteria for fibromyalgia are pain of at least 3 months duration occurring in at least six body sites that is accompanied by fatigue or sleep disturbances judged to be of at least moderate severity by a clinician. Other common features include tenderness, executive functioning deficits, and sensory intolerance [2]. Common comorbidities include several psychiatric conditions. Identified risk and vulnerability factors for developing fibromyalgia include female gender, middle to older age, limited physical activity, genetic factors, premorbid psychosocial stress, and co-occurring mental health symptoms [3]. Recent research suggests that up to 50% of risk may be attributable to genetics, specifically the expression of hypo-methylated DNA and microRNAs [4].

Methodology

A recent systematic review of studies examining associations between traumatic life events and development of fibromyalgia supported associations between both physically traumatic events and psychologically traumatic events. There is further evidence that traumatic experiences and chronic stress may result in epigenetic alterations of genes associated with DNA repair [5]. Psychosocial resilience and protective factors include strong social support, active coping strategies, acceptance, psychological flexibility, and increased self-efficacy as shown in (Figure 1). These have been shown to be beneficial in reducing experiential pain and improving general wellbeing. Diagnostically, medically unexplained chronic pain is closely related to somatic symptom disorders, as identified inDSM-5 [6]. However, there is evidence that individuals with somatic symptom disorders and fibromyalgia present with differing symptomology and behaviours. A study that separated fibromyalgia patients by whether they fulfilled DSM-5 criteria for a somatic symptom disorders reported that the study groups differed in the level of self-reported symptoms. In contrast, the study groups did not differ on objective measures of health care utilization or disability [7]. Although psychiatric symptoms were prevalent in both groups, a higher proportion of the fibro-myalgia patients meeting somatic symptom disorders criteria also met criteria for an anxiety or depressive disorder. The authors commented that disproportionate and persistent worry about health symptoms may be better attributed to the comorbid depressive or anxiety disorders than to fibromyalgia [8]. As noted in several re-cent reviews, fibromyalgia is more accurately classified as having both physical and psychological dimensions rather than categorizing it as either a physical disorder or a psychiatric disorder. A recent prospective population-based cohort study re-ported a bidirectional relationship between chronic pain conditions and psychiatric disorders, as developing one in-creased the risk for developing the other. The incidence rate ratio for receiving a fibromyalgia diagnosis after developing a psychiatric disorder was

Figure 1: Strong support and increased self-efficacy.

***Corresponding author:** Tanaka P, Department of Medicine and Health Sciences, Universiti Sultan Zainal Abidin, Malaysia, Tel: 096658237, E-mail: tanakap@gmail.com

Received: 19-Jun-2023, Manuscript No.JPAR-23-108489; **Editor assigned:** 22-Jun-2023, PreQC No. JPAR-23-108489(PQ); **Reviewed:** 06-Jul-2023, QC No. JPAR-23-108489; **Revised:** 11-Jul-2023, Manuscript No. JPAR-23-108489(R); **Published:** 18-Jul-2023, DOI: 10.4172/2167-0846.1000525

Citation: Tanaka P (2023) Neurobiological Indicators of Altered Centralized Pain Processing in Fibromyalgia. J Pain Relief 12: 525.

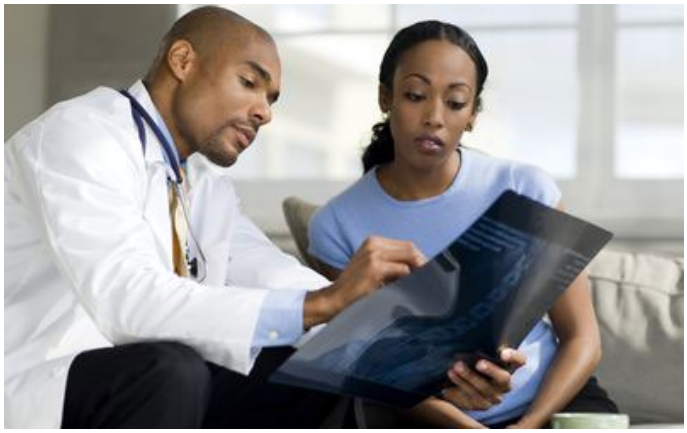

Figure 2: Identifying Changes in perception of peripherally delivered stimuli.

5.54. The IRR for receiving a psychiatric diagnosis after developing fibromyalgia was 4.05 [9]. As noted by the authors, these results suggest shared bio-psychosocial vulnerabilities between persistent pain and psychiatric disorders. Centrally mediated amplification of pain, an adaptive response to limit further injury, normally subsides with healing. Quantitative sensory testing is a standardized methodology for assessing reactions to delivery of quantified peripheral stimuli. Quantitative sensory testing provides several metrics that are used to identify changes in perception or processing of peripherally delivered stimuli that indicate presence of central sensitization as shown in (Figure 2). These include pain resulting from typically non-painful stimuli, increased sensitivity to painful stimuli, enhanced progressive increase in pain with repeated exposure, and impaired conditioned pain modulation [10].

Discussion

Central sensitization has been demonstrated in both secondary chronic pain conditions and in primary chronic pain conditions. Many studies utilizing QST have demonstrated presence of central sensitization in patients with fibromyalgia [11]. A meta-analysis of studies comparing fibromyalgia and healthy control groups on Quantitative sensory testing metrics confirmed enhanced temporal summation and impaired conditioned pain modulation in fibromyalgia patients. A few studies have utilized Quantitative sensory testing T in combination with clinical measures to evaluate treatment-related changes in patients with fibromyalgia [12]. A randomized-blinded clinical trial comparing amitriptyline and melatonin reported improvement in conditioned pain modulation and slightly better symptom reduction in the groups receiving melatonin. A small study that administered Quantitative sensory testing prior to and during treatment with pregabalin reported gradual improvements in pain thresholds and conditioned pain modulation as well as reductions in other symptoms. A pilot study of mindful yoga for fibromyalgia reported improved pain tolerance and decreased pain after sensations accompanied by clinically meaningful improvements on symptom severity, pain, and pain catastrophizing. Overall, these studies indicate the presence of central sensitization prior to treatment initiation in patients with fibromyalgia that is as least partially normalized treatment [13]. MRI studies have used voxel-based morphometry to identify differences in regional brain volumes between fibromyalgia and healthy control groups. Two meta-analyses of such studies reported similar areas of decreased volume in anterior and posterior cingulate cortices. Of these meta-analyses, one also identified other areas of decreased and increased volume in fibromyalgia. Single studies have reported differences in multiple other regions. A longitudinal study in fibromyalgia patients with insomnia assessed regional cortical thickness in areas previously identified as altered in either condition before and after treatment. Finding support the potential reversibility of some of these differences [14]. Very little is known regarding the types of tissue changes that underlie identified volumetric differences. One study combined multiple imaging approaches with hierarchical multiple regression analyses to assess contributions of neuronal density and water content in areas that differed in volume between fibromyalgia and healthy control groups. Flumazenil positron emission tomography binding provided a surrogate measure for neuronal density. This ligand binds to the benzodiazepine site on the GABAA receptor complex. MRI T1relaxation time measurement provided a surrogate measure for water content. GABAA receptor binding did not differ between the groups in any region of interest, suggesting absence of NeuroDegeneration in fibromyalgia. Decreased water content accounted for a substantial proportion of variance in ROIs with lower volume in the fibromyalgia group. Both GABAA receptor binding and increased water content contributed to variance in ROIs of higher volume in the fibromyalgia group. As noted by the authors, these results might indicate presence of Neuro-inflammatory oedema. A multisite study utilized PBR28 PET to compare trans-locator protein binding between fibromyalgia and healthy control groups. This study identified multiple cortical areas with higher binding in the fibromyalgia group, indicating presence of glial activation. Exploratory analyses indicated that the only clinical variable that correlated with binding was fatigue. Fibromyalgia patients with higher levels of fatigue had higher TSPO binding in anterior and middle/posterior cingulate cortices. L-deprenyl-D2PET, considered a marker specific to astroglia, did not differ between the groups. Thus, areas of increased TSPO binding likely indicate presence of microglial activation in fibromyalgia. As discussed by the authors, the functional significance of these changes is presently undetermined. Meta-analyses of functional MRI studies in which painful stimuli were administered have reported generally similar patterns of activations in healthy individuals and in patients with chronic pain conditions. One meta-analysis found that although findings varied considerably across individual functional MRI studies, the frequency of an area being reported was similar for both groups. Although the regions commonly activated by painful stimuli have been historically referred to as the pain matrix, there is considerable evidence that these areas cannot be considered pain-specific. This was most clearly demonstrated in an fMRI study in which areas activated by noxious stimuli were compared between healthy individuals and patients with congenital insensitivity to pain. The same set of brain regions was activated in both groups. The areas matched the previously identified signature for pain. As noted by the authors, their results confirm that activations indicate high salience rather than pain. The presence in fibromyalgia of elevated sensitivity to other types of sensory input supports the recently proposed generalized or global state of sensory amplification as a result of top-down central mechanisms. Recent study utilized machine learning based on functional MRI responses to sensory stimuli to identify a brain signature for fibromyalgia. The derived multisensory evoked classifier map had high accuracy in correctly identifying fibromyalgia from healthy controls. Fibromyalgia was characterized by increased activation in hetero model and self-referential regions and reduced activation in primary/secondary visual and auditory regions, lateral prefrontal, cerebellum, diencephalon and midbrain. As noted in a recent review, although multivariate methods are quite useful in the research setting, they are much less likely to become useful in the clinical context. The other major fMRI approach to identifying neurobiological differences

associated with fibromyalgia does not require stimulation of any type. Instead, functional MRI acquired in a resting state is used to assess spontaneous changes in activation. One use of resting state functional MRI is evaluation of functional connectivity between brain regions.

Conclusion

The most common approach is to use an ROI as a seed and identify voxels throughout the brain in which spontaneous changes in local signal intensity are highly similar to the seed. Although multiple studies have reported significant differences between fibromyalgia and healthy groups, there is relatively little consistency across studies. This is likely a result of differences in methodology and the small numbers of study subjects examined. One research group recently pooled resting state fMRI data from their previous studies and used graph theoretical methods to assess functional connectivity between 264 ROIs.

Acknowledgement

None

Conflict of Interest

None

References

1. Cohen SP, Mao J (2014) Neuropathic pain: mechanisms and their clinical implications. BMJ UK 348:1-6.
2. Mello RD, Dickenson AH (2008) Spinal cord mechanisms of pain. BJA US 101:8-16.
3. Bliddal H, Rosetzsky A, Schlichting P, Weidner MS, Andersen LA, et al. (2000) A randomized, placebo-controlled, cross-over study of ginger extracts and ibuprofen in osteoarthritis. Osteoarthr Cartil EU 8:9-12.
4. Maroon JC, Bost JW, Borden MK, Lorenz KM, Ross NA,et al (2006) Natural anti-inflammatory agents for pain relief in athletes. Neurosurg Focus US 21:1-13.
5. Birnesser H, Oberbaum M, Klein P, Weiser M (2004) The Homeopathic Preparation Traumeel® S Compared With NSAIDs For Symptomatic Treatment Of Epicondylitis. J Musculoskelet Res EU 8:119-128.
6. Ozgoli G, Goli M, Moattar F (2009) Comparison of effects of ginger, mefenamic acid, and ibuprofen on pain in women with primary dysmenorrhea. J Altern Complement Med US 15:129-132.
7. Raeder J, Dahl V (2009) Clinical application of glucocorticoids, antineuropathics, and other analgesic adjuvants for acute pain management. CUP UK: 398-731.
8. Świeboda P, Filip R, Prystupa A, Drozd M (2013) Assessment of pain: types, mechanism and treatment. Ann Agric Environ Med EU 1:2-7.
9. Nadler SF, Weingand K, Kruse RJ (2004) The physiologic basis and clinical applications of cryotherapy and thermotherapy for the pain practitioner. Pain Physician US 7:395-399.
10. Trout KK (2004) The neuromatrix theory of pain: implications for selected non-pharmacologic methods of pain relief for labor. J Midwifery Wom Heal US 49:482-488.
11. Bidaisee S, Macpherson CNL (2014) Zoonoses and one health: a review of the literature. J Parasitol 2014:1-8.
12. Cooper GS, Parks CG (2004) Occupational and environmental exposures as risk factors for systemic lupus erythematosus. Curr Rheumatol Rep EU 6:367-374.
13. Parks CG, Santos ASE, Barbhaiya M, Costenbader KH (2017) Understanding the role of environmental factors in the development of systemic lupus erythematosus. Best Pract Res Clin Rheumatol EU 31:306-320.
14. Barbhaiya M, Costenbader KH (2016) Environmental exposures and the development of systemic lupus erythematosus. Curr Opin Rheumatol US 28:497-505.