THE EUROPEAN SOCIETY OF MEDICINE
Medical Research Archives, Volume 12 Issue 12

RESEARCH ARTICLE

Fibromyalgia: Another Aetiological Approach

Golstein Marc [1]

[1] Rheumatology Department, Clinique Saint-Jean, Bd du Jardin Botanique 32, B-1000 Brussels, Belgium

OPEN ACCESS

PUBLISHED
31 December 2024

CITATION
Golstein, M., 2024. Fibromyalgia: Another Aetiological Approach. Medical Research Archives, [online] 12(12).
https://doi.org/10.18103/mra.v12i12.6093

DOI
https://doi.org/10.18103/mra.v12i12.6093

ISSN
2375-1924

ABSTRACT

Fibromyalgia and diffuse pain disorders have been the subject of thousands of specialised publications and more than 56,000,000 references suggested by public search engines.

Nevertheless, the aetiology of diffuse pain syndrome remains poorly understood, though it accounts for nearly 20% of rheumatology consultations. Treatment is not very systematised and the results of treatment procedures remain of limited efficacy in terms of work capacity. The socio-economic consequences for patients with fibromyalgia are on the same level as those seen in patients diagnosed with rheumatoid arthritis. It would appear desirable to review the aetiological approach to be able to treat diffuse pain disorders more effectively. The association between violence experienced during childhood and the onset of fibromyalgia has been previously suggested without being considered a necessary and sufficient cause. However, thanks to the development of medical brain imaging techniques and the knowledge of epigenetic mechanisms, it seems that a previous history of sexual abuse and physical violence experienced during childhood could effectively be one of/or the cause of the onset of fibromyalgia.

Introduction

According to the PubMed website more than 14800 articles concerning fibromyalgia and more than 56 million references are suggested by public search engines. Starting in 1944, Kelly[1,2,3], in his article entitled "Fibrositis", described a list of subjective symptoms summarising 9 types of pain: headaches, scapular pain, forearm, and hand pain, the concept of pleurodynia, intercostal muscle pain, abdominal pain, lumbar pain, sciatic-like pain, knee pain, plantar pain and foot cramps. This original description was summarised by the American College of Rheumatology (ACR) in its criteria published in 1990, as well as in 2010[4]. In 2019, those ACR criteria were discussed and slightly modified by the AAPT group of experts[5]. Initially, Kelly suggested a "neurological" aetiology or possibly a "psychological" origin of the symptoms. After various classifications mentioned above and 80 years of thousands of publications, the progress in characterizing the syndrome or the disease remains thin. The discussion about the difference between widespread pain and multisite appears far removed from fibromyalgia patient's concerns (Table 1).

Table 1. Signs and symptoms of fibromyalgia according to Kelly (1944, 1945 and 1946) and according to the American College of Rheumatology (ACR 1990, 2010 and 2010 amended) and AAPT

	Kelly 1944 to 1946	ACR 1990	ACR 2010	ACR 2010 amended	AAPT 2018
Duration	NM	3 months	3 months	3 months	3 months
Tender points Widespread pain index (WPI)	+	≥ 11/18	≥ 7 and SS ≥ 5; or WPI: 3 to 6 and SS ≥ 9	≥ 13/31	>6 to 9 sites
Diffuse pain	NM	Mid-body left or right, under the waist and over the waist	+	+	+
Severity score (SS)	0	0	0	0	0
Sensitivity	0	88.4%	88.1%	NM	NM
Specificity	0	81.1%	88.1%	NM	NM
Cognitive disorders	+	0	+	+	+
Fatigue	0	0	+	+	+
Non-restful sleep (0-3)	0	0	+	+	+
Somatic disorders	+	0	+	+	+
Absence of other pathologies	+	+	+	+	+

Ref. 1-3; ACR Fibromyalgia guidelines (https://www.rheumatology.org/I-Am-A/Patient-Caregiver/Diseases-Conditions/Fibromyalgia).

AAPT: ACTTION (The Analgesic, Anesthetic, and Addiction Clinical Trial Translations Innovations Opportunities and Networks)

APS (American Pain Society) Pain Taxonomy

NM = Not Mentioned; **SS** = Severity Score; **0** = not taken into consideration; **+** = taken into consideration.

Faced with this stagnation, another aetiological approach could be envisaged, including sexual violence as a triggering factor. Sexual abuse-related pathologies are subjects not easily approached in the medical literature, and more particularly in the context of fibromyalgia. Using keywords "sexual abuse and fibromyalgia", only 102 studies have been referenced on Pubmed site, the first one published in 1992[6] mentioned the concept of sexual abuse noted in children with unexplained pain disorders. In 1995, Hudson et al.[7] invalidated the involvement of sexual abuse in fibromyalgia, by referring to retrospective studies, methodology bias in the abovementioned studies, and a similar frequency of sexual abuse in patients with proven inflammatory rheumatism. Recently L Clauw[8] criticized another innovative approach[9] using the same kind of arguments to reject the role of acute stress or sexual abuse as a causal event of fibromyalgia. However, the literature on the subject quasi-ignored the epigenetic role of the environment. Further publications relate that the prevalence of sexual abuse is higher in a rheumatological population and especially in patients with fibromyalgia[10,11]. The subject is not discussed in main rheumatologic journals, though pathologies involving unexplained and/or chronic pain account for nearly 20% of rheumatology consultations.

The influence of the general environment

EFFECT OF GENDER ON THE QUALITY OF PUBLICATIONS

Following Schiebinger[12,13,14], the diversity of genders improves the quality of the drafting of scientific articles. Many clinical studies do not consider the specific characteristics of gender in the analysis of the effects of medicines. In addition, most publications were written by men. The effect of gender could explain why the topic of sexual abuse in inflammatory or non-inflammatory rheumatological diseases has garnered so little attention till the 21st century[11,15]

"COST-EFFICACY" STUDIES OF FIBROMYALGIA TREATMENT

Recent cost-effective analyses about fibromyalgia are rare and only few meta-analyses are available without answering to the efficacy of any treatment. None of the studies can precisely determine which therapeutic strategies enable the patient to resume full-time or part-time work after having been incapacitated due to

fibromyalgia knowing that full-time or part-time work incapacity touch 64% of patients[16]. Recently a cost-utility study about non-pharmaceutical therapeutic procedures as cognitive and physical rehabilitation showed a reduction of costs after one year of follow-up[17].
Nevertheless, the medico-social problem remains unresolved but leads to ever-increasing expenses in terms of healthcare.

ESTIMATION OF COSTS RELATED TO FIBROMYALGIA
In 2009 in the United States, a person with fibromyalgia will cost as much as a person with rheumatoid arthritis, 10,800 dollars per year. A patient with both disorders will cost 19,395 dollars per year[18] and not establishing the diagnosis leads to additional expenses. Medical expenditure linked to fibromyalgia[20,21] remains high and is equivalent in Europe and the United States, with an average of 7,800 euros per year. Fibromyalgia patients[22] consulted various medical and non-medical practices used in fibromyalgia patients, including those of chiropractors, osteopaths, environmental and ecological clinicians, acupuncturists, naturopaths, homeopaths, psychiatrists, and psychologists. This non-exhaustive list demonstrates how unsatisfied and powerless patients feel with current evidence-based medicine. The average number of medical and non-medical visits is 26 per year. The number of types of doctors and other therapists consulted became an additional clinical criterion for practicians to diagnose fibromyalgia.

Medical expenses have risen over the years, from 1,000 euros/year in 1991 to 5500 euros/year in Catalonia[20]. Equally, the indirect costs are induced essentially by work incapacity estimated at 10,800 dollars per year in 2009 with an average cost of 72,950 dollars for the duration of his or her active life, considering that 34% of patients will be on disability for about 20 years on average. Faced with this ever-increasing expense, the idea of a multidisciplinary treatment with social and educational support was proposed to try to limit costs and work incapacities. Unfortunately, this type of approach does not currently make it possible to control costs even non-pharmaceutical programs of rehabilitation as mind fullness intervention seems to be slightly effective[23]. We can therefore question the efficiency of current treatment methods related to the poor results in terms of healing and workability. In addition, the latest meta-analyses on the subject concluded that more in-depth, randomized, controlled, prospective studies need to be conducted[24]. Facing stagnation, modifying the aetiological approach to the disease might be relevant.

CHILDHOOD MALTREATMENT AND SEXUAL ABUSE
Considering the poor efficacy and efficiency of multiple therapeutic processes, it seems reasonable to reconsider childhood maltreatment as one of the starting points causing sleep disturbance, fatigue, widespread pain, multiple site pain and/or fibromyalgia. After a certain latency period, people who have suffered maltreatment develop pain syndrome more often than those who have not suffered this type of trauma[25,26]. Furthermore, according to certain authors, the frequency of physical violence or sexual abuse is very high, reaching a prevalence of 62% among patients with fibromyalgia[27]. Childhood maltreatment is not the only source of this type of disorder. Episodes of physical or verbal violence during adulthood and socio-economic precarity, among others, are both commonly related causes. This might, therefore, explain the significant number of patients with multiple pain disorders. In addition, an in vivo study demonstrates that anxiety and social instability are transmitted beyond three generations by female mice, independently of genetic heritage[28]. Intra-familial violence and sexual abuse may also mimic a familial pattern of fibromyalgia[29]. An anxiety-provoking environment could be the cause of chronic pain. When we compile all these data, we gain a better understanding of the reasons for the absence of convincing therapeutic results. This also supports the idea of the need to treat this disorder differently, as it can probably be transmitted not only genetically but by the transgenerational repetition of physical and verbal abuse. Despite enormous amounts delivered to the care and treatment of fibromyalgia, the excessively low percentage of cured patients should lead us to consider other pathogenic explanations that are unfortunately darker than a genetic predisposition or a possible infectious agent. The multiplication of publications concerning childhood and adult maltreatment due to physical or verbal violence or sexual abuse is slowly revealing one of the deeper causes of these somatoform disorders, but probably also other observable pathologies (see DSM-5). The hidden face of this fibromyalgia syndrome, which seems to be the human reflection of the violence encountered, or even generated, in our societies, should be approached fully and free of taboos.

Another aetiological approach

Progress in the epigenetic and cerebral plasticity fields has opened new aetiological perspectives allowing us not only to explain the large number of patients suffering from fibromyalgia, but also to consider an additional approach to explaining other observable organic pathologies.

THE ROLE OF EPIGENETIC FACTORS
We know that nutrition influences gene expression[30] and in 2002, an epidemiology study showed that the nutrition of the grandparents conditioned the predisposition of their descendants to developing cardiovascular and metabolic diseases (onset of diabetes mellitus), independently of genetic factors[31]. Since then, many articles have passed the preponderance of epigenetics on to genetics to explain the onset of a pathology[32,33]. Physical and mental trauma were then incriminated as a cause of fibromyalgia[34]. Epigenetic changes were demonstrated in many genes coding for associated substances to chronic pain, depression, and post-traumatic stress disorder[35,36] as well DNA methylation and up or down gene regulation associated with fibromyalgia patients[37].

Recently, post-traumatic stress disorder appears to be correlated to the emergence of auto-immune diseases empowering the role of a violent environment[38,39] on the occurrence of organic diseases.

THE NEURONAL DEVELOPMENT AND THE SYNAPTIC PLASTICITY
The study of the stages of neurogenesis reveals that at the age of 2 years, humans have the most possibilities for

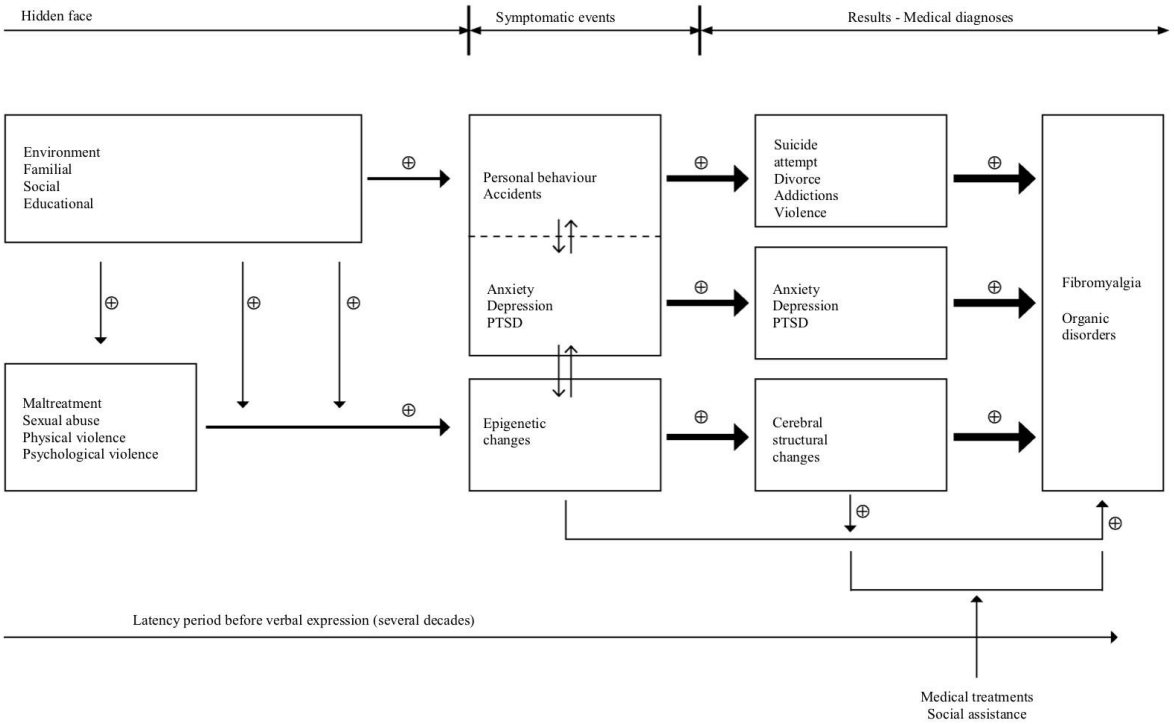
neuronal connections, and their learning and observation capacity is at its peak. Then, depending on the learning and social conditioning, and therefore on the child's environment, the number of synapses decreases[40], as the learning reflexes and circuits for memorisation and thought have been acquired. Recent brain imaging techniques have enabled us to evaluate the number of synaptic connections and cerebral volume with extreme precision. The cerebral consequences of psychological trauma or maltreatment and sexual abuse during childhood have been observed [41]. Significant morphological changes have thus been observed in several regions of the brain, resulting from the trauma experienced and the adaptation process. People who have suffered various episodes of maltreatment during their childhood develop changes, including in the volume of the grey matter, the frontal-occipital cortex, and the parietal gyrus. These objective deficiencies also appear to be correlated with the severity of the maltreatment [42,43].

Recent studies objective specific brain MRI imaging changes on hippocampal and amygdala subregions related to sexual abuse in case of depression disorder[44,45]. MRI imaging also supports childhood sexual abuse's implication on the onset of an adult post-traumatic stress disorder [9,46]. The hypothesis of sexual abuse during childhood as an aetiological factor of fibromyalgia is slowly taking an objective form.

DISCUSSION AND PROPOSAL OF AN AETIOLOGICAL MECHANISM

Despite successive modified criteria of classification (Figure 1) and the abundant literature, deficiencies in the treatment of patients with fibromyalgia are observed. The most recent meta-analyses reveal the heterogenicity of the studies and the low long-term impact of the various treatments on the disease itself and on the ability of patients to return to work.

Figure 1. Hypothesis of the development of a diffuse pain syndrome



PTSD = post-traumatic stress disorder

On the one hand, treatment for fibromyalgia is stagnating, while on the other, in recent years the veil has been lifted on violence against women. However, the pain felt by patients is expressed during medical or rheumatology consultations, while psychological suffering is discussed with psychiatrists. Indeed, the frequency of sexual abuse and childhood maltreatment is most often put forth, or even demonstrated, in the neuro-psychiatric fields and forensic science[47]. There is an initial reasoning bias, which consists of sidestepping this cause based on the practically equivalent frequency of a history of sexual abuse in patients with fibromyalgia and in the control group, which also includes inflammatory rheumatism; this implicitly sidesteps, without proof, the possibility that epigenetic changes caused by sexual abuse could lead also to a pro-inflammatory imbalance in predisposed subjects. The other reasoning bias is to require prospective longitudinal studies by comparing the outcomes of sexually abused children and "healthy controls". This requirement is simply impossible to meet, as it would involve including mistreated and abused children, who, based on a randomisation process, would have to be either left in contact with abusers or cared for in a specialised structure, and then compared with a control group. In addition, the latency period between the time of the sexual abuse and the verbal expression of the victim is a major obstacle to the comparison of groups or observational studies. For more than 20 years, rheumatologists have simply adapted their diagnostic criteria (ACR 1990, 2010, 2010, AAPT 2018) considering the pain to be treated, without providing further therapeutic results. The recent data make it possible to observe epigenetic transcriptions of mediators and neurotransmitters involved in the processes of pain,

depression, post-traumatic stress disorder and synaptic connections in patients with fibromyalgia. Medical imaging shows the presence of brain lesions related to fibromyalgia and childhood maltreatment. There is still no demonstration of the correlation between the epigenetic expression of substances involved in synaptic plasticity and cerebral morphological changes. However, the epigenetic arguments appear to converge towards an aetiological hypothesis combining the current knowledge. All that remains to demonstrate a correlation between cerebral morphological and biochemical changes, to encounter a better approach to fibromyalgia's aetiology.

Conclusion

For almost 80 years, billions of euros and dollars have been spent and thousands of publications have been written on the subject without satisfactory patient results. The administration of drugs remains the first choice of treatment in rheumatology consultations, The emergence of knowledge in epigenetics and functional imaging offers new perspectives for understanding the appearance of diffuse pain in the context of violent acts and sexual abuse. This approach could provide the missing knowledge needed to improve the management of fibromyalgia.

Financing and conflicts of interests

The author did not receive any financing.

The author does not declare any conflicts of interest

Bibliography

1. Kelly M. Fibrositis and reality. Ann Rheum Dis., 1944, 4(2): 46-49.
2. Kelly M. The nature of fibrositis. Ann Rheum Dis., 1945, 5(1): 1-7.
3. Kelly M. The nature of fibrositis: III. Multiple Lesions and the Neural Hypothesis. Ann Rheum Dis., 1946, 5(5): 161-167.
4. Wolf F, Clauw DJ, Fitzcharles M.A et al, The American College of Rheumatology Preliminary Diagnostic Criteria for Fibromyalgia and Measurement of Symptom Severity, Arthritis Care Research, Vol.62, N° 5, May 2010, pp 600-610
5. Lesley M. Arnold, Robert M. Bennett, Leslie J. Crofford, Linda E. Dean, Daniel J. Clauw, Don L. Goldenberg, Mary-Ann Fitzcharles, Eduardo S. Paiva, Roland Staud, Piercarlo Sarzi-Puttini, Dan Buskila, and Gary J. Macfarlane, AAPT Diagnostic Criteria for Fibromyalgia, The Journal of Pain, Vol 20, No 6 (June), 2019: pp 611−628
6. Malleson P.N., al-Matar M., Pettry R.E. Idiopathic musculoskeletal pain syndromes in children. J Rheumatol.,1992,19(11):1786 1789.
7. Hudson J.I., Pope H.G. Does childhood sexual abuse cause fibromyalgia? Arthritis Rheum., 1995, 38(2): 161-163.
8. Clauw DJ , Reply to Hypothetical model ignores many important pathophysiologic mechanisms in fibromyalgia, Nature Reviews Rheumatology, vol 19, May 2023, 322-323
9. Pinto AM, Geenen R, Wager TD, Lumley MA, Häuser W, Kosek E, Ablin JN, Amris K, Branco J, Buskila D, Castelhano J, Castelo-Branco M, Crofford LJ, Fitzcharles MA, López-Solà M, Luís M, Marques TR, Mease PJ, Palavra F, Rhudy JL, Uddin LQ, Castilho P, Jacobs JWG, da Silva JAP Emotion regulation and salience network: a hypothetical integrative model of fibromyalgia, Nature Reviews. Rheumatology,2023, Jan;19(1):44-60
10. Boisset-Pioro M.H., Esdaile J.M., Fitzcharles M.A. Sexual and physical abuse in women with fibromyalgia syndrome. Arthritis Rheum., 1995, 38(2): 235-241.
11. Gota C.E., Kaouk S., Wilke W.S., Fibromyalgia and Obesity: The Association Between Body Mass Index and Disability, Depression, History of Abuse, Medications, and Comorbidities. J. Clin. Rheumatol., 2015, 21(6): 289-295.
12. Nielsen M.W., Alegria S., Börjeson L., Etzkowitz H., Falk-Krzesinski H.J., Joshi A., Leahey E., Smith-Doerr L., Woolley A.W., Schiebinger L. Opinion: Gender diversity leads to better science. Proc. Natl. Acad. Sci. USA., 2017, 114(8): 1740-1742.
13. Buitendijk S., Corda D., Flodström A., Holdcroft A., Hunter, J., Pollitzer E., Rees T., Rice C., Schiebinger L., Schraudner M., Sjørup K., Tarrach R. Women in science and medicine, Lancet, 2011, 377(9768): 811.
14. Schiebinger L., Women's health and clinical trials, J. Clin. Invest., 2003, 112(7): 973-977.
15. Hauser W., Hoffmann E.M.., Wolfe F., Worthing A.B., Stahl N., Rothenberg R., Walitt B., Self-reported childhood maltreatment, lifelong traumatic events and mental disorders in fibromyalgia syndrome: a comparison of US and German outpatients. Clin. Exp. Rheumatol., 2015, 33(1 Suppl 88): S86-92.
16. Wolfe F., Anderson J., Harkness D., Bennett R.M., Caro X.J., Goldenberg D.L., Russell I.J., Yunus M.B. Work and disability status of persons with fibromyalgia. J. Rheumatol., 1997, 24(6): 1171-1178
17. Arfuch V, Aguilar Martin C, Berenguera A, Caballol Angelats R, Queiroga Gonçalves A, Carrasco-Quero N, Gonzalvez Serra G, Sancho Sol M, Fuste Anguera I, Friberg E , Petterson E, Casajuana M ; cost-utility of a multicomponent intervention for fibromyalgia versus usual care: a pragmatic randomised controlled trial; J Rehabil Med 2023;55:jm12361
18. Annemans L., Wessely S., Spaepen E., Caekelbergh K., Caubère J.P., Le lay K., Taïeb C., Health economic consequences related to the diagnosis of fibromyalgia syndrome. Arthritis Rheum. 2008, 59(12): 895-902.
19. Reisine S., Fifield J., Walsh S., Dauser Forrest D., Employment and health status changes among women with fibromyalgia: a five-year study. Arthritis Rheum. 2008, 59(12): 1735-1741.
20. Oliva-Moreno J and Vilaplana-Prieto C; social costs associated with fibromyalgia in Spain; Health Economics review (2024) 14/51; doi.org/10.1186/s13561-024-00527-1
21. Arfuch V, Aguilar Martin C, Berenguera A, Caballol Angelats R, Carrasco-Quero N, Gonzalvez Serra G, Sancho Sol M, Fuste Anguera I, Fernandez Saez J, Queiroga Gonçalves A, Casajuana M ; cost-utility analysis of a multicomponent intervention for fibromyalgia in primary care versus usual clinical practice: study protocol for an economic evaluation of a randomised control trial; BMJ open 2021;11:e043562. Doi:10.1136:bmjopen-2020-043562
22. Bombardier C.H., Buchwald D., Chronic fatigue, chronic fatigue syndrome, and fibromyalgia. Disability and health-care use. Med. Care, 1996, 34(9): 924-930.
23. Zhang L, Lopes S, Lavelle T, Ogata JonesK, Chen L , Jindal M , Zinzow H, Shi L ; economic evaluation of mindfulness-based interventions: a systematic review; mindfulness(2022)13:2359-2378
24. Palstam A., Mannerkorpi K., Workability in fibromyalgia: an update in the 21st century. Curr. Rheumatol. Rev., 2017, 13(3): 180-187.
25. Kleinstäuber M, Scgröder A , Daehler S , Pallesen K, Rask Ch , Sanyer M , Van den Bergh O, Petersen M, Rosmalen J ; aetiological understanding of fibromyalgia, irritable bowel syndrome, chronic fatigue syndrome and classificatory analogues: a systematic review; clinical psychology in Europe 2023, vol.5(3)article e11179.
26. Gardoki-Souto I, Redolar-Ripoll D, Fontana M, Hogg B, Castro M, Blanch J, Ojeda F, Solanes A, Radua J, Valente-Gomez A, Cirici R, Perez V, Amann B, Moreno-Alcazar; prevalence and characterization of psychological trauma in patients with fibromyalgia: a cross-sectional study; Pain Research and Management vol 2022, Article ID 2114451, 16 pages
27. Hauser W., Kosseva M., Üceyler N., Klose P., Sommer C., Emotional, physical, and sexual abuse in fibromyalgia syndrome: a systematic review with meta-analysis. Arthrisis Care Res., 2011, 63(6): 808-820.
28. Saavedra-Rodriguez L., Feig L.A., Chronic social instability induces anxiety and defective social

interactions across generations, Biol. Psychiatry, 2013, 73(1): 44-53.
29. Golstein MA, Steinfeld SD, Non-genetic familial transmission of fibromyalgia: role of sexual abuse? Clin Exp Rheumatol.2022 jun, 40(6):1221-1222
30. Wolff G.L., Kodell R.L., Moore S.R., Cooney C.A., Maternal epigenetics and methyl supplements affect agouti gene expression in Avy/a mice. FASEB J., 1998, 12(11): 949-957.
31. Kaati G., Bygren L.O., Edvinsson S., Cardiovascular and diabetes mortality determined by nutrition during parents' and grandparents' slow growth period. Eur. J. Hum. Genet., 2002, 10(11): 682 – 688.
32. Reddy M.A., Natarajan R., Recent developments in epigenetics of acute and chronic kidney diseases. Kidney Int., 2015, 88(2): 250-261.
33. van der Harst, P., de Windt L.J., Chambers J.C., Translational Perspective on Epigenetics in Cardiovascular Disease. J. Am. Coll. Cardiol., 2017, 70(5): 590-606.
34. Ovrom E, Mostert K, Khakhkhar S, McKee D, Yang P, Her Y; a comprehensive review of genetic and epigenetic contributions to the development of fibromyalgia; biomedicines 2023,11,1119
35. Low L.A., Schweinhardt P., Early life adversity as a risk factor for fibromyalgia in later life. Pain Res.Treat., 2012, 140832.
36. Menzies V., Lyon, D.E., Archer K.J., Zhou Q., Brumelle J., Jones, K.H., Gao G., York T.P., Jackson-Cook C., Epigenetic alterations and an increased frequency of micronuclei in women with fibromyalgia. Nurs. Res. Pract., 2013, 795784.
37. Burri A., Marinova Z., Robinson M.D., Kühnel B., Waldenberger M., Wahl S., Kunze S., Gieger C., Livshits G., Williams F., Are epigenetic factors implicated in chronic widespread pain? PLoS. One, 2016, 11(11): e0165548.
38. Brite J, Miller-Archie SA, Cone J,The relationship between 9/11 exposure, systemic autoimmune disease and post-traumatic stress disorder:a mediational analysis; int.j.environ.res.public health 2022,19, 6514
39. Song H, Fang F, Tomasson G, Arnberg FK, Mataix-Cols D, Fernadez de la Cruz L,Almqvist C, association of stress-related disorders with subsequent autoimmune disease; JAMA June 19, 2018 vol 319 ,23, 2388-240
40. Bruer J.T., Tout est-il joué avant 3 ans ? Editions Odile Jacob, 2002.
41. Cassiers L.L.M., Sabbe B.G.C., Schmaal L., Veltman D.J., Penninx B.W.J.H., Van Den Eede F., Structural and functional brain abnormalities associated with exposure to different childhood trauma subtypes: a systematic review of neuroimaging findings. Front. Psychiatry, 2018, 9: 329.
42. Whittle S, Simmons J, Hendriksma S , Vijayakumar N , Byrne M , Dennison M , Allen N ; Childhood maltreatment , psycholopathology and the development of hippocampal subregions during adolescence ; BrainBehav 2017 ; 7 : e00607
43. Lim L., Hart H., Mehta M., Worker A., Simmons A., Mirza K., Rubia K., Grey matter volume and thickness abnormalities in young people with a history of childhood abuse. Psychol Med., 2018, 48(6):1034-1046.
44. Luo Q, Chen J, Li Y, Wu Z, Lin W, Yao J, Yu H, Wu H, Peng H; aberrant static and dynamic functional connectivity of amygdala subregions in patients with major depressive disorder and childhood maltreatment; Neuroimage: Clinical 36(2022) 103270
45. Kim S, An S, Han J , Kang Y, Bae E, Tae W-S, Ham B-J, Han K-M; childhood abuse and cortical gray matter volume in patients with major depressive disorder; Psychiatry Res 2023 Jan:319:114990 doi/ 10.1016/j
46. Harb F, Liuzzi M, Huggins A, Webb E, Fitzgerald J, Kurkowski J, deRoon-Cassini T, Larson Ch ; childhood maltreatment and amygdala-mediate Anxiety and post-traumatic stress following adult trauma; Biological Psychiatry: Global Open Science July 2024;4.
47. Beyer Eg M , Graesholt-Knudsen T, Bang Madsen K, Obel C ,Vesterby Charles A , Ingemann-Hansen O ; Distinct age-related differences among victimes in cases of suspected child-abuse , J Forensic Sci 2024;69:259-263