Wróblewski Hubert, Chojęta Dariusz, Zimna Aleksandra, Zygmunt Ewelina, Kozłowska Anna, Mierzwa Monika, Wróblewska Kinga. Psychiatric manifestations of rheumatic diseases. Journal of Education, Health and Sport. 2022;12(8):52-60. eISSN 2391-8306. DOI <u>https://dx.doi.org/10.12775/JEHS.2022.12.08.005</u> https://apcz.umk.pl/JEHS/article/view/JEHS.2022.12.08.005 https://zenodo.org/record/6595419

The journal has had 40 points in Ministry of Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of December 21, 2021. No. 32343. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical Culture Sciences (Field of Medical sciences and health sciences); Health Sciences (Field of Medical Sciences and Health Sciences); Health Sciences (Field of Medical Sciences and Health Sciences); Health Sciences (Field of Medical Sciences and Health Sciences); Health Sciences (Field of Medical Sciences and Health Sciences); Health Sciences (Field of Medical Sciences and Health Sciences); Health Sciences); Health Sciences (Field of Medical Sciences and Health Sciences); Health Sciences); Health Sciences (Field of Medical Sciences and Health Sciences); Health Sciences (Field of Medical Sciences and Health Sciences); Health Sciences); Health Sciences (Field of Medical Sciences and Health Sciences); Health Sciences); Health Sciences (Field of Medical Sciences and Health Sciences); Health Sciences); Health Sciences (Field of Medical Sciences and Health Sciences); Health Sciences (Field of Medical Sciences and Health Sciences); Health Sciences (Field of Medical Sciences and Health Sciences); Health Sciences (Field of Medical Sciences and Health Sciences); Health Sciences (Field of Medical Sciences and Health Sciences); Health Sciences (Field of Medical Sciences and Health Sciences); Health Sciences (Field of Medical Sciences and Health Sciences); Health Sciences (Field of Medical Sciences and Health Sciences); Health Sciences (Field of Medical Sciences and Health Sciences); Health Sciences (Field of Medical Sciences (Paravers); Nauki o Zdrowiu); Nauki o Zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu); Medical Sciences Sciences (Denos Access at Licenses Open Journal Systems of Nicolaus Copernicus University in Torun, Poland Open Access. This article is distributed and er

Received: 02.05.2022. Revised: 15.05.2022. Accepted: 30.05.2022.

# Psychiatric manifestations of rheumatic diseases

## Hubert Wróblewski, Dariusz Chojęta, Aleksandra Zimna, Ewelina Zygmunt, Anna Kozłowska, Monika Mierzwa, Kinga Wróblewska

Faculty of Medicine, Medical University of Lublin

ORCID ID and email:

Hubert Wróblewski https://orcid.org/0000-0002-1666-1650; hwwroblewski@gmail.com Dariusz Chojęta https://orcid.org/0000-0002-6474-854X; dariusz.chojeta@gmail.com Aleksandra Zimna https://orcid.org/0000-0002-8712-3497; aleksandra\_zimna97@wp.pl Ewelina Zygmunt https://orcid.org/0000-0002-3724-2164;ewelinazygmunt26@gmail.com Anna Kozłowska https://orcid.org/0000-0001-6719-9331;aniakozlowska6@o2.pl Monika Mierzwa https://orcid.org/0000-0002-6418-7535; akinom142@gmail.com Kinga Wróblewska https://orcid.org/0000-0002-6418-7535; akinom142@gmail.com

## Abstract

**Introduction and purpose of the work:** Rheumatic diseases are chronic diseases that cause symptoms in many systems of the human body. Their most common symptoms include pain and symptoms of arthritis, their deformities, fatigue, and malaise. The aim of the article is to present the symptoms and mental disorders occurring in the course of selected rheumatic diseases.

State of knowledge: The psychological symptoms are characteristic of systemic lupus erythematosus. Specified is a form of lupus called NSPLE (neuropsychiatric systemic lupus

erythematosus), which includes neuropsychiatric symptoms in the course of systemic lupus erythematosus. Psychiatric symptoms are also present in the course of other rheumatic diseases. Neuropsychiatric symptoms may affect up to 80% of patients with primary Sjogren's syndrome, with 50% to 80% ahead of diagnosis. It has been proven that systemic slcerosis causes microvascular damage, which may cause neuropsychiatric symptoms in the form of mood disorders, anxiety and cognitive disorders. In one study, 59% of patients with fibromyalgia experienced mania, which was more than twice as high as in the control group. **Summary:** In the course of all rheumatic diseases presented by us, there are symptoms and mental disorders. They are often mood, cognitive and sleep disturbances. It should be emphasized that the etiology of psychiatric symptoms is multifactorial.

#### Key words: rheumatic diseases, psychiatric symptoms, depression

## Introduction

As is well known, rheumatic diseases are chronic diseases that cause symptoms in many systems of the human body. It is estimated that almost every family in Europe is affected in some way. Their most common symptoms include pain and symptoms of arthritis, their deformities, fatigue, and malaise [1]. There is a known link between the autoimmune processes that underlie rheumatic diseases and mental disorders [2]. Therefore, the aim of our article is to present the symptoms and mental disorders occurring in the course of selected rheumatic diseases.

### State of the art

#### Systemic lupus erythematosus

The psychological symptoms are characteristic of systemic lupus erythematosus. The disease classification criteria according to EULAR / ACR 2019, used to diagnose the disease (European League Against Rheumatism / American College of Rheumatology classification criteria for systemic lupus erythematosus) include symptoms such as: delirium and psychosis[3]. Moreover, a form of lupus called NSPLE (neuropsychiatric systemic lupus erythematosus) is specified, which includes neuropsychiatric symptoms in the course of systemic lupus erythematosus. In their meta-analysis, Meszaros et al. emphasize the fact that psychiatric symptoms occur in the vast majority of patients suffering from systemic lupus

erythematosus (SLE). Its most common indicators are cognitive dysfunction (even in 80% of people) and depression (even in 39%)[4], although other studies report a slightly higher incidence of anxiety disorders than depression[5]. In most cases, the cognitive decline is mild to moderate[6], while severe cognitive impairment affects from 3% to 5%[7]. Disturbances in attention, visual and verbal memory and executive functions are characteristic [5]. In turn, psychosis is extremely rare, most often secondary in patients treated with high doses of glucocorticosteroids [8,9]; in one study it occurred in 1 in 85 subjects[10]. Interestingly, psychosis develops most often in the first year of the disease and its symptoms disappear after intensive immunosuppressive treatment [11]. It should be emphasized that some patients experience symptoms for the first time after initiating glucocorticoid therapy, making it sometimes difficult to decide what is causing them [12]. A cohort study by Fernandez et al. also showed a higher incidence of psychiatric symptoms among patients receiving corticosteroids, but the relationship was not statistically significant[10].

#### **Primary Sjogren's Syndrome**

Taiwanese authors showed a significantly increased risk of depression, anxiety and sleep disorders in patients with primary Sjogren's syndrome compared to the general population, and the risk was higher in women, but it should be remembered that Sjogren's syndrome affects the female gender much more often [13]. Also the occurrence of bipolar disorder [14] and schizophrenia [15] it is more common among people with Sjogren's syndrome. Importantly, neuropsychiatric symptoms may affect up to 80% of patients with primary Sjogren's syndrome, with 50% - 80% of cases ahead of diagnosis[16]. Patients with primary Sjogren's syndrome may also have an increased incidence of cognitive impairment, which may precede the diagnosis of the disease by an average of two years. In most cases, they are presented as brain fog or MCI (Mild Cognitive Impairment) [17]. According to the data presented by Morreale et al. 31.1% of 87 patients with recently diagnosed primary Sjogren's syndrome had cognitive dysfunctions consistent with dementia[18] and in another study, 11% of people were diagnosed with severe severe cognitive impairment [19]. Interestingly, Chinese scientists have shown that people with primary Sjogren's syndrome are neurotic [20]. The literature also includes case reports of patients suffering from this rheumatic disease presenting psychotic symptoms, therefore primary Sjogren's syndrome should be considered in the differential diagnosis of people showing new psychotic symptoms [21,22].

#### **Rheumatoid arthritis**

One of the studies reporting the prevalence of psychiatric disorders in people with rheumatoid arthritis showed a higher incidence of depression (incidence rate [IRR] 1.46 [95% confidence interval (95% CI) 1.35-1.58, anxiety disorders (IRR 1, 24 [95% CI 1.15-1.34], bipolar disorder (IRR 1.21 [95% CI 1.00-1.47][23]. The results of studies on the incidence of schizophrenia are interesting. The first of them was carried out in the 1950s, when the protective effect of schizophrenia on the development of rheumatoid arthritis was

demonstrated [24]. This is somewhat contradicted by the study by Eaton et al., according to which the risk of developing rheumatoid arthritis (RA) is slightly higher compared to the general population. The authors emphasized, however, that the study required a diagnosis of RA before the diagnosis of schizophrenia, while in most cases this rheumatic disease begins somewhat later.[25]. Regarding the prevalence of schizophrenia in RA patients, studies have shown both a reduced risk of developing the disease[26], increased (hazard ratio [HR] = 0.69, 95% CI = 0. 59-0.80), similar to ankylosing spondylitis[27] and no relationship[23].

#### Systemic sclerosis

It has been proven that systemic sclerosis causes microvascular damage, which may cause neuropsychiatric symptoms in the form of mood disorders, anxiety and cognitive disorders [28]. The prevalence of major depressive disorders is estimated from 17% to 69% [29]. Compared to rheumatoid arthritis patients, people with systemic sclerosis experience less severe body pain and disability, but tend to report more symptoms of depression [30]. Interestingly, people suffering from this rheumatic disease showed significantly more severe symptoms of depression and anxiety in the study than patients with melanoma [31]. A study by Yilmaz et al. showed significantly lower results in neuropsychiatric tests assessing cognitive functions than control groups, however, according to the authors, problems with attention and memory may also be influenced by chronic drug use and the duration of the disease [32]. There have also been reports of psychotic symptoms in the course of scleroderma, such as paranoid delusions, perceptual disturbances, disorientation [32]. On the other hand, a study conducted on 30 patients with scleroderma showed significantly increased symptoms of anxiety, feeling of guilt, symptoms of depression[33].

#### Fibromyalgia

Fibromyalgia is characterized by extensive pain accompanied by fatigue, memory and sleep disturbances. Patients suffering from this disease are more likely to suffer from depression, anxiety disorders, obsessive-compulsive disorder or post-traumatic stress disorder [34]. The meta-analysis by Alciati et al. showed the prevalence of severe depressive episodes up to 70% -86% [35]. On the other hand, people with a history of bipolar disorder and fibromyalgia have a high percentage of manic or hypomanic symptoms [35]. In the study by Cart et al. the proportion of patients with mania symptoms was 59%, which was more than twice as high as in the control group [36]and this was also confirmed in another study[37]. The risk of suicide in people suffering from fibromyalgia is even ten times higher, which may be related to the high prevalence of bipolar disorder in this group of patients [35,38]. In terms of sleep disorders, such as difficulty falling asleep, night awakenings or sleep not providing sufficient rest, it has been estimated that it may affect over 90% of patients. Importantly, non-regenerative sleep is classified as a highly disruptive symptom, along with pain, morning stiffness and fatigue.[39].

#### Ankylosing spondylitis

Another rheumatic disease in which symptoms of depression, anxiety disorders and sleep disturbances are common is ankylosing spondylitis. It should be emphasized that, apart from the above-mentioned symptoms, there are few studies on other disorders in the literature. In one study, disease activity, functional performance, and the incidence of pain and fatigue were positively correlated with symptoms of somatization, sleep disturbance, phobic anxiety, depression, psychoticism, and paranoid thoughts [40].

#### **Rheumatic fever**

Studies have been carried out to determine the prevalence of symptoms and mental disorders among people with rheumatic fever, especially in terms of obsessive-compulsive disorder. Already in an article published in 2000, it was shown in this group of people, where people with Sydenham's chorea presented more frequent severe depressive disorders, tics and hyperactivity disorder. Moreover, the symptoms of ADHD (attention deficit hyperactivity disorder), were associated with a higher risk of developing Sydenham's Chorea[41]. The fact of the higher incidence of obsessive-compulsive disorder was confirmed by studies conducted by Alvareng et al. in the group of people with heart disease or a history of rheumatic fever[41] and made by the same scientist on a sample of 678 people [42]. In contrast, another Brazilian study found that Generalized Anxiety Disorder was more common in first-degree relatives of people with febrile neutropenia[43].

#### **Summary**

In the course of all rheumatic diseases presented by us, there are symptoms and mental disorders. They are often mood, cognitive and sleep disturbances. Moreover, the occurrence of psychotic symptoms can also be observed. Probably some of them may be caused by the stress associated with the disease, but it seems that psychiatric symptoms have a multifactorial etiology and are also related to the mechanisms underlying rheumatic diseases and microvascular changes.

#### **Bibliography**

- [1] 10 things you should know about rheumatic diseases n / a: https: //www.eular.org/myUploadData/files/10%20thin. www.eular.org (accessed May 29, 2022).
- [2] Jeppesen R, Benros ME. Autoimmune Diseases and Psychotic Disorders. Front Psychiatry 2019; 10: 131. https://doi.org/10.3389/FPSYT.2019.00131.

- [3] Aringer M, Costenbader K, Daikh D, Brinks R, Mosca M, Ramsey-Goldman R, et al. 2019 European League Against Rheumatism / American College of Rheumatology classification criteria for systemic lupus erythematosus. Ann Rheum Dis 2019; 78: 1151–9. https://doi.org/10.1136/annrheumdis-2018-214819.
- [4] Meszaros ZS, Perl A, Faraone S V. Psychiatric symptoms in systemic lupus erythematosus: a systematic review. J Clin Psychiatry 2012; 73: 993–1013. https://doi.org/10.4088/JCP.11R07425.
- [5] Fanouriakis A, Bertsias G, Govoni M. Editorial: Lupus and the Brain: Advances in Neuropsychiatric Systemic Lupus Erythematosus. Front Med 2019; 6. https://doi.org/10.3389/FMED.2019.00052.
- [6] Kozora E, Thompson LL, West SG, Kotzin BL. Analysis of cognitive and psychological deficits in systemic lupus erythematosus patients without overt central nervous system disease. Arthritis Rheum 1996; 39: 2035–45. https://doi.org/10.1002/ART.1780391213.
- [7] Huerta PT, Gibson EL, Rey C, Huerta TS. Integrative neuroscience approach to neuropsychiatric lupus. Immunol Res 2015; 63: 11–7. https://doi.org/10.1007/S12026-015-8713-6.
- [8] Sergent JS, Lockshin MD, Klempner MS, Lipsky BA. Central nervous system disease in systemic lupus erythematosus: Therapy and prognosis. Am J Med 1975; 58: 644–54. https://doi.org/10.1016/0002-9343(75)90500-8.
- [9] Chau SY, Mok CC. Factors predictive of corticosteroid psychosis in patients with systemic lupus erythematosus. Neurology 2003; 61: 104–7. https://doi.org/10.1212/WNL.61.1.104.
- [10] Fernandez H, Cevallos A, Jimbo Sotomayor R, Naranjo-Saltos F, Mera Orces D, Basantes E. Mental disorders in systemic lupus erythematosus: a cohort study. Rheumatol Int 2019; 39: 1689–95. https://doi.org/10.1007/S00296-019-04423-4.
- [11] Pego-reigosa JM, Isenberg DA. Psychosis due to systemic lupus erythematosus: characteristics and long-term outcome of this rare manifestation of the disease. Rheumatology (Oxford) 2008; 47: 1498– 502.https://doi.org/10.1093/RHEUMATOLOGY/KEN260.
- [12] Fujieda Y. Diversity of neuropsychiatric manifestations in systemic lupus erythematosus. Immunol Med 2020; 43: 135–41. https://doi.org/10.1080/25785826.2020.1770947.
- [13] Hsieh MC, Hsu CW, Lu MC, Koo M. Increased risks of psychiatric disorders in patients with primary Sjögren's syndrome-a secondary cohort analysis of nationwide, population-based health claim data. Clin Rheumatol 2019; 38: 3195–203. https://doi.org/10.1007/S10067-019-04705-Z.
- [14] Wang LY, Chiang JH, Chen SF, Shen YC. Systemic autoimmune diseases are associated with an increased risk of bipolar disorder: A nationwide population-based cohort study. J Affect Disord 2018; 227: 31–7. https://doi.org/10.1016/J.JAD.2017.10.027.
- [15] Eaton WW, Byrne M, Ewald H, Mors O, Chen CY, Agerbo E, et al. Association of

schizophrenia and autoimmune diseases: Linkage of Danish national registers. Am J Psychiatry 2006; 163: 521–8. https://doi.org/10.1176/APPI.AJP.163.3.521/ASSET/IMAGES/LARGE/Q228T4.JPEG.

- [16] Ravan JR, Chatterjee S, Singh P, Maikap D, Padhan P. Autoimmune Rheumatic Diseases Masquerading as Psychiatric Disorders: A Case Series. Mediterr J Rheumatol 2021; 32: 164. https://doi.org/10.31138/MJR.32.2.164.
- [17] Manzo C, Martinez-Suarez E, Kechida M, Isetta M, Serra-Mestres J. Cognitive Function in Primary Sjögren's Syndrome: A Systematic Review. Brain Sci 2019; 9. https://doi.org/10.3390/BRAINSCI9040085.
- [18] Morreale M, Francia A, Marchione P, Manuppella F, Giacomini P. Intracranial hemodynamic changes in primary Sjögren syndrome: a transcranial Doppler casecontrol study. Neurol Sci 2015; 36: 1589–95. https://doi.org/10.1007/S10072-015-2204-3.
- [19] Tezcan ME, Kocer EB, Haznedaroglu S, Sonmez C, Mercan R, Yucel AA, et al. Primary Sjögren's syndrome is associated with significant cognitive dysfunction. Int J Rheum Dis 2016; 19: 981–8. https://doi.org/10.1111/1756-185X.12912.
- [20] Wang Y, Wang SL, Zou YZ LG. Psychiatric and central nervous system involvement in Sjogren's syndrome. Zhonghua Kou Qiang Yi Xue Za Zhi 2004; 39 (2): 158-: 158-60.
- [21] Hammett EK, Fernandez-Carbonell C, Crayne C, Boneparth A, Cron RQ, Radhakrishna SM. Adolescent Sjogren's syndrome presenting as psychosis: a case series. Pediatrician Rheumatol Online J 2020; 18. https://doi.org/10.1186/S12969-020-0412-8.
- [22] Wong JKF, Nortley R, Andrews T, D'Cruz D. Psychiatric manifestations of primary Sjögren's syndrome: a case report and literature review. BMJ Case Rep 2014; 2014. https://doi.org/10.1136/BCR-2012-008038.
- [23] Marrie RA, Hitchon CA, Walld R, Patten SB, Bolton JM, Sareen J, et al. Increased Burden of Psychiatric Disorders in Rheumatoid Arthritis. Arthritis Care Res 2018; 70: 970–8. https://doi.org/10.1002/ACR.23539/ABSTRACT.
- [24] Jeppesen R, Benros ME. Autoimmune diseases and psychotic disorders. Front Psychiatry 2019; 10: 131. https://doi.org/10.3389/FPSYT.2019.00131/BIBTEX.
- [25] Eaton WW, Byrne M, Ewald H, Mors O, Chen CY, Agerbo E, et al. Association of schizophrenia and autoimmune diseases: linkage of Danish national registers. Am J Psychiatry 2006; 163: 521–8. https://doi.org/10.1176/APPI.AJP.163.3.521.
- [26] Cullen AE, Holmes S, Pollak TA, Blackman G, Joyce DW, Kempton MJ, et al. Associations Between Non-neurological Autoimmune Disorders and Psychosis: A Meta-analysis. Biol Psychiatry 2019; 85: 35–48. https://doi.org/10.1016/J.BIOPSYCH.2018.06.016.
- [27] Sellgren C, Frisell T, Lichtenstein P, Landen M, Askling J. The association between schizophrenia and rheumatoid arthritis: a nationwide population-based Swedish study on intraindividual and familial risks. Schizophr Bull 2014; 40: 1552–9. https://doi.org/10.1093/SCHBUL/SBU054.

- [28] McNair S, Hategan A, Bourgeois JA, Losier B. Neuropsychiatric symptoms in scleroderma. Psychosomatics 2013; 54: 382–6. https://doi.org/10.1016/J.PSYM.2012.09.002.
- [29] GM, Bhat KM, AP, GL, MG C. Psychiatric Symptoms and Quality of Life in Systemic Sclerosis. Clin Pract Epidemiol Ment Health 2012; 8:30. https://doi.org/10.2174/1745017901208010030.
- [30] Danieli E, Airò P, Bettoni L, Cinquini M, Antonioli CM, Cavazzana I, et al. Healthrelated quality of life measured by the Short Form 36 (SF-36) in systemic sclerosis: correlations with indexes of disease activity and severity, disability, and depressive symptoms. Clin Rheumatol 2005; 24: 48–54. https://doi.org/10.1007/S10067-004-0970-Z.
- [31] Mozzetta A, Antinone V, Alfani S, Neri P, Bonda PGF, Pasquini P, et al. Mental health in patients with systemic sclerosis: a controlled investigation. J Eur Acad Dermatol Venereol 2008; 22: 336–40. https://doi.org/10.1111/J.1468-3083.2007.02426.X.
- [32] Yilmaz N, Mollahasanoglu A, Gurvit H, Can M, Tuncer N, Ananc N, et al. Dysexecutive syndrome: A specific pattern of cognitive impairment in systemic sclerosis. Cogn Behav Neurol 2012; 25: 57–62. https://doi.org/10.1097/WNN.0B013E3182593C75.
- [33] Angelopoulos N V., Drosos AA, Moutsopoulos HM. Psychiatric symptoms associated with scleroderma. Psychother Psychosom 2001; 70: 145–50. https://doi.org/10.1159/000056240.
- [34] Clauw DJ. Fibromyalgia: a clinical review. JAMA 2014; 311: 1547–55. https://doi.org/10.1001/JAMA.2014.3266.
- [35] Alciati A, Sgiarovello P, Atzeni F, Sarzi-Puttini P. Psychiatric problems in fibromyalgia: clinical and neurobiological links between mood disorders and fibromyalgia. Reumatismo 2012; 64: 268–74. https://doi.org/10.4081/REUMATISMO.2012.268.
- [36] Carta MG, Cardia C, Mannu F, Intilla G, Hardoy MC, Anedda C, et al. The highfrequency of manic symptoms in fibromyalgia does influence the choice of treatment? Clin Pract Epidemiol Ment Health 2006; 2. https://doi.org/10.1186/1745-0179-2-36.
- [37] Dell'Osso L, Bazzichi L, Consoli G, Carmassi C, Carlini M, Massimetti E, Giacomelli C, Bombardieri S CA. A. Manic spectrum symptoms are correlated to the severity of pain and the health-related quality of life in patients with fibromyalgia. Clin Exp Rheumatol 2009; Sep-Oct; 27: 57–61.
- [38] Dreyer L, Kendall S, Danneskiold-Samsøe B, Bartels EM, Bliddal H. Mortality in a cohort of Danish patients with fibromyalgia: increased frequency of suicide. Arthritis Rheum 2010; 62: 3101–8. https://doi.org/10.1002/ART.27623.
- [39] Roizenblatt S, Neto NSR, Tufik S. Sleep disorders and fibromyalgia. Curr Pain Headache Rep 2011; 15: 347–57. https://doi.org/10.1007/S11916-011-0213-3.
- [40] Durmus D, Sarisoy G, Alayli G, Kesmen H, Çetin E, Bilgici A, et al. Psychiatric symptoms in ankylosing spondylitis: their relationship with disease activity, functional

capacity, pain and fatigue. Compr Psychiatry 2015; 62: 170–7. https://doi.org/10.1016/J.COMPPSYCH.2015.07.016.

- [41] Mercadante MT, Busatto GF, Lombroso PJ, Prado L, Rosario-Campos MC, Do Valle R, et al. The psychiatric symptoms of rheumatic fever. Am J Psychiatry 2000; 157: 2036–8. https://doi.org/10.1176/APPI.AJP.157.12.2036.
- [42] de Alvarenga PG, Floresi AC, Torres AR, Hounie AG, Fossaluza V, Gentil AF, et al. Higher prevalence of obsessive-compulsive spectrum disorders in rheumatic fever. Gen Hosp Psychiatry 2009; 31: 178–80. https://doi.org/10.1016/J.GENHOSPPSYCH.2008.11.003.
- [43] Seixas AAA, Hounie AG, Fossaluza V, Curi M, Alvarenga PG, De Mathis MA, et al. Anxiety disorders and rheumatic Fever: is there an association? CNS Spectr 2008; 13: 1039–46. https://doi.org/10.1017/S1092852900017090.