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## Article

# The Association Between the Occurrence of Sensory Integration Disorders, Depression, and Chronic Fatigue Syndrome in Patients with Relapsing-Remitting Multiple Sclerosis

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## Abstract

**Background:** Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system associated with both motor and non-motor symptoms. Depression and chronic fatigue syndrome (CFS) are frequent in relapsing–remitting MS (RRMS), but the role of sensory integration disorders (SID) remains unclear. **Methods:** This cross-sectional study included 205 RRMS patients (147 females, 58 males; aged 19–69 years) treated at the Pomeranian Medical University, Szczecin (2022–2023). SID were evaluated using the Daniel Travis Questionnaire, depression using the Beck Depression Inventory (BDI), fatigue using the Fatigue Scale for Motor and Cognitive Functions (FSMC), and disability using the Expanded Disability Status Scale (EDSS). MRI T2 lesion counts and relapse rates were analyzed using non-parametric tests ( $p < 0.05$ ). **Results:** SID were significantly associated with depression severity. Patients with moderate to severe depression showed greater impairment in sensory discrimination, motor abilities, and emotional functioning ( $p < 0.05$ ). Higher disability (EDSS  $> 3$ ) and longer disease duration correlated with worse SID scores. Relapse frequency was linked to poorer sensory-seeking and emotional domains, while no association was found between SID and CFS or MRI lesion load. **Conclusions:** SID are prevalent in RRMS and correlate with depression, disease duration, and disability, suggesting potential therapeutic value in sensory-based rehabilitation.

**Keywords:** multiple sclerosis; sensory integration disorder; depression; fatigue; relapsing–remitting MS

## Introduction

Multiple sclerosis (MS) is a chronic, incurable disease of the central nervous system, the direct cause of which remains unknown, although an autoimmune background is assumed. The disease has a varied course, but systematically leads to neurological deterioration and is the most common non-traumatic cause of disability in young adults. The disease process involves the formation of diffuse foci of demyelination, as well as degeneration of the white and gray matter of the central nervous system. Depending on the location of the foci of damage, a range of clinical manifestations are observed [1,2].

In addition to the symptoms of focal damage to the central nervous system in patients with MS, attention is also drawn to the high frequency of non-motor symptoms such as chronic fatigue syndrome (CFS), which can affect up to 80% of patients, depression (15–56% of patients in the later stages of the disease), cognitive dysfunction (11–67% of patients) [3].

CFS in MS is defined as a multifactorial pathology—both as a result of damage to the central nervous system in the course of MS, as well as a disorder caused by general weakness, sleep and

mood disturbances, and side effects of the disease modifying treatment used [4]. CFS definitely negatively affects the quality of life of patients with MS [5].

Depressive disorders are present in approximately 50% of MS patients. They are two to three times more common in this group than in the general population. They negatively impact quality of life and treatment outcomes and become significantly more common as the disease progresses [6,7]. The pathophysiological basis of this process in MS is multifactorial, similar to that in CFS. Neuroanatomical factors such as activation of hippocampal microglia, spreading demyelinating lesions, and atrophy of the cerebral cortex in strategic regions have been implicated, as well as adaptive factors resulting from the diagnosis of a severe, incurable, and potentially progressive degenerative disease [7]. Common mechanisms have been suggested to play a role in the development of both CFS and depression, including psychological factors or brain damage in specific neuroanatomical pathways [7,8].

Recently, increasing importance has also been placed on somatosensory integration disorders [9–11].

The basis of somatosensory integration is that human motor and cognitive functioning is closely linked to the integration of stimuli from visual, auditory, tactile, olfactory, gustatory, vestibular and proprioceptive receptors. These stimuli are appropriately organized in the central nervous system and then used to formulate perception, learning, behavior, emotions, movement planning, muscle tension, among others.

Sensory integration dysfunctions influence the ability to organize sensory information, motor and cognitive performance.

One of the most well-established approaches to SID has been proposed by Winnie Dunn and her four-quadrant model of sensory processing [12].

According to this model, sensory processing consists of a neurological threshold (high or low) and a behavioral response.

A high neurological threshold refers to individuals who are hypersensitive and may represent two behavioral patterns, depending on their response strategy:

(1) sensation-seeking - the individual represents an active response strategy and will seek out stimulus-rich environments to enhance the response;

(2) low registration - the individual represents a passive response strategy and will show slow or no response to stimuli.

Low neurological threshold, on the other hand, refers to hypersensitivity and the following two behavioral patterns:

(3) sensation avoidance-an active response strategy that results in the avoidance of sensations that are uncomfortable for the person;

(4) sensitivity to sensations-a passive response strategy to sensations that may be unpleasant [12–14].

In both SID and MS, there may be some common symptoms, such as sensory abnormalities-central and musculoskeletal pain, limb paresthesias, allodynia (hypersensitivity in response to stimuli), dysesthesias, decreased vibration sensation or Lhermitte's sign [9,15]. Sensory integration disorders in patients with MS mainly involve the motor and sensory spheres [10].

To date, few studies have been conducted in area of sensory integration disorders in patients with MS.

Stern et al. showed that individuals with higher sensory sensitivity, sensation avoidance and a low registration pattern had higher levels of anxiety compared to the general population, as well as lower mental and physical health-related quality of life. The pattern of sensation-seeking, on the other hand, showed the opposite characteristics, which the authors believe could suggest a potential protective factor in MS [16]. Hebert et al. showed that sensory integration disorders influenced postural disorders in patients with MS [17]. Another study observed that training targeting sensory integration disorders had a beneficial effect on balance disorders in MS patients, as well as on quality of life and improvements in their perceived fatigue [18,19].

As of today, the association between the occurrence of chronic fatigue syndrome and depressive disorders in patients with MS seems fairly well documented, while little is known about the association of these disorders with somatosensory integration disorders. The association of somatosensory integration disorders with the course of MS has not yet been studied.

## Aims

The purpose of this study is to demonstrate whether there is an association between somatosensory integration disorders in patients with relapsing- remitting MS and other features, such as: the occurrence of chronic fatigue syndrome, depression and whether somatosensory integration disorders in patients with the relapsing- remitting form of MS is related to the duration and severity of the disease.

## Material and Methods

The study included 205 patients (147 females and 58 males), aged 19 to 69 years with a diagnosis of the relapsing- remitting form of MS, treated in the National Health Insurance Drug Program at the Department of Neurology of the Pomeranian Medical University in Szczecin between January 2022 and March 2023.

Patients with MS meeting the following criteria were included in the study:

- age over 18 years,
- a diagnosis of a relapsing- remitting form of multiple sclerosis,
- active disease- modifying treatment in the NHI Drug Program
- the absence of a disease relapse detected in the last 8 weeks as a factor that could significantly affect the patients' perceived level of fatigue and tiredness

All patients signed informed consent to participate in the study.

The following were excluded from the study:

- patients under 18 years of age,
- patients with secondary or primary progressive forms of the disease,
- patients who had experienced a relapse 8 weeks prior to study eligibility.

**The Daniel Travis questionnaire for people over the age of 18 was used to investigate somatosensory integration disorders** [Supplementary materials].

It distinguishes between the domains of general modulation (9 statements), overreactivity (26 statements), inadequate response/sensory seeking (20 statements), sensory discrimination (26 statements), sensory-based motor abilities (19 statements), and social and emotional (22 statements).

Each symptom was rated by the survey participant using a 5-point Likert scale from 0 (never occurred) to 4 (occurs regularly). If the problem had occurred in the past but no longer occurs, the participant entered a P. The sum obtained by adding the values in each domain indicated the severity of the somatosensory integration disorder in that domain.

An increased frequency or high severity of symptoms may suggest a sensory integration disorder; however, further evaluation is needed.

The Daniel Travis questionnaire was previously used on the Polish population with the supervision of a certified sensory integration therapist. In our study, one of the authors is a certified Ayres Sensory Integration Therapist and Sensorisch-Integrative Ayres Therapie.

**Depressive disorders** were diagnosed by assessment based on the Beck Depression Inventory scale (BDI). This is a scale used in the screening diagnosis of depression, by Aaron Beck.

This test consists of 21 questions, which the patient answers independently. There are 4 possible answer variants, which are scored differently. Subsequent response variants correspond to increased intensity of symptoms, so they are appropriately incrementally scored from 0 to 3 points [91].

The level of depression is calculated from the number of points obtained after summing.

For the purpose of statistical calculations, a division into the following subgroups was adopted:

- subgroup A with a total score of 0-11- no depression or depressed mood;

- subgroup B with a total score of 12- 19- mild depression
- subgroup C with a total score of 20-25- moderate depression;
- subgroup D with a total score of 26 or more- severe depression [Supplementary materials].

**The degree of disability resulting from the disease** was determined based on the 10-point EDSS scale.

This scale consists of functional subscales to assess the function of vision, brainstem, pyramidal system, cerebellum, sensory system, sphincter and higher cerebral functions, and also includes an assessment of mobility and self-care. A score of 0 indicates normal neurological status, and 10 indicates death from MS.

Based on the sum of scores in each functional subscale, the patient gets a final score - both whole and half points are possible. A score of more than 4 points already means a reduction in walking distance to 500, 200 and 100 meters, respectively, 6 points means permanent or intermittent unilateral walking assistance, 7 points means moving mainly in a wheelchair, and 9 points means a recumbent patient [Supplementary materials].

Depending on the EDSS score for the purpose of statistical calculations, patients were divided into two subgroups:

- subgroup E- EDSS scale score greater than or equal to 3
- subgroup F- EDSS scale score less than 3

A score of 3 on the EDSS scale indicates a noticeable disability. In terms of the scale, this is either moderate impairment in one functional subscale score or mild functional impairment in 3 or 4 functional subscales; the patient remains fully walking.

**The disease duration** was determined on the basis of available medical records assuming the time from the establishment of the MS diagnosis. The history of the first symptoms was also taken into account, and those patients whose time from the first symptoms of the disease to the establishment of the diagnosis was longer than one year were not included in the study.

For the purpose of statistical calculations, patients were divided into subgroups in this respect:

- subgroup G- duration of disease up to 5 years
- subgroup H- disease duration between 5 and 10 years
- subgroup J- disease duration of more than 10 years

#### **Chronic fatigue syndrome**

The occurrence of chronic fatigue syndrome was based on a questionnaire survey including a validated questionnaire for chronic fatigue syndrome - Fatigue Syndrome Scale for Motor and Cognitive Functions (FSMC) [supplementary materials].

A license was purchased to use this scale for the purposes of the conducted study (scale by Prof. Dr. Iris- Katharina Penner, agreement between Pomeranian Medical University in Szczecin and Clinical Neuroscience Consulting GmbH, Chemin du Chardon Bleu 24, 1882 Gryon, Switzerland, signed on 25.04.2018).

This questionnaire consists of 20 questions, which are answered by the patient on a 5-point Likert scale from 1 ("doesn't affect me at all") to 5 ("fully affects me"). The individual questions are grouped into those relating to the spheres of cognitive fatigue and motor fatigue. The maximum possible sum of points is 100, and total fatigue syndrome is diagnosed with a sum of points greater than or equal to 43. Values between 43 and 52 points indicate mild fatigue syndrome, between 53 and 62 indicate moderate fatigue syndrome, and values above 63 indicate severe fatigue syndrome. In terms of questions on cognitive functioning, total scores between 22 and 27 indicate mild "cognitive fatigue," between 28 and 33 indicate moderate "cognitive fatigue," and above 33 indicate severe fatigue syndrome in terms of cognitive functioning. The same is true for questions on "motor fatigue," where score values between 22 and 26 indicate "mild motor fatigue," 27 to 31 for "moderate motor fatigue," and above 32 for "severe motor fatigue."

Patients with a total score greater than or equal to 43 were classified as those with chronic fatigue syndrome and patients with a total score less than 43 were classified as those without chronic fatigue syndrome.

**Evaluation of the number of hyperintense lesions in T2-dependent sequences on MRI** of the brain in patients with the relapsing- remitting form of MS

In each patient, the most recent of the control routinely performed MRI examinations of the brain with contrast were considered. MRI examinations of the brain with contrast were performed at the Department of Imaging Diagnostics and Interventional Radiology at USK 1 PUM in Szczecin (headed by Prof. Wojciech Poncyłjusz, MD, PhD). A 1.5 Tesla MRI model Discovery 450 from General Electric with gradients of 50 mT (multitesla/meter) in all three axes was used.

The number of hyperintense lesions in T2- dependent sequences was assessed.

For statistical purposes, patients were divided into three subgroups:

- subgroup K—number of changes in the T2-dependent sequence below 10
- subgroup L—number of changes in the T2-dependent sequence between 10 and 20
- subgroup M - number of changes in the T2-dependent sequence above 20

**The disease activity** was defined as the number of relapses in the last year. For the purposes of statistical analysis, patients were divided into three subgroups:

- subgroup N- patients who have not experienced a relapse of the disease during the last year
- subgroup O- patients who have experienced one relapse of the disease during last year
- subgroup P- patients who experienced two or more relapses during the last year

The association of somatosensory integration disorders with chronic fatigue syndrome and disease duration and severity was also analyzed, taking into account annual relapse rate, degree of disability level on the EDSS scale, and radiological disease activity.

**Statistical analysis**

Quantitative variables were analyzed using the arithmetic mean, taking into account the minimum, maximum and standard deviation values, in addition to the median, lower and upper quartiles.

For the analysis of qualitative variables, percentages and counts of the variable were used. Levene's test revealed heterogeneity of variance across groups and subgroups of patients ( $p<0.05$ ). Accordingly, and due to the distribution of the data analyzed in the study deviating from the normal distribution (Shapiro-Wilk test,  $p<0.05$ ), groups of variables were compared using non-parametric tests: for two groups the Whitney U-Mann test, for three groups the Kruskal-Wallis rank ANOVA test and the median test.

For the analysis of qualitative variables, Pearson's chi-square test was used for 2 x 2 tables.

The behavior of the variables was illustrated using tables and histograms.

The significance level for the analyzed variables was taken as  $p< 0.05$ .

The licensed program STATISTICA version 13.3 was used for statistical analysis.

For the presented study, an exemption was obtained from the need to obtain an opinion from the Bioethics Committee with the number KB.006.34.2023

**Results**

**Table 1.** Characteristics of the study group of patients with relapsing-remitting MS.

| Data            |        | n=205        |
|-----------------|--------|--------------|
| sex             | female | 147 (71.70%) |
|                 | male   | 58 (28.29%)  |
| Age ( mean)     |        | 39.08        |
| Beck Depression | A      | 137 (67.16%) |

|                                                |   |               |
|------------------------------------------------|---|---------------|
| Inventory                                      | B | 36 (17.65%)   |
|                                                | C | 17 (8.33%)    |
|                                                | D | 15 (7.35%)    |
| EDSS                                           | E | 44 (21.46%)   |
|                                                | F | 160 (78.04%)  |
| Disease duration                               | G | 60 (29.26%)   |
|                                                | H | 77 (37.56%)   |
|                                                | J | 68 (33.17%)   |
| Patients with chronic fatigue syndrome         |   | 135 (65.85%)  |
| Patients without chronic fatigue syndrome      |   | 70 (34.15%)   |
| Number of lesions in T2-weighted images on MRI | K | 20 (9.75%)    |
|                                                | L | 78 (38.04%)   |
|                                                | M | 107 (52.19%)  |
| Disease activity                               | N | 156 (76.097%) |
|                                                | O | 34 (16.585% ) |
|                                                | P | 14 (6.829%)   |

Women predominated in the study group (71.70% vs. 28.29%). Most of the patients (61.16%) did not show symptoms of depression. In the study group, most patients had a disability level resulting from the disease according to the EDSS scale lower than 3 points (78.04% vs. 21.46%). The vast majority of patients experienced chronic fatigue syndrome (65.85% vs. 34.14%). In the study group, most patients did not experience a relapse of the disease in the last year (76.097%).

Table 2 presents SI disorders in patients with relapsing-remitting MS who experienced mood swings without depressive disorders (group A), with mild depressive disorders (group B), with moderate depressive disorders (group C), and with severe depressive disorders (group D)

**Table 2.** Sensory integration disorders and depressive disorders.

| Variables                                                               |              | Subgroup A     | Subgroup B     | Subgroup C     | Subgroup D     | p-value |
|-------------------------------------------------------------------------|--------------|----------------|----------------|----------------|----------------|---------|
|                                                                         |              | n=137          | n=36           | n=17           | n=15           |         |
| General modulation<br><br>(points; mean ± SD)                           | gr A vs gr B | 9.027 ± 6.111  | 11.812 ± 7.566 | -              | -              | 0.796   |
|                                                                         | gr A vs gr C | 9.027 ± 6.111  | -              | 11.352 ± 6.688 |                | 1.000   |
|                                                                         | gr A vs gr D | 9.027 ± 6.111  | -              | -              | 14.266 ± 8.379 | 0.083   |
|                                                                         | gr B vs gr C | -              | 11.812 ± 7.566 | 11.812 ± 7.566 | -              | 1.000   |
|                                                                         | gr B vs gr D | -              | 11.352 ± 6.688 | -              | 14.266 ± 8.379 | 1.000   |
|                                                                         | gr C vs gr D | -              | -              | 11.812 ± 7.566 | 14.266 ± 8.379 | 1.000   |
| Over-Responsiveness<br><br>(points; mean ± SD)                          | gr A vs gr B | 24.194± 17.556 | 30.937± 19.124 | -              | -              | 0.414   |
|                                                                         | gr A vs gr C | 24.194± 17.556 | -              | 26.000±14.387  | -              | 1.000   |
|                                                                         | gr A vs gr D | 24.194± 17.556 |                |                | 37.000±24.833  | 0.280   |
|                                                                         | gr B vs gr C | -              | 30.937± 19.124 | 26.000±14.387  |                | 1.000   |
|                                                                         | gr B vs gr D | -              | 30.937± 19.124 |                | 37.000±24.833  | 1.000   |
|                                                                         | gr C vs gr D | -              |                | 26.000±14.387  | 37.000±24.833  | 1.000   |
| Under-Responsiveness<br><br>/Sensory Seeking<br><br>(points; mean ± SD) | gr A vs gr B | 18.513± 12.681 | 25.656± 10.997 | -              | -              | 0.040*  |
|                                                                         | gr A vs gr C | 18.513± 12.681 | -              | 20.294±12.553  | -              | 1.000   |
|                                                                         | gr A vs gr D | 18.513± 12.681 | -              | -              | 23.200±13.148  | 1.000   |
|                                                                         | gr B vs gr C | -              | 25.656± 10.997 | 20.294±12.553  | -              | 0.705   |
|                                                                         | gr B vs gr D | -              | 25.656± 10.997 | -              | 23.200±13.148  | 1.000   |
|                                                                         | gr C vs gr D | -              | -              | 20.294±12.553  | 23.200±13.148  | 1.000   |
| Sensory Discrimination<br><br>(points; mean ± SD)                       | gr A vs gr B | 14.972± 13.863 | 26.187± 18.774 | -              | -              | 0.017*  |
|                                                                         | gr A vs gr C | 14.972± 13.863 | -              | 22.117± 14.456 | -              | 0.333   |
|                                                                         | gr A vs gr D | 14.972± 13.863 | -              | -              | 35.000± 27.498 | 0.011*  |

|                                                            |                 |                |                |                |                |        |
|------------------------------------------------------------|-----------------|----------------|----------------|----------------|----------------|--------|
|                                                            | gr B vs gr C    | -              | 26.187± 18.774 | 22.117± 14.456 | -              | 1.000  |
|                                                            | gr B vs gr D    | -              | 26.187± 18.774 | -              | 35.000± 27.498 | 1.000  |
|                                                            | gr C vs gr D    | -              | -              | 22.117± 14.456 | 35.000± 27.498 | 1.000  |
| Sensory-Based<br>Motor Abilities<br>(points; mean ±<br>SD) | gr A vs gr B    | 16.263± 12.548 | 25.468± 18.656 | -              | -              | 0.112  |
|                                                            | gr A vs gr C    | 16.263± 12.548 | -              | 21.235± 11.070 | -              | 0.634  |
|                                                            | gr A vs gr D    | 16.263± 12.548 | -              | -              | 33.933±20.686  | 0.007* |
|                                                            | gr B vs gr C    | -              | 25.468± 18.656 | 21.235± 11.070 | -              | 1.000  |
|                                                            | gr B vs gr D    | -              | 25.468± 18.656 | -              | 33.933±20.686  | 1.000  |
|                                                            | gr C vs gr D    | -              | -              | 21.235± 11.070 | 33.933±20.686  | 1.000  |
| Social and<br>Emotional<br>(points; mean ±<br>SD)          | gr A vs gr<br>B | 19.180± 13.472 | 32.781± 20.298 | -              | -              | 0.006* |
|                                                            | gr A vs gr<br>C | 19.180± 13.472 | -              | 21.647± 13.605 | -              | 1.000  |
|                                                            | gr A vs gr<br>D | 19.180± 13.472 | -              | -              | 36.666± 22.388 | 0.014* |
|                                                            | gr B vs gr C    | -              | 32.781± 20.298 | 21.647± 13.605 | -              | 0.450  |
|                                                            | gr B vs gr<br>D | -              | 32.781± 20.298 | -              | 36.666± 22.388 | 1.000  |
|                                                            | gr C vs gr<br>D | -              |                | 21.647± 13.605 | 36.666± 22.388 | 0.279  |

Statistically worse results were demonstrated in the following domains: hypersensitivity, sensory discrimination, motor skills, social and emotional skills in subgroups diagnosed with depression compared to the subgroup without depression. The worst results in these domains were obtained by patients with severe depression.

Table 3 presents SI disorders in patients with MS who obtained an EDSS score for assessing the severity of disability of less than or equal to 3 (group E) and above 3 (group F).

Table 3. Sensory integration disorders in patients with MS and EDSS score.

| Variables                                                    | EDSS subgroup E<br><br>n=44 | EDSS subgroup F<br><br>n=160 | p-value |
|--------------------------------------------------------------|-----------------------------|------------------------------|---------|
| General modulation<br><br>(points; mean ± SD)                | 8.291± 6.483                | 9.977± 7.196                 | 0.116   |
| Over-Responsiveness<br><br>(points; mean ± SD)               | 20.571± 17.254              | 27.545± 20.626               | 0.054*  |
| Under-Responsiveness<br>/Sensory Seeking (points; mean ± SD) | 18.838± 12.425              | 17.454± 12.505               | 0.454   |
| Sensory Discrimination<br><br>(points; mean ± SD)            | 13.956± 14.705              | 23.090± 22.028               | 0.013*  |
| Sensory-Based Motor Abilities<br><br>(points; mean ± SD)     | 13.049± 13.162              | 25.545± 18.662               | 0.000*  |
| Social and Emotional<br><br>(points; mean ± SD)              | 18.987± 16.080              | 22.750± 19.241               | 0.289   |

Patients with a more severe degree of disability (scoring more than 3 points on the EDSS scale) had significantly more severe sensory hypersensitivity (p=0.054\*), sensory discrimination (p=0.013\*) and motor function (p=0.00\*) disorders.

Table 4 Shows SI disorders and disease duration from 0 to 5 years (group G), from 5 to 10 years (group H), and from 10 years (group J) in patients with relapsing-remitting MS.

Table 4. Sensory intergation disorders and disease duration.

| Variables                                     |              | Subgroup G<br><br>n=60 | Subgroup H<br><br>n=77 | Subgroup J<br><br>n=68 | p-value |
|-----------------------------------------------|--------------|------------------------|------------------------|------------------------|---------|
| General modulation<br><br>(points; mean ± SD) | gr G vs gr H | 6.916±6.410            | 9.454±6.936            | -                      | 0.038*  |
|                                               | gr G vr gr J | 6.916±6.410            | -                      | 9.173±6.375            | 0.037*  |
|                                               | gr H vr gr J | -                      | 9.454±6.936            | 9.173±6.375            | 1.000   |
| Over-                                         | gr G vs gr H | 17.950±15.839          | 22.870±18.088          | -                      | 0.390   |

|                                                                                       |              |               |               |               |        |
|---------------------------------------------------------------------------------------|--------------|---------------|---------------|---------------|--------|
| Responsiveness<br><br>s<br><br>(points; mean ±<br><br>SD)                             | gr G vr gr J | 17.950±15.839 | -             | 24.492±19.849 | 0.213  |
|                                                                                       | gr H vr gr J | -             | 22.870±18.088 | 24.492±19.849 | 1.000  |
| Under-<br>Responsiveness<br><br>/Sensory<br>Seeking<br><br>(points; mean ±<br><br>SD) | gr G vs gr H | 18.233±12.995 | 19.085±12.165 | -             | 1.000  |
|                                                                                       | gr G vr gr J | 18.233±12.995 | -             | 17.260±12.206 | 1.000  |
|                                                                                       | gr H vr gr J | -             | 19.085±12.165 | 17.260±12.206 | 0.589  |
| Sensory<br>Discrimination<br><br>(points; mean ±<br><br>SD)                           | gr G vs gr H | 12.033±13.675 | 16.220±14.626 | -             | 0.146  |
|                                                                                       | gr G vr gr J | 12.033±13.675 | -             | 18.797±20.895 | 0.232  |
|                                                                                       | gr H vr gr J | -             | 16.220±14.626 | 18.797±20.895 | 1.000  |
| Sensory-Based<br>Motor Abilities<br><br>(points; mean ±<br><br>SD)                    | gr G vs gr H | 11.200±11.732 | 15.441±13.258 | -             | 0.206  |
|                                                                                       | gr G vr gr J | 11.200±11.732 | -             | 19.884±18.881 | 0.042* |
|                                                                                       | gr H vr gr J | -             | 15.441±13.258 | 19.884±18.881 | 1.000  |
| Social and<br>Emotional<br><br>(points; mean ±<br><br>SD)                             | gr G vs gr H | 17.316±15.738 | 21.298±16.911 | -             | 0.420  |
|                                                                                       | gr G vr gr J | 17.316±15.738 | -             | 20.057±17.616 | 1.000  |
|                                                                                       | gr H vr gr J | -             | 21.298±16.911 | 20.057±17.616 | 1.000  |

It should be noted that patients with a shorter disease duration (less than 5 years) have significantly better overall SI parameters compared to groups with a disease duration of more than 5 years (more than 5 years p=0.038\* and more than 10 years p=0.037\*). Of course, As the duration of the disease increases, patients have poorer motor function compared to those with shorter disease duration (over 10 years of disease p=0.042\*), which is characteristic of the course of MS.

Patients with chronic fatigue syndrome scored worse on the somatosensory integration assessment in each domain than patients without fatigue. However, the differences were not statistically significant (p>0.5).

Table 5 presents sensory integration disorders in patients who have not experience a relapse of the disease during the last year (group N), experienced one relapse during last year (group O), and experienced two or more relapses during the last year (group P).

Table 5. Sensory integration disorders and disease activity.

| Variables                                                        |              | Subgroup N    | Subgroup O    | Subgroup P    | p-value |
|------------------------------------------------------------------|--------------|---------------|---------------|---------------|---------|
|                                                                  |              | n=156         | n=34          | n=14          |         |
| General modulation<br><br>(points; mean ± SD)                    | gr N vs gr O | 8.885± 6.940  | 7.235± 5.554  | -             | 0.783   |
|                                                                  | gr N vs gr P | 8.885± 6.940  | -             | 9.500± 5.761  | 1.000   |
|                                                                  | gr O vs gr P | -             | 7.235± 5.554  | 9.500± 5.761  | 0.519   |
| Over-Responsiveness<br><br>(points; mean ± SD)                   | gr N vs gr O | 21.821±18.498 | 21.000±17.250 | -             | 1.000   |
|                                                                  | gr N vs gr P | 21.821±18.498 |               | 27.428±17.447 | 0.496   |
|                                                                  | gr O vs gr P | -             | 21.000±17.250 | 27.428±17.447 | 0.653   |
| Under-Responsiveness /Sensory Seeking<br><br>(points; mean ± SD) | gr N vs gr O | 17.993±12.078 | 17.323±12.124 | -             | 1.000   |
|                                                                  | gr N vs gr P | 17.993±12.078 | -             | 27.642±14.221 | 0.039*  |
|                                                                  | gr O vs gr P | -             | 17.323±12.124 | 27.642±14.221 | 0.071   |
| Sensory Discrimination<br><br>(points; mean ± SD)                | gr N vs gr O | 15.872±17.624 | 13.382±13.268 | -             | 1.000   |
|                                                                  | gr N vs gr P | 15.872±17.624 | -             | 22.571±15.785 | 0.183   |
|                                                                  | gr O vs gr P | -             | 13.382±13.268 | 22.571±15.785 | 0.201   |
| Sensory-Based Motor Abilities<br><br>(points; mean ± SD)         | gr N vs gr O | 15.585±15.981 | 13.735±12.083 | -             | 1.000   |
|                                                                  | gr N vs gr P | 15.585±15.981 | -             | 22.214±14.417 | 0.107   |
|                                                                  | gr O vs gr P | -             | 13.735±12.083 | 22.214±14.417 | 0.169   |
| Social and Emotional<br><br>(points; mean ± SD)                  | gr N vs gr O | 19.689±17.050 | 15.205±13.035 | -             | 0.721   |
|                                                                  | gr N vs gr P | 19.689±17.050 | -             | 32.142±17.474 | 0.025*  |
|                                                                  | gr O vs gr P | -             | 15.205±13.035 | 32.142±17.474 | 0.007*  |

There were statistically significantly worse results in the domains of under- responsiveness/ sensory seeking ( $p=0.039^*$ ) and social and emotional abilities in the group of patients with one ( $p=0.025^*$ ) and two relapses ( $p=0.007^*$ ) in the last year compared to the group of patients without relapses.

No association was found between scores in any of the SID domains and the number of hyperintense lesions in the T2-weighted sequence in brain MRI.

## Discussion

One of the well-described features of CFS is hypersensitivity, not only to pain, but also to all external stimuli, from profound sensitivity in the neurovegetative system, sensory organs and in some central nervous system functions, to psychological aspects and sleep control [20].

Few studies have examined the characteristics of noise and lights hypersensitivities in adults with CFS or MS. For instance, studies have found prevalence rates of lights hypersensitivity among people with CFS to vary between 48–90. No study has determined prevalence rates for noise hypersensitivity among people with ME/CFS or MS [21].

According to data in the literature, patients with MS show features of somatosensory integration disorder regardless of their cognitive abilities, and impaired sensory processing translates into greater disease severity [18].

It has been noted that patterns of low registration, sensation avoidance and sensory sensitivity predispose to high cognitive fatigue and low quality of life, while sensation seeking predisposes to low cognitive fatigue and high quality of life [17].

From these observations arose our hypothesis that in CFS we can expect to see impaired somatosensory integration, especially in the domains of hypersensitivity, social and emotional abilities, and perhaps also hypersensitivity as sensation and stimulus avoidance or motor dysfunction.

The patients analyzed in the study with fatigue syndrome scored worse on the somatosensory integration assessment compared to patients without fatigue. However, the differences were not statistically significant.

Worse scores in the evaluation of somatosensory integration disorders in the analyzed group of MS patients were also associated with depression. This was true for sensory hypersensitivity, sensory discrimination, motor skills, and social and emotional abilities. In terms of general sensory processing, a score on the borderline of statistical significance was found. Of these patients, those with severe depression had the worst results.

The relationship between depressive disorders and somatosensory integration disorders can also be seen in the results of other studies [22].

The results suggest a reciprocal relationship between somatosensory integration disorder and depression. It remains an open question as to what results. Depression, by negatively affecting concentration and attention, may significantly impair somatosensory integration [23,24].

Reports on the effect of sensory stimulation via the visual, auditory, olfactory and gustatory systems on modulating depression, on the other hand, suggest an effect of somatosensory integration disorders on depression [25,26].

The results do not allow us to find a link between the occurrence of chronic fatigue syndrome and somatosensory integration disorders in patients with the relapsing- remitting form of multiple sclerosis. Analysis of the data indicates that these are rather two separate symptoms.

In contrast, a clear correlation was found between the presence of depression and somatosensory integration disorders in these patients. This is particularly true for sensory hypersensitivity, sensory discrimination, motor skills, and social and emotional abilities. Therapy aimed at improving these functions could enhance the effects of antidepressant treatment in this group of patients, and by affecting depression, perhaps also play a beneficial role in reducing fatigue syndrome in patients with MS.

Disorders of somatosensory integration, although unrelated to CFS, were nevertheless significant in the context of the disease itself. Worse scores in sub-sensitivity and social and emotional abilities were associated with greater disease activity.

Impaired emotional processing is an inherent feature of MS, and available studies report the appearance of emotional disturbances in the early stages of the disease [27].

The patients analyzed in the study with a higher degree of disability according to the EDSS scale were distinguished by significantly worse motor abilities and sensory discrimination disorders. A significantly worse score in motor abilities was observed with longer disease duration. The same was true for overall sensory processing.

Thus, impaired motor abilities should be associated with worse motor skills as measured by the EDSS scale, as well as with longer disease duration, which in most cases is closely related-motor disability increases with longer disease duration.

Longer disease duration may be associated with a greater risk of somatosensory integration disorders in general stimulus processing and motor skills. Hypersensitivity and poorer social and emotional abilities are associated with greater annual relapse rate. A higher degree of disability according to the EDSS scale is associated with poorer sensory discrimination scores and motor abilities.

Further research is needed to answer whether particular parameters of MS can affect somatosensory integration disorders in different modalities, or whether somatosensory integration disorders themselves affect the course of MS.

Undoubtedly, the non-motor symptoms of MS analyzed in the study presented here pose both diagnostic and therapeutic challenges. There is a need to develop better tools for their assessment, to objectify the results obtained, as well as to develop synergistic methods of therapy and rehabilitation.

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## References

1. Riley C. Stwardnienie rozsiane i pokrewne choroby demielinizacyjne. W: Louis ED, Mayer SA, Rowland LP, Turaj W. Merrit Neurologia. Wyd. 13 Wrocław: Wydaw. Edra Urban& Partner 2017. s. 659-674 ISBN 97883-65625-93-9
2. Rzepiński J, Maciejek Z. Heterogenność etiopatogenezy stwardnienia rozsianego w kontekście danych klinicznych, immunohistochemicznych, autopsyjnych oraz aktualnych możliwości terapeutycznych Pol. Przegl. Neurol. 2018; 14(1): 1-9.
3. Inojosa H, Schrieffer D, Ziemssen T. Clinical outcome measures in multiple sclerosis: A review. Autoimmun Rev 2020; 5:102512.

4. Chalah M, Riachi N, Ahdab R, Creange A, Lefaucheur JP, Ayache S. Fatigue in Multiple Sclerosis: Neural Correlates and the Role of Non- Invasive Brain Stimulation. *Front Cell Neuroscience*. 2015; 9:460.
5. Fredrikson S, Kam-Hansen S. The 150-year anniversary of multiple sclerosis: does its early history give an aetiological clue? *Perspect Biol Med* 1989; 32:238.
6. Patten SB, Marrie RA, Carta MG. Depression in multiple sclerosis. *Int Rev Psychiatry*. 2017; 5: 463-472
7. Longinetti E, Frisell T, Englund S, Reutfors J, Fang F, Piehl F. Risk of depression in multiple sclerosis across disease-modifying therapies. *Mult Scler*. 2022; 4:632-641
8. Tecchio F, Cancelli A, Cottone C, Zito G, Pasqualetti P, Ghazaryan A, Rossini P, Filippi M.M. Multiple sclerosis fatigue relief by bilateral somatosensory cortex neuromodulation. *J Neurol*. 2014; 8:1552-8.
9. Thompson, T.L.; Amedee, R. Vertigo: A Review of Common Peripheral and Central Vestibular Disorders. *Ochsner J*. 2009; 9: 20–26.
10. Patten, S.B.; Svenson, L.W.; Metz, L.M. Descriptive Epidemiology of Affective Disorders in Multiple Sclerosis. *CNS Spectr*. 2005; 10: 365–371
11. Herrera, W.G. Vestibular and other balance disorders in multiple sclerosis. Differential diagnosis of disequilibrium and topognostic localization. *Neurol. Clin*. 1990; 8: 407–420.
12. Dunn, W. The Impact of Sensory Processing Abilities on the Daily Lives of Young Children and Their Families: A Conceptual Model. *Infants Young Child*. 1997; 9: 23–25.
13. Mross K, Jankowska M, Meller A, Machowska-Sempruch K, Nowacki P, Masztalewicz M, Pawlukowska W. Sensory Integration Disorders in Patients with Multiple Sclerosis. *J Clin Med*. 2022;11:5183.
14. Ayres, A.J. *Sensory Integration and the Child: Understanding Hidden Sensory Challenges*; Western Psychological Services: Los Angeles, CA, USA, 2005
15. Christogianni, A.; Bibb, R.; Davis, S.L.; Jay, O.; Barnett, M.; Evangelou, N.; Filingeri, D. Temperature sensitivity in multiple sclerosis: An overview of its impact on sensory and cognitive symptoms. *Temperature* 2018; 5: 208–223.
16. Stern, B.Z.; Strober, L.B.; Goverover, Y. Relationship between Sensory Processing Patterns, Trait Anxiety, and Health-Related Quality of Life in Multiple Sclerosis. *J. Health Psychol*. 2021. 26; 2106–2117.
17. Hebert J, Corboy J. The association between multiple sclerosis-related fatigue and balance as a function of central sensory integration. *Gait Posture* 2013; 38:37-42.
18. Gandolfi M, Munari D, Geroi C, Gajofatto A, Benedetti M, Midiri A, Carla F, Picelli A, Waldner A, Smania N. Sensory integration balance training in patients with multiple sclerosis: A randomized, controlled trial. *Mult Scler* 2015; 11:1453-62.
19. Christogianni, A., Bibb, R., & Filingeri, D. (2024). High-density thermal sensitivity maps of the body of people with multiple sclerosis: Implications for inclusive personal comfort systems. *Journal of thermal biology*, 123, 103887. <https://doi.org/10.1016/j.jtherbio.2024.103887>
20. Engel-Yeger, B.; DeLuca, J.; Hake, P.; Goverover, Y. The Role of Sensory Processing Difficulties, Cognitive Impairment, and Disease Severity in Predicting Functional Behavior among Patients with Multiple Sclerosis. *Disabil. Rehabil*. 2021; 43: 1129–1136.
21. Maeda KI, Islam MF, Conroy KE, Jason L. Health outcomes of sensory hypersensitivities in myalgic encephalomyelitis/chronic fatigue syndrome and multiple sclerosis. *Psychol Health Med*. 2023 Dec;28(10):3052-3063. doi: 10.1080/13548506.2023.2195670. Epub 2023 Mar 28. PMID: 36977713; PMCID: PMC10533743
22. Storozheva ZI, Akhapiin RV, Bolotina OV, Korendrukina A, Novototsky-Vlasov VY, Shcherbakova IV, Kirenskaya AV. Sensorimotor and sensory gating in depression, anxiety, and their comorbidity. *World J Biol Psychiatry*. 2021 22:183-193.
23. Oakley B, Loth E *Int Rev Psychiatry*. 2021 May;33(3):280-299., Murphy DG. Autism and mood disorders.
24. Rong H, Lai X, Jing R, Wang X, Fang H, Mahmoudi E. Association of Sensory Impairments with Cognitive Decline and Depression Among Older Adults in China. *JAMA Netw Open*. 2020 Sep 1;3(9)
25. Canbeyli R. Sensorimotor modulation of mood and depression: an integrative review. *Behav Brain Res*. 2010 5;207(2):249-64
26. Canbeyli R. Sensory stimulation via the visual, auditory, olfactory and gustatory systems can modulate mood and depression. *Eur J Neurosci*. 2022 Jan;55(1):244-263

27. Colbeck, M. Sensory Processing, Cognitive Fatigue, and Quality of Life in Multiple Sclerosis: Traitement de l'Information Sensorielle, Fatigue Cognitive et Qualité de Vie des Personnes Atteintes de Sclérose en Plaques. *Can. J. Occup. Ther.* 2018; 85: 169–175

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