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Review

Personality Traits and Fatigue in Multiple Sclerosis: A Narrative Review

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Abstract: (1) Background: Multiple sclerosis (MS) is a chronic neurodegenerative autoimmune disease. Fatigue is a prevalent and debilitating symptom that significantly impacts the quality of life of these patients. A relationship between personality traits and fatigue in MS has been hypothesized but not clearly defined. (2) Methods: A literature search was carried out from databases up to April 2023 for studies correlating personality traits and fatigue in patients suffering from MS. (3) Results: A total of ten articles was included; most of the studies depict a neuroticism–fatigue correlation; however, they were not consistent in terms of the fatigue, personality, and covariate assessments. (4) Conclusions: The clinical and methodological heterogeneity of the included studies prevented us from drawing any firm conclusion on the link between personality traits and fatigue in MS. Several models of personality and different fatigue assessments have been found. Despite this, a common pathway shows that the neuroticism trait or similar personality patterns has a role in fatigue diagnosis. This may be a useful target to improve the quality of life and enhance the modification of the disease treatment results. Further homogeneous and longitudinal studies are needed.

Keywords: multiple sclerosis; personality traits; fatigue; neurodegenerative disease; big five factor

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1. Introduction

Multiple sclerosis (MS) is an autoimmune-mediated neurodegenerative disease of the central nervous system (CNS) characterized by inflammatory demyelination with axonal degeneration [1]. MS typically affects young adults (mean age of onset, 20–30 years) but the rate of late-onset disease is also growing, and it is characterized by a peculiar course and therapeutic approach [2–7].

MS can lead to physical disability, cognitive impairment, and a decreased quality of life and its manifestations include a variety of symptoms. These can include "invisible" symptoms not externally evident to others, such as fatigue, mood disorders, cognitive impairments, pain, bladder/bowel dysfunction, sexual dysfunction, and vision changes [7–12]. These symptoms significantly impact the subject's life and negatively affect daily activities, work, family interactions, and social life [13,14]. The therapeutic armamentarium has grown substantially in the last few years. New high-efficacy therapies also lead to an increased risk of infections or cancers due to the prolonged immunosuppression, especially since they are chronic and lifelong therapies [15–18].

The therapeutic choice is strictly personalized and is based on demographical, clinical, and radiological characteristics [19–25]. Biomarkers that can predict disability progression, monitor ongoing disease activity, and assess the treatment response are integral in making important decisions regarding MS treatment [26–29]. Previous studies [10,30–32] have identified fatigue as a key and prevalent symptom in MS, with a greater prevalence of approximately 80% in the primary progressive form compared with the relapsing–remitting form's prevalence of about 60% [33]. Fatigue is characterized by an overwhelming sense of tiredness, a lack of energy, and a feeling of exhaustion compared to the actual level of activity exerted [34,35]. It is defined as "a subjectively perceived lack of physical and/or mental energy that interferes with habitual and desired activities" [35,36]. It does not appear to be correlated with sex [37] or disease severity; it can be found from the early stages of the disease [38] and it can sometimes be the most important symptom in relapses [39]. Research has also shown that there is a negative correlation between fatigue and the level of disability measured with the Expanded Disability Status Scale (EDSS), resulting in higher levels of fatigue for patients with lower levels of disability [35]. The pathophysiological mechanisms of fatigue in MS are complex and multifaceted [32]. It is currently thought that fatigue arises from multiple different underlying mechanisms, which can make treatment difficult and often results in a trial-and-error approach [32,40]. Many theories have been formulated as hypoactivity of the hypothalamic–pituitary–adrenal axis, autonomic nervous system alterations characterized by sympathetic overactivity and low vagal tone, as well as immune abnormalities (an abnormal imbalance between pro- and anti-inflammatory cytokines) [41,42]. Fatigue has been also related to higher white- and grey-matter atrophy and higher lesion load on magnetic resonance imaging, whilst female sex and higher levels of education seemed to have a protective role towards fatigue [43].

Fatigue strongly affects the quality of life of MS patients, limiting them in daily activities, relationships, and work and thus their lowering quality of life; moreover, it is often found in association with psychiatric symptoms such as depression, anxiety, and insomnia, but also with pain [10,30,31,44]. Various factors such as sleep disturbances, endocrine dysfunction, and mood disorders can contribute to the development or exacerbation of fatigue, necessitating careful investigation for the potential underlying causes [45]. The association with anxiety and depression could be explained by the underlying pathogenic mechanisms such as alteration of HPA [46] and noradrenergic pathways as well as the involvement of pro-inflammatory cytokines [30,47–49].

Fatigue is a persistent symptom in MS. In fact, despite the success of disease-modifying therapy in decreasing inflammation, no effects on fatigue have been reported [50]. A recently approved disease-modifying therapy for MS, ponesimod, was compared to teriflunomide in the Oral Ponesimod Versus Teriflunomide In Relapsing Multiple Sclerosis (OPTIMUM) trial [51]. In addition to standard MS treatment measures such as disability and relapse rate, participants in the study were evaluated using a specially developed scale called the fatigue, symptom, and impact questionnaire-RMS (FSIQ-RMS) [51]. Here, the mean difference in FSIQ-RMS, −3.57 (−0.01 vs. 3.56; $p < 0.001$) [51].

About symptomatic treatments targeting fatigue, it has been proposed that fatigue may improve with a different, non-pharmacological or psychological approach rather than specific neurological therapies [52]. Among the pharmacological treatments of MS-related fatigue, methylphenidate, modafinil, and amantadine are commonly prescribed medications for alleviating fatigue in multiple sclerosis (MS) [53]; however, the evidence supporting their efficacy is sparse and conflicting [53–55].

Among neurological deficits that may occur in people with MS, neuropsychiatric changes are common and personality disturbances are found in 20–40% of people with MS, including social inappropriateness, disinhibition, apathy, emotional instability, and impulsivity [56]. These personality disturbances affect all aspects of social, personal, and professional activity, treatment compliance, and quality of life (QOL) [57].

Few studies have evaluated personality traits in people with early or early-diagnosed MS. Baseline personality traits are important to recognize early in the diagnosis of MS since they may have a negative impact on the progression of neurological symptoms [58]. Indeed, it is well-known that personality traits may play a pivotal role in the acceptance of the illness and in adaptive coping mechanisms [59–62] and several studies have considered traits to investigate patients' responses to disease [63–65]. Personality traits reflect people's characteristic patterns of perceiving, relating to, and thinking about the environment and oneself and they are relatively stable over time [66,67].

In clinical research, personality traits are characterized through different psychological models. The theory of Hans Eysenck [68,69] suggests that personality differences are determined genetically, therefore attributing a pivotal role to temperaments and recognizing three dimensions: extroversion/introversion, neuroticism/stability, and Psychoticism/socialization (PEN). Millon's psychosocial theory [70] focusses on a personality model defined by constitutional elements and past experiences. Such styles might become pathological due to a poor ability to withstand stress, to poor adaptive flexibility, and to a tendency to repeat harmful dynamics without the ability to learn from experience. Psychopathology could derive from the combination of maladaptive coping mechanisms and the associated interpersonal relationships [71]. According to Cloninger's theory [72], personality is naturally broken down into the psychobiological dimensions of temperament and character; this model proposes that personality is strongly influenced by both genetic (temperament) and environmental (character) variables. The five-factor model of personality [73] identifies the following five personality traits: neuroticism, extraversion, agreeableness, conscientiousness, and openness. In MS patients, a high level of neuroticism and a low level of extraversion and conscientiousness [74] have been observed. Moreover, these traits have been associated with a greater risk of depression and symptoms of anxiety [75], with less physical activity [76], a more cautious approach to life associated with dysfunctional behaviours and lower levels of resilience with dysfunctional coping mechanisms and a higher risk of psychiatric disorders [59].

Personality traits and MS have been studied, but no clear relationship between personality and overall function in MS has been described. For these reasons, we aimed to describe the state-of-the-art understanding of this area of MS investigation. In detail, we focussed our attention on personality factors and the perception of fatigue in people with MS.

2. Methods

We carried out a search on PubMed and Web of Science until 12 April 2023 by using the following search string: ("multiple sclerosis"[All Fields] AND "fatigue"[All Fields] AND ("personality"[All Fields] OR "personality traits"[All Fields] OR "Five factor model"[All Fields] OR "Temperament and Character Inventory"[All Fields] OR "TCI-R"[All Fields] OR "FFM"[All Fields] OR ("mmpi"[All Fields] OR "mmpi"[All Fields]) OR "PID"[All Fields])). The eligibility criteria were as follows: (1) studies correlating personality traits and fatigue on pwMS; (2) studies written in English. The exclusion criteria were: (1) non-peer reviewed data (e.g., abstracts or trial registry repositories); (2) any other publication different from research studies (e.g., review, case report, commentary, editorial). The relevant data were extracted in a predefined form. The following characteristics were collected: first author and year of publication, country where the study was conducted, study design, MS population characteristics including the EDSS mean measure, personality trait model/tool used, fatigue scale assessed, other clinically relevant data measured, and main results.

3. Results

The flow chart in Figure 1 shows the screening process. A total of 136 papers was identified. After title and abstract screening, 110 records were excluded, leaving 26 studies. After a full-text screening we included a total of ten studies [77–86] matching our inclusion criteria. All of them used a cross-sectional study design. Four studies compared findings with a group of healthy controls [77,82–84]. The included studies were conducted in

various countries (Croatia, Germany, Iran, Italy, the Netherlands, Switzerland, Spain, and the United States). The earliest publication date was 2003 and the most recent was 2021. The most common clinical status of the population studied was relapse–remitting multiple sclerosis (RRMS). Table 1 presents a detailed summary of the core characteristics of the included studies.

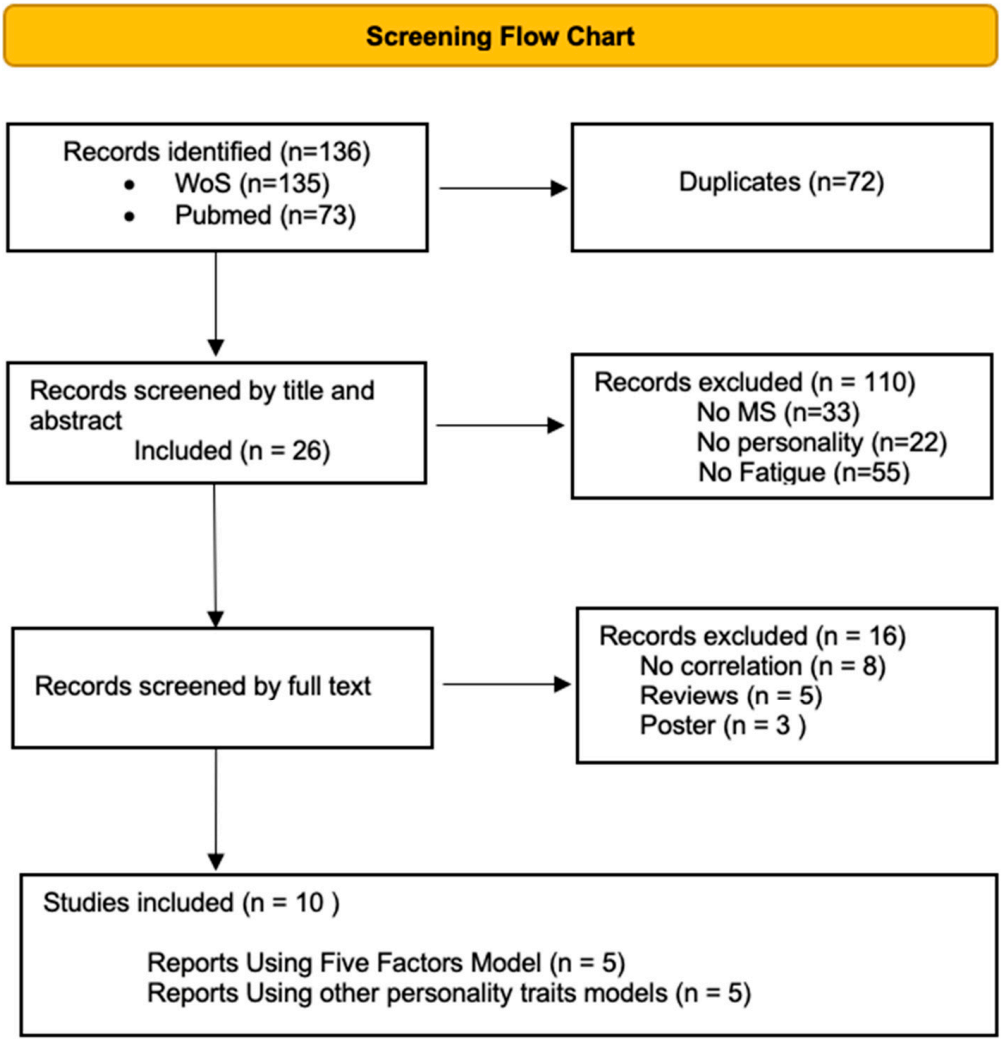

Figure 1. PRISMA flow chart.

Table 1. Studies included and described in the narrative review.

	Personality Trait Assessment	Fatigue Assessment	Other Assessments	Results
		Five-Factor Model		
Penner (2007) [82] Switzerland Cross-sectional study Participants: 41 Mean Age (SD): 41.80 (10.95) Female/Male: 24/17 MS Diagnosis: McDonald's criteria Clinical status: 68.3% of patients have RR MS, 7.3% PP MS, 24.4% SP MS EDSS mean (SD): 3.1 (1.71) Years of illness (SD): 8 (7.22) Healthy controls: yes (41 controls)	NEO Five-Factor Inventory (NEO-FFI) • N, Neuroticism, • A, Agreeableness, • C, Consciousness, • O, Openness, • E, Extroversion (only Neuroticism and Extroversion were assessed)	Fatigue Severity Scale (FSS) Modified fatigue impact scale (MFIS) • Scale for Mental fatigue • Scale for Physical fatigue	• Beck Depression Inventory (BDI) • Action control assessment (HAKEMP-90)	• MS patients were more neurotic and less extraverted compared to controls; • Personality traits not directly related to fatigue after controlling for depression. • Comparisons (Cohen's d) between patients with MS and healthy controls: ○ MFIS: 1.49 ○ FSS: 1.49
Fernandez-Muños (2015) [78] Spain Cross-sectional study Participants: 108 Mean Age (SD): 44 (9) Female/Male: 59/49 MS Diagnosis: Modified McDonald's criteria Clinical status: 74% of patients have RR MS, 8% PP MS, 18% SP MS EDSS mean (SD): 3.6 (1.6) Years of illness (SD): 12.8 (8) Healthy control: No	NEO Five-Factor Inventory (NEO-FFI) • N, Neuroticism, • A, Agreeableness, • C, Consciousness, • O, Openness, • E, Extroversion	Fatigue Impact Scale (FIS)	• Pain Rating scale (NPRS) • Functional Assessment of Multiple Sclerosis scale (FAMS) • Beck Depression Inventory (BDI-II) • Short-Form Health Survey 36 (SF-36)	• Personality traits were not associated with self-perceived fatigue.

Table 1. *Cont.*

	Personality Trait Assessment	Fatigue Assessment	Other Assessments	Results
Strober (2017) [85] United States Cross-sectional study Participants: 37 type D pos on 230 pwMS Mean Age (SD): 41.81 (9.82) Type D pos Female/Male: 33/4 Type D pos MS Diagnosis: McDonald's criteria Clinical status: 97% RR MS EDSS mean (SD): NA Years of illness (SD): 7.18 (7.05) TypeD pos Healthy controls: no	NEO Five-Factor Inventory 3 (NEO-FFI-3) • N, Neuroticism, • A, Agreeableness, • C, Consciousness, • O, Openness, • E, Extroversion International Personality Item Pool LOC scale (IPIP-LOC) Neuroticism (T > 60) and higher IPIP social discomfort were assessed to determine Type D personality	Modified fatigue impact scale (MFIS) • MFIS physical • MFiS cognitive • MFiS psychosocial	• MOS Pain Effects Scale (MOS-PES) • Pittsburgh Sleep Quality Index (PSQI) • Multiple Sclerosis Self-Management Scale (MSSM-R) • Disability Management Self-Efficacy Scale (DMSES) • Morisky Adherence Questionnaire (MAQ) • COPE inventory • General Self-Efficacy Scale (GSE) • Chicago Multiscale Depression Inventory (CMDI) • State Trait Anxiety Inventory (STAI) • Flourishing Scale (FS) • Perceived Stress Scale (PSS)	• Type D+ individuals were found to report more severe symptoms of fatigue.
Sindermann (2018) [83] Germany Cross-sectional study Participants: 52 Mean Age (SD): 45.13 (9.56) Female/Male: 43/9 MS Diagnosis: McDonald's criteria Clinical status: 54% of patients have RR MS, 17% PP MS, 13% SP MS, 2% CIS, and 13% other. EDSS mean (SD): NA Years of illness (SD): 8.67 (7.36) Healthy controls: yes (screened by BDI-II score < 13)	NEO Five-Factor Inventory (NEO-FFI) • N, Neuroticism, • A, Agreeableness, • C, Consciousness, • O, Openness, • E, Extroversion	Fatigue Scale for Motor and Cognitive Functions (FSMC) • Scale for Cognitive fatigue • Scale for Motor fatigue	• Allgemeine Depressionsskala (ADS; translated from German as the General Depression Scale)	• Low extraversion predicts motor fatigue; • High neuroticism predicts for general and cognitive fatigue.

Table 1. *Cont.*

	Personality Trait Assessment	Fatigue Assessment	Other Assessments	Results
Spiegelberg (2021) [84] Germany Cross-sectional study Participants: 30 Mean Age (SD): 46.1 (9.6) Female/Male: 21/9 MS Diagnosis: McDonald's criteria Clinical status: 80% of patients have RR MS, 13.3% SP MS, 3.3% CIS, and 3.3% other. EDSS median (range): 2.8 (1.5–7–5) Years of illness (SD): 9.1 (8.9) Healthy controls: yes	NEO Five-Factor Inventory (NEO-FFI) • N, Neuroticism, • A, Agreeableness, • C, Consciousness, • O, Openness, • E, Extroversion (Only Neuroticism was assessed)	Fatigue Scale for Motor and Cognitive Functions (FSMC) • Scale for Cognitive fatigue • Scale for Physical	• Cognitive Failures Questionnaire (CFQ) • Center for Epidemiologic Studies-Depression scale (CES-D) • Affective Neuroscience Personality Scale (ANPS) (only FEAR subscale was assessed)	• High neuroticism had a stronger correlation with cognitive fatigue than with motor fatigue. • Comparisons (Cohen's d) between patients with MS and healthy controls: ○ FSMCc: 1.65 ○ FSMCph: 2.59
		Freiburg Personality		
Merkelbach (2003) [81] Germany Cross-sectional study Participants: 80 Mean Age (SD): 38.50 (9.0) Female/Male: 62/18 MS Diagnosis: Modified McDonald's criteria Clinical status: 61.25% of patients have RR MS, 13.75% PP MS, 25% SP MS, EDSS mean (SD): 3.2 (1.4) Years of illness (SD): 9.10 (6.20) Healthy control: No	German Freiburg Personality Inventory—revised (FPI-R) • LEB, Life Satisfaction • SOZ, Social Orientation • LEI, Achievement Orientation • GEH, Inhibitedness • ERR, Excitability • AGGR Aggressiveness • BEAN, Strain • KORP, Somatic Complaints • GES, Health Concerns • OFF, Frankness • E, Extraversion • N, Neuroticism	Fatigue Severity Scale (FSS) Chronic Fatigue Scale (CFS)	• Revised Clinical Interview Schedule (CIS-R)	• Neuroticism was related to fatigue symptoms; • Neuroticism was a predictor for more chronic and more severe fatigue.

Table 1. *Cont.*

	Personality Trait Assessment	Fatigue Assessment	Other Assessments	Results
Eysenck PEN system for personality				
Van Der Werf (2003) [86] Netherlands Cross-sectional study Participants:89 Mean Age (range): 41.9 (25–69) Female/Male: 63/26 MS Diagnosis: revised Poser criteria Clinical status: 58.4% of patients have RR MS, 41.6% SP MS and PP MS. EDSS mean (SD): 4.4 (1.8) Years of illness (SD): 9.1 (8.9) Healthy controls: No	Eysenck Personality Questionnaire (EPQ) • P, Psychoticism • E, Extroversion • N, Neuroticism Subscale neuroticism was assessed as EI, emotional instability	Subjective Fatigue of the Checklist Individual Strength (CIS-Fatigue).	• Illness Cognition Questionnaire (ICQ) • Depressed Mood of the Impact of Rheumatic Diseases on General Health and Lifestyle (IRGL),	• Emotional instability leads to helplessness, which in turn affected the MS-associated fatigue.
Skinnerian reinforcement theory				
Besharat (2011) [77] Iran Cross-sectional study Participants: 120 Mean Age (SD): 32.82 (8.22) Female/Male: 79/41 MS Diagnosis: Modified McDonald's criteria Clinical status: 32.5% of patients have RR MS, 12.1% PP MS, 4.2% SP MS EDSS mean (SD): NA Years of illness (SD): 6.84 (3.99) Healthy control: yes	Positive and negative perfectionism scale (PANPS) • PP, positive perfectionism; • NP, negative perfectionism	Modified fatigue impact scale (MFIS) Fatigue severity scale (FSS)	• Beck depression inventory (BDI)	• Negative perfectionism was related to higher fatigue symptoms. • Comparisons (Cohen's d) between patients with MS and healthy controls: ○ MFIS: 1.90 ○ FSS: 1.29

Table 1. *Cont.*

	Personality Trait Assessment	Fatigue Assessment	Other Assessments	Results
		Millon's model		
Incerti (2015) [79] Italy D: Cross-sectional study Participants: 77 Mean Age (SD): 43.1 (9.8) Female/Male: 56/21 MS Diagnosis: Modified McDonald's criteria Clinical status: 82.4% of patients have RR MS, 20.7% SP MS EDSS mean (SD): 3.2 (1.6) Years of illness (SD): 12.9 (7.5) Healthy control: No	Millon Clinical Multiaxial Inventory-III (MCMI-III): • 14 personality traits scales • 10 Clinical states scales	Modified fatigue impact scale (MFIS)	• Full cognitive functions assessment • the State Trait Anxiety Inventories Y1 and Y2 (STAI Y1-Y2) • Chicago Multiscale Depression Inventory (CMDI)	• Depression, avoidance, dependence, and masochism personality traits were directly related to fatigue symptoms; • Lower histrionism and narcissism correlated with higher fatigue symptoms.
		Temperament and character theory		
Matesic (2020) [80] Croatia Cross-sectional study Participants: 201 Mean Age (SD): 39.40 (10.81) Female/Male: 153/48 MS Diagnosis: Modified McDonald's criteria Clinical status: 81.6% of patients have RR MS, 5% PP MS, 10.9% SP MS, 2.5% PR MS EDSS mean (SD): 2.6 (2.12) Years of illness (SD): 7.96 (6.38) Healthy control: No	Temperament and Character Inventory Revised (TCI-R),Four temperament dimensions • NS, Novelty Seeking • HA, Harm Avoidance, • RD, Reward Dependence • PS, Persistence. Three character dimensions • SelfD, Self-Directedness, • CO, Cooperativeness, • ST, Self-Transcendence.	Modified fatigue impact scale (MFIS)	• Depression scale from the Hospital Anxiety and Depression Scale (HADS)	• MS fatigue was to some degree dependent upon premorbid personality; • Harm avoidance predicted fatigue; • Low self-directiveness predicted higher fatigue.

SD: standard deviation; NA: not available; MS: multiple sclerosis; RR MS: relapsing–remitting multiple sclerosis, PP MS: primary progressive multiple sclerosis, SP MS: secondary progressive multiple sclerosis, CIS: clinically isolated syndrome; EDSS: expanded disability severity score.

Fatigue was measured with different tools valid for MS-related fatigue symptoms. One article [78] assessed fatigue with the Fatigue Impact Scale (FIS) [87], while five studies [77,79,80,82,85] used the modified version of the Fatigue Impact Score (MFIS) [88]. The Fatigue Severity Score (FSS) [89] was administered in three different studies [77,81,82]. Merkelbach et al. [81] added the assessments of the chronic symptomatology with the Chronic Fatigue Scale (CFS) [90] and the subjective consequences of fatigue with the Revised Clinical Interview Schedule (CIS-R). Van der Werf et al. [86] assessed fatigue by using the Fatigue subscale of the Checklist Individual Strength (CIS) [91]. Finally, two studies [83,84] used the Fatigue Scale for Motor and Cognitive functions (FCSM) [92]. Nine studies assessed depression as a confounding factor [77–80,82–86]. Among them, three evaluated cognition as well [79,84,86].

We found that five studies [78,82–85] used the five-factor model (FFM) [93,94] to assess personality traits. Among these, Fernández-Muñoz et al. [78] found no significant association between personality traits measured with the NEO Five-Factor Inventory (NEO-FFI) [93] and perceived fatigue measured with Fatigue Impact Scale (FIS) [87]. Penner et al. [82] assessed only the neuroticism and extroversion subscales of the NEO-Five-Factor Inventory, finding that pwMS had a higher score in neuroticism and lower score in extroversion than healthy controls. Despite this result, after controlling for depression, these traits were not related to fatigue, which was assessed with both the Fatigue Severity Scale (FSS) and the Modified Fatigue Impact Scale. In their study, Sindermann et al. [83] assessed personality using the NEO-FFI. High neuroticism predicted cognitive fatigue, while low extroversion was the best predictor for motor fatigue. Spiegelberg et al. [84] confirmed the same finding as Sindermann et al. [83] concerning neuroticism and cognitive fatigue, assessing only the neuroticism subscale of NEO-FFI and comparing it with both FSMC subscales. Strober et al. [85] screened the study population using the neuroticism subscale of the NEO-Five-Factor Inventory-3 (NEO-FFI-3) [95] and the social discomfort subscale of the International Personality Item Pool (IPIP) [96]. PwMS who had higher score on the IPIP social discomfort scale had a T-score greater than 60 on the NEO neuroticism and were identified as having type D personality [97]. This group reported more severe fatigue symptoms compared to pwMS without type D personality.

The included studies evaluated personality traits with different assessment tools. Besharat et al. [77] considered the Skinnerian reinforcement theory (Skinner 1969) to define perfectionism as a personality dimension [98], differentiating two kinds of perfectionism, a positive and a negative (maladaptive) one. The Positive and Negative Perfectionism Scale (PANPS) [99] was administered and was correlated with the total scores of fatigue assessed with MFIS and FSS. Negative perfectionism was directly and significantly associated with MS-related fatigue. Incerti et al. [79] explored personality traits with the Millon Clinical Multiaxial Inventory-III (MCMI-III) [100], following Millon's model of abnormal personality and coding for DSM IV-TR personality diagnosis. It was found that a higher fatigue score on MFIS correlated with higher scores in several personality traits, such as depression (D), avoidance (Avo), dependence (Dep), and masochism (Mas). Moreover, a higher fatigue score was associated with lower scores in histrionic (His) and narcissistic (Nar) traits. Indeed, the authors noted that fatigue had stronger correlations with clinically significant syndromes such as dysthymia, somatoform disorder, and major depression disorder, as MCMI-III was able to detect them. In their study, Matesic et al. [80] used Cloninger's psychobiological temperament and character theory for personality through the Temperament and Character Inventory Revised (TCI-R) [101,102]. According to this theory, personality is composed of four temperamental dimensions, heritable and early manifesting, and three-character dimensions, changeable throughout age and life events [101,102]. Their results showed that personality traits directly and indirectly predict MS-related fatigue assessed with MFIS [101,102]. In fact, it was indicated that MS fatigue is dependent upon premorbid harm avoidance. In addition, low self-directedness, as a character dimension, predicted fatigue as well. Merkelbach et al. [81] used the German Freiburg Personality Inventory Revised (FPI-R) [103] tool to assess personality traits, including neuroticism and

extroversion. Comparing these two traits with different fatigue assessments tools, such as the Fatigue Severity Scale (FSS) and the Chronic Fatigue Scale (CFS), higher results were found to correlate with higher neuroticism. Moreover, neuroticism has been found to be a strong predictor for severity and chronicity, as their direct correlation with the total scores of both scales showed [81]. Finally, Van der Werf et al. [86] assessed personality traits using the Eysenck Personality Questionnaire (EPQ) [104], focusing on the neuroticism subscale, which result was reported as emotional instability. In their study they correlated through several models the different clinical values with each other, including subjective fatigue assessed with a subscale of the Checklist Individual Strength (CIS-Fatigue) [86]. The findings showed that emotional instability, evidenced by a high neuroticism, led to increased helplessness, which in turn affected fatigue secondarily [86].

4. Discussion

This narrative review was conducted to provide an updated summary of the previous evidence on the association between personality traits and fatigue in pwMS. Previous systematic reviews on personality traits and MS have focused on the type of personality traits and how they may impact the primary clinical manifestations and disabilities in people with MS. Limited attention has been given to the association between personality traits and fatigue in MS, and the most recent review on this topic is not up to date [74].

From this review, an association between fatigue and personality traits [77,79–81,83–86] emerges, albeit not definitively. The studies under consideration have used different models for the evaluation of personality traits. It is important to proceed with caution when interpreting the data from these studies due to the limited sample size and the varying methodologies used.

Five studies used scales based on the psychological five-factor model [105]. Among them, three [83–85] found that neuroticism and/or extroversion were the dimensions that showed a stronger correlation with fatigue.

Elevated neuroticism, defined as behavioural rigidity and a low ability to react to adversity, is the trait most associated with greater levels of fatigue [81,83–86]. The degree to which basic traits underlie vulnerable narcissism, with a particular emphasis on the importance of neuroticism and agreeableness, has been investigated in a study involving adolescents and young adults [106]; here, analyses demonstrated an association between vulnerable narcissism and neuroticism [106]. This connection between vulnerable narcissism and neuroticism was confirmed by another study indicating that vulnerable narcissism is largely a manifestation of neuroticism [107]. This appears consistent with data in the literature that report that high neuroticism is related to increased somatization and the development of fatigue [76]. Specifically, Strober et al. [85] used a neuroticism subscale from NEO-PPI to determine how many pwMS had a type D personality, defined with high neuroticism and increased psychosocial discomfort [108]. In their results, pwMS scoring higher in neuroticism (hence, included in the type D group) were correlated with more severe symptoms such as increased fatigue and pain, reduced self-effectiveness in disease management, more depressive symptoms, less family support, an increase in perceived stress, and a lower quality of life [85].

Two studies have shown that neuroticism is directly associated with fatigue [83,84]. In their findings, neurotic patients tended to report higher cognitive fatigue, defined as a psychological state characterized by feelings of tiredness and impaired cognitive functioning arising from high cognitive demands [83,84]. In general, neurotic people, associated with anxiety, emotional instability, and mood swings, have more problems with concentration and learning new information [109,110]; on the other hand, physical fatigue is related to low extroversion [83]. This may be explained by greater extroversion likely being associated with experiential behaviours that favour the development of physical activity and lead to better physical performance and greater mobility in adults [76].

High neuroticism, strain, and excitability are traits that characterize a high proportion of MS patients (with a higher prevalence in SMRR) and these results are in line with several

studies that have reported how disease management from the point of view of thoughts, behaviour, and emotions was unrelated to the type of evolution of MS [111]. In fact, personality traits clearly affect the impact of physical disability, leading to an overestimation of the perception of fatigue, which in turn leads to a worse perception of physical disability [81].

Contrary to what has been reported so far, Penner [82] and Fernandez [78] did not find a direct correlation between high neuroticism and fatigue.

Fernandez-Munos [78] did not find a correlation between perceived fatigue and personality traits. In fact, they did not find a correlation between fatigue and depression either. They explained this result because of the rarity of depressive symptoms in their sample. This may be said for dysfunctional personality traits as well [78].

Conversely, Penner [82] initially found a correlation between high neuroticism and fatigue; however, it emerged that the only predictors of fatigue were action control and disability by controlling depression as a covariate. These data probably derive from a different methodology implemented in the assessment of depressive symptoms [78].

Despite the use of the same personality model, there was no homogeneity in the assessment of depression. These results may be explained by the frequent comorbidity between depression and fatigue in pwMS.

In the literature, it has been shown that patients with depression present more severe symptoms of fatigue, suggesting that mood disturbance and fatigue are connected to each other in a strong circular relation [112] that cannot be easily discerned by sensitive yet nonspecific self-report tools.

In fact, Strober [85] does not make any correction of the data based on the depressive symptomatology; Sindermann et al. [83], exclude from their population BDI scores greater than 13; Spiegelberg [84], meanwhile, administered the CES-scaleD, considering it more suitable compared to the BDI scale because it contains fewer physical symptom items and is therefore better able to prevent false positives caused by MS itself.

It is certain that patients suffering from neurological pathologies have a higher prevalence of developing depressive symptoms [113–115] and one of the key physical symptoms of this disorder is precisely fatigue. Penner [82] believes that fatigue can be considered a direct symptom of depression. However, none of this evidence can be replicated or reproduced since different scales of evaluation are used [116].

Fatigue and depression may manifest with the same symptoms, such as a loss of motivation and anhedonia, making these conditions difficult to differentiate [112]. Depressive symptoms should be carefully evaluated using scales that allow the exclusion of the overlap of physical symptoms associated with MS with those arising on a psychological basis [112].

In fact, many of the correlations that emerged from that review were found to be strictly dependent on the different scales used.

In the remaining five articles, personality was assessed through different psychological models with various grades of comparability between each other.

Merkelbach et al. [81] used the FPI-R scale for personality assessment. This scale assessed twelve different personality factors, including neuroticism and extroversion [103]. Both these traits were found to be significantly related to fatigue in MS [81]. They concluded that personality traits clearly impact physical disability, leading to an overestimation of the perception of fatigue, which in turn leads to a worse perception of physical disability [81]. In some parts, their conclusion may be compared to previously commented-on studies even if their assessment is not strictly related to the five-factor model [81].

One study used the Eysenck model [68]. It emerged that elevated neuroticism, understood as emotional instability, is associated with increased feelings of impotence caused by the inability for patients to change their neurological condition. Both MS, as an unpredictable changing stressor, and emotional instability, as personality vulnerability, might lead to higher helplessness, which in turn affects the MS-associated depression and fatigue [68].

Hence, higher neuroticism produces more helplessness, which is indeed related to fatigue not only as a direct consequence of depression [86]. In a direct comparison of their

models, Costa and McCrae reported that Eysenck's neuroticism and extroversion are completely consistent with the corresponding factors theorized in the five=-factor model [117].

The literature confirms that high neuroticism and low extroversion are fatigue-related personality traits that could directly determine the fatigue symptom through a patient's subjective experience of a lack of mental/physical energy, or indirectly by psychological, neuroendocrine, and neurovegetative dysregulation, which would lead to dysfunctional management of the disease (i.e., emotion-centred coping) [42], regardless of the theoretical basis used.

In the study by Matesic et al. [80], the authors investigated the relationship between personality and fatigue in pwMS following the Cloninger theory of temperaments and character. Their results showed that high harm avoidance and low self-directedness directly predicted fatigue, highlighting and underlining how fatigue in MS may be related in part to the premorbid personality. Regarding low self-management, this led to poor management of the disease, leaving patients mentally and physically exhausted [84]. What emerges is that fatigue in MS might stem both from the direct effects of genetically determined temperament, as well as from traits shaped by the environment that develop in later stages of life [84].

Moreover, it emerges that MS patients who have high levels of negative perfectionism and depressive symptoms are correlated with higher fatigue levels [77]. Perfectionism is a personality trait characterized by the search for impeccability and the definition of high standards of performance [98,118]. Two types of perfectionism are recognized, the positive and the negative [119]. In the first case, individuals take pleasure in the search for excellence by recognizing their individual limits, while in the second case the individuals aim to achieve unrealistic objectives and it is therefore considered a mismatching trait [120]. In this article, after correcting for depression, it was evidenced that negative perfectionism correlated with increased fatigue levels, emphasizing how the standards set by individuals with traits of negative perfectionism increase discomfort and somehow lead to an increase in fatigue itself [120]. This appears consistent with data in the literature underlining how the standards set by individuals with traits of negative perfectionism increase discomfort in MS patients, who certainly have limitations associated with pathology [30,121].

Moreover, this trait is stressful, characterized by an excessive emotional resonance towards failure, and often aims at implementing behaviours that go beyond the real possibilities.

Incerti et al. [79] reported that personality traits such as depression, avoidance, addiction, and masochism were related to high fatigue levels. Moreover, histrionicism and narcissism were negatively related to fatigue, unlike in other studies, in which the high neuroticism, loss of empathy, and low pleasantness, elements characterizing high narcissism and histrionicism, correlated directly with fatigue [122,123].

However, in our opinion, these data are associated with the use of a scale aimed at diagnosing personality disorders and not at identifying personality traits. In fact, the authors found a correlation of fatigue with diseases such as dysthymia, major depressive disorder, and somatoform disorder.

Furthermore, this review has highlighted how the studies are uneven in the definition of fatigue. Fatigue is a complex and multidimensional phenomenon that consists of subjective and objective components. In MS, fatigue can be primary or secondary. Primary fatigue is a direct consequence of the disease, while secondary fatigue is a consequence of reduced functional capabilities, chronic pain, and treatment side effects. It may be defined as a decrease in physical and/or mental performance [124]. Nevertheless, the present literature clearly reports that the definition of patients with fatigue often depends on the type of scale used and it might not represent the actual experience of the patient.

In future studies, homogeneous scales should be used that also allow the differentiation of stretch and state fatigue, such as the FSMC scale and the WEIMuS.

Despite the great lack of homogeneity, personality has a pivotal role in fatigue symptomatology. However, the studies under consideration are of a cross-sectional design that does not allow the analysis of direct causal links between personality and fatigue.

Moreover, personality is composed of a premorbid and an experiential part. It should first be assessed whether these dysfunctional personality traits are already present in the premorbid phase, predisposing patients to the development of fatigue, or are the result of maladaptive coping mechanisms and/or the consequence of the inflammatory action associated with the disease. For this purpose, it would be useful to carry out longitudinal studies on naïve patients to analyse over time the direct fatigue–personality causality relationship.

In any case, detecting dysfunctional personality traits may be useful throughout the progression of the neurodegenerative disease to easily achieve and maintain improvements related to disease-modifying therapies.

5. Limitations

Medical disabling and progressive conditions could influence personality. No evidence has conclusively shown whether there is a causal link between brain structural damage and personality changes due to inflammation or if these traits are directly related to the MS diagnosis itself. Moreover, anxiety and depression may be considered as confounding factors. Indeed, these symptoms may be higher during active phases or in patients who do not have an adequate MDT response, leading to a worse fatigue experience, regardless of the personality traits presented.

Although the ICD-10 defines a diagnostic personality change ("Enduring personality changes, not attributable to brain damage and disease" F62.0), they were performed to determine whether MS could alter personality due to chronic, persistent pain or because of MS-related psychiatric symptoms (e.g., higher demands of others, higher dependence and expectation).

6. Conclusions

This narrative review identified eight studies that found a correlation between personality traits and fatigue. Although some studies have suggested that neuroticism is associated with fatigue in MS patients, these data should be interpreted with extreme caution given the small number of studies under consideration, but especially due to the lack of a common methodology. Future studies should employ unique personality models, utilize fatigue scales with higher specificity and sensitivity indices to increase homogeneity, and carefully study depressive symptoms. This should include removing fatigue-related items from the scales to avoid overlap and eliminate the methodological issues, while also conducting a psychiatric evaluation. Fatigue has been suggested by many authors as a "marker" of disease activity, progression, and prognosis. Thus, it is important to define the role of personality traits, especially because no univocal way to measure them is available and all the data collected are based on self-reported questionnaires.

Given the significant impact of fatigue on the quality of life for MS patients, the limited evidence currently available underscores the importance of further studies. These should aim to identify personality traits that can inform targeted intervention strategies to improve the quality of life of MS patients.

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References

1. McGinley, M.P.; Goldschmidt, C.H.; Rae-Grant, A.D. Diagnosis and Treatment of Multiple Sclerosis: A Review. *JAMA* **2021**, *325*, 765–779. [CrossRef]
2. D'Amico, E.; Patti, F.; Zanghì, A.; Chisari, C.G.; Fermo, S.L.; Zappia, M. Late-onset and young-onset relapsing-remitting multiple sclerosis: Evidence from a retrospective long-term follow-up study. *Eur. J. Neurol.* **2018**, *25*, 1425–1431. [CrossRef]
3. Naseri, A.; Nasiri, E.; Sahraian, M.A.; Daneshvar, S.; Talebi, M. Clinical Features of Late-Onset Multiple Sclerosis: A Systematic Review and Meta-analysis. *Mult. Scler. Relat. Disord.* **2021**, *50*, 102816. [CrossRef]
4. Zanghì, A.; Avolio, C.; Amato, M.P.; Filippi, M.; Trojano, M.; Patti, F.; D'amico, E.; Register, F.T.I.M. First-line therapies in late-onset multiple sclerosis: An Italian registry study. *Eur. J. Neurol.* **2021**, *28*, 4117–4123. [CrossRef] [PubMed]
5. Zanghì, A.; D'amico, E.; Fermo, S.L.; Patti, F. Exploring polypharmacy phenomenon in newly diagnosed relapsing–remitting multiple sclerosis: A cohort ambispective single-centre study. *Ther. Adv. Chronic Dis.* **2021**, *12*, 2040622320983121. [CrossRef] [PubMed]
6. Mirmosayyeb, O.; Brand, S.; Barzegar, M.; Afshari-Safavi, A.; Nehzat, N.; Shaygannejad, V.; Bahmani, D.S. Clinical Characteristics and Disability Progression of Early- and Late-Onset Multiple Sclerosis Compared to Adult-Onset Multiple Sclerosis. *J. Clin. Med.* **2020**, *9*, 1326. [CrossRef] [PubMed]
7. Solaro, C.; Trabucco, E.; Uccelli, M.M. Pain and Multiple Sclerosis: Pathophysiology and Treatment. *Curr. Neurol. Neurosci. Rep.* **2012**, *13*, 320. [CrossRef] [PubMed]
8. D'amico, E.; Zanghì, A.; Serra, A.; Murabito, P.; Zappia, M.; Patti, F.; Cocuzza, S. Management of dysphagia in multiple sclerosis: Current best practice. *Expert Rev. Gastroenterol. Hepatol.* **2019**, *13*, 47–54. [CrossRef] [PubMed]
9. Zanghì, A.; Cimino, S.; Urzì, D.; Privitera, S.; Zagari, F.; Lanza, G.; Patti, F.; D'amico, E. Pharmacotherapeutic management of lower urinary tract symptoms in Multiple Sclerosis patients. *Expert Opin. Pharmacother.* **2020**, *21*, 1449–1454. [CrossRef]
10. Lakin, L.; Davis, B.E.; Binns, C.C.; Currie, K.M.; Rensel, M.R. Comprehensive Approach to Management of Multiple Sclerosis: Addressing Invisible Symptoms—A Narrative Review. *Neurol. Ther.* **2021**, *10*, 75–98. [CrossRef] [PubMed]
11. Racke, M.K.; Frohman, E.M.; Frohman, T. Pain in Multiple Sclerosis: Understanding Pathophysiology, Diagnosis, and Management through Clinical Vignettes. *Front. Neurol.* **2022**, *12*, 799698. [CrossRef] [PubMed]
12. Nazari, F.; Shaygannejad, V.; Sichani, M.M.; Mansourian, M.; Hajhashemi, V. Sexual dysfunction in women with multiple sclerosis: Prevalence and impact on quality of life. *BMC Urol.* **2020**, *20*, 15. [CrossRef] [PubMed]
13. Lorefice, L.; Fenu, G.; Frau, J.; Coghe, G.; Marrosu, M.G.; Cocco, E. The burden of multiple sclerosis and patients' coping strategies. *BMJ Support. Palliat. Care* **2018**, *8*, 38–40. [CrossRef] [PubMed]
14. Zanghì, A.; D'Amico, E.; Luca, M.; Ciaorella, M.; Basile, L.; Patti, F. Mental health status of relapsing-remitting multiple sclerosis Italian patients returning to work soon after the easing of lockdown during COVID-19 pandemic: A monocentric experience. *Mult. Scler. Relat. Disord.* **2020**, *46*, 102561. [CrossRef]
15. D'Amico, E.; Chisari, C.G.; Arena, S.; Zanghì, A.; Toscano, S.; Fermo, S.L.; Maimone, D.; Castaing, M.; Sciacca, S.; Zappia, M.; et al. Cancer Risk and Multiple Sclerosis: Evidence from a Large Italian Cohort. *Front. Neurol.* **2019**, *10*, 337. [CrossRef]
16. D'amico, E.; Zanghì, A.; Leone, C.; Tumani, H.; Patti, F. Treatment-Related Progressive Multifocal Leukoencephalopathy in Multiple Sclerosis: A Comprehensive Review of Current Evidence and Future Needs. *Drug Saf.* **2016**, *39*, 1163–1174. [CrossRef] [PubMed]
17. Soelberg Sorensen, P. Safety concerns and risk management of multiple sclerosis therapies. *Acta Neurol. Scand.* **2017**, *136*, 168–186. [CrossRef]
18. Chen, C.; Zhang, E.; Zhu, C.; Wei, R.; Ma, L.; Dong, X.; Li, R.; Sun, F.; Zhou, Y.; Cui, Y.; et al. Comparative efficacy and safety of disease-modifying therapies in patients with relapsing multiple sclerosis: A systematic review and network meta-analysis. *J. Am. Pharm. Assoc.* **2023**, *63*, 8–22.e23. [CrossRef]
19. D'amico, E.; Leone, C.; Zanghì, A.; Fermo, S.L.; Patti, F. Lateral and escalation therapy in relapsing-remitting multiple sclerosis: A comparative study. *J. Neurol.* **2016**, *263*, 1802–1809. [CrossRef] [PubMed]
20. D'Amico, E.; Zanghì, A.; Gastaldi, M.; Patti, F.; Zappia, M.; Franciotta, D. Placing CD20-targeted B cell depletion in multiple sclerosis therapeutic scenario: Present and future perspectives. *Autoimmun. Rev.* **2019**, *18*, 665–672. [CrossRef] [PubMed]
21. D'amico, E.; Zanghì, A.; Sciandra, M.; Borriello, G.; Callari, G.; Gallo, A.; Salemi, G.; Cottone, S.; Buccafusca, M.; Valentino, P.; et al. Discontinuation of teriflunomide and dimethyl fumarate in a large Italian multicentre population: A 24-month real-world experience. *J. Neurol.* **2019**, *266*, 411–416. [CrossRef] [PubMed]
22. D'amico, E.; Zanghì, A.; Sciandra, M.; Lanzillo, R.; Callari, G.; Cortese, A.; Lus, G.; Lucchini, M.; Buccafusca, M.; Bonavita, S.; et al. Dimethyl fumarate vs. Teriflunomide: An Italian time-to-event data analysis. *J. Neurol.* **2020**, *267*, 3008–3020. [CrossRef]
23. Zanghì, A.; Gallo, A.; Avolio, C.; Capuano, R.; Lucchini, M.; Petracca, M.; Bonavita, S.; Lanzillo, R.; Ferraro, D.; Curti, E.; et al. Exit Strategies in Natalizumab-Treated RRMS at High Risk of Progressive Multifocal Leukoencephalopathy: A Multicentre Comparison Study. *Neurotherapeutics* **2021**, *18*, 1166–1174. [CrossRef]
24. D'amico, E.; Zanghì, A.; Callari, G.; Borriello, G.; Gallo, A.; Graziano, G.; Valentino, P.; Buccafusca, M.; Cottone, S.; Salemi, G.; et al. Comparable efficacy and safety of dimethyl fumarate and teriflunomide treatment in Relapsing-Remitting Multiple Sclerosis: An Italian real-word multicenter experience. *Ther. Adv. Neurol. Disord.* **2018**, *11*, 1756286418796404. [CrossRef]
25. Manjunatha, R.T.; Habib, S.; Sangaraju, S.L.; Yepez, D.; Grandes, X.A. Multiple Sclerosis: Therapeutic Strategies on the Horizon. *Cureus* **2022**, *14*, e24895. [CrossRef] [PubMed]

26. D'amico, E.; Zanghì, A.; Manuti, V.; Allegretta, C.; Amoruso, A.; Serviddio, G.; Avolio, C. MicroRNAs 181a and 125a are highly expressed in naïve RRMS: A pilot case–control study. *J. Neurol.* **2023**, *270*, 1150–1153. [CrossRef] [PubMed]
27. D'amico, E.; Zanghì, A.; Parrinello, N.L.; Romano, A.; Palumbo, G.A.; Chisari, C.G.; Toscano, S.; Di Raimondo, F.; Zappia, M.; Patti, F. Immunological Subsets Characterization in Newly Diagnosed Relapsing–Remitting Multiple Sclerosis. *Front. Immunol.* **2022**, *13*, 819136. [CrossRef]
28. Paul, A.; Comabella, M.; Gandhi, R. Biomarkers in Multiple Sclerosis. *Cold Spring Harb. Perspect. Med.* **2019**, *9*, a029058. [CrossRef]
29. Yang, J.; Hamade, M.; Wu, Q.; Wang, Q.; Axtell, R.; Giri, S.; Mao-Draayer, Y. Current and Future Biomarkers in Multiple Sclerosis. *Int. J. Mol. Sci.* **2022**, *23*, 5877. [CrossRef]
30. Bol, Y.; Duits, A.A.; Hupperts, R.M.; Vlaeyen, J.W.; Verhey, F.R. The psychology of fatigue in patients with multiple sclerosis: A review. *J. Psychosom. Res.* **2009**, *66*, 3–11. [CrossRef]
31. Plow, M.; Gunzler, D.D.; Chang, J.H.C. Characterizing fatigue phenotypes with other symptoms and clinically relevant outcomes among people with multiple sclerosis. *Qual. Life Res.* **2023**, *32*, 151–160. [CrossRef] [PubMed]
32. Manjaly, Z.-M.; Harrison, N.A.; Critchley, H.D.; Do, C.T.; Stefanics, G.; Wenderoth, N.; Lutterotti, A.; Müller, A.; Stephan, K.E. Pathophysiological and cognitive mechanisms of fatigue in multiple sclerosis. *J. Neurol. Neurosurg. Psychiatry* **2019**, *90*, 642–651. [CrossRef] [PubMed]
33. Rooney, S.; Wood, L.; Moffat, F.; Paul, L. Prevalence of fatigue and its association with clinical features in progressive and non-progressive forms of Multiple Sclerosis. *Mult. Scler. Relat. Disord.* **2019**, *28*, 276–282. [CrossRef]
34. Wan, J.-J.; Qin, Z.; Wang, P.-Y.; Sun, Y.; Liu, X. Muscle fatigue: General understanding and treatment. *Exp. Mol. Med.* **2017**, *49*, e384. [CrossRef]
35. Flachenecker, P. Definitions, Epidemiology, and Etiological Factors. In *Fatigue in Multiple Sclerosis: Background, Clinic, Diagnostic, Therapy*; Penner, I.-K., Ed.; Springer International Publishing: Cham, Swizerland, 2023; pp. 9–26.
36. Gümüş, H. Fatigue Can Be Objectively Measured in Multiple Sclerosis: Multipl Sklerozda Yorgunluk Objektif Olarak Ölçülebilir. *Noro Psikiyatr Ars.* **2018**, *55* (Suppl. 1), S76–S79. [PubMed]
37. Colosimo, C.; Millefiorini, E.; Grasso, M.G.; Vinci, F.; Fiorelli, M.; Koudriavtseva, T.; Pozzilli, C. Fatigue in MS is associated with specific clinical features. *Acta Neurol. Scand.* **1995**, *92*, 353–355. [CrossRef]
38. von Bismarck, O.; Dankowski, T.; Ambrosius, B.; Hessler, N.; Antony, G.; Ziegler, A.; Hoshi, M.-M.; Aly, L.; Luessi, F.; Groppa, S.; et al. Treatment choices and neuropsychological symptoms of a large cohort of early MS. *Neurol.-Neuroimmunol. Neuroinflamm.* **2018**, *5*, e446. [CrossRef]
39. Flachenecker, P.; Müller, G.; König, H.; Meissner, H.; Toyka, K.V.; Rieckmann, P. ["Fatigue" in multiple sclerosis. Development and and validation of the "Würzburger Fatigue Inventory for MS"]. *Nervenarzt* **2006**, *77*, 165–166, 168–170, 172–174. [CrossRef]
40. Braley, T.J.; Chervin, R.D. Fatigue in Multiple Sclerosis: Mechanisms, Evaluation, and Treatment. *Sleep* **2010**, *33*, 1061–1067. [CrossRef]
41. Angioni, D.; Giudici, K.V.; Martinez, M.M.; Rolland, Y.; Vellas, B.; Barreto, P.D.S. Neuroimaging markers of chronic fatigue in older people: A narrative review. *Aging Clin. Exp. Res.* **2021**, *33*, 1487–1492. [CrossRef]
42. Schreiber, H.; Lang, M.; Kiltz, K.; Lang, C. Is personality profile a relevant determinant of fatigue in multiple sclerosis? *Front Neurol.* **2015**, *6*, 2. [CrossRef] [PubMed]
43. Ellison, P.M.; Goodall, S.; Kennedy, N.; Dawes, H.; Clark, A.; Pomeroy, V.; Duddy, M.; Baker, M.R.; Saxton, J.M. Neurostructural and Neurophysiological Correlates of Multiple Sclerosis Physical Fatigue: Systematic Review and Meta-Analysis of Cross-Sectional Studies. *Neuropsychol. Rev.* **2022**, *32*, 506–519. [CrossRef]
44. AlSaeed, S.; Aljouee, T.; Alkhawajah, N.M.; Alarieh, R.; AlGarni, H.; Aljarallah, S.; Ayyash, M.; Abu-Shaheen, A. Fatigue, Depression, and Anxiety Among Ambulating Multiple Sclerosis Patients. *Front. Immunol.* **2022**, *13*, 844461. [CrossRef]
45. Ayache, S.S.; Chalah, M.A. Fatigue in multiple sclerosis–Insights into evaluation and management. *Neurophysiol. Clin.* **2017**, *47*, 139–171. [CrossRef] [PubMed]
46. Dean, J.; Keshavan, M. The neurobiology of depression: An integrated view. *Asian J. Psychiatry* **2017**, *27*, 101–111. [CrossRef] [PubMed]
47. Lee, C.-H.; Giuliani, F. The Role of Inflammation in Depression and Fatigue. *Front. Immunol.* **2019**, *10*, 1696. [CrossRef]
48. Dantzer, R.; O'Connor, J.C.; Freund, G.G.; Johnson, R.W.; Kelley, K.W. From inflammation to sickness and depression: When the immune system subjugates the brain. *Nat. Rev. Neurosci.* **2008**, *9*, 46–56. [CrossRef]
49. Concerto, C.; Rodolico, A.; Ciancio, A.; Messina, C.; Natale, A.; Mineo, L.; Battaglia, F.; Aguglia, E. Vitamin D and Depressive Symptoms in Adults with Multiple Sclerosis: A Scoping Review. *Int. J. Environ. Res. Public Health* **2021**, *19*, 199. [CrossRef]
50. Putzki, N.; Katsarava, Z.; Vago, S.; Diener, H.; Limmroth, V. Prevalence and Severity of Multiple-Sclerosis-Associated Fatigue in Treated and Untreated Patients. *Eur. Neurol.* **2008**, *59*, 136–142. [CrossRef]
51. Kappos, L.; Fox, R.J.; Burcklen, M.; Freedman, M.S.; Havrdová, E.K.; Hennessy, B.; Hohlfeld, R.; Lublin, F.; Montalban, X.; Pozzilli, C.; et al. Ponesimod Compared with Teriflunomide in Patients with Relapsing Multiple Sclerosis in the Active-Comparator Phase 3 OPTIMUM Study: A Randomized Clinical Trial. *JAMA Neurol.* **2021**, *78*, 558–567. [CrossRef]
52. Nourbakhsh, B.; Waubant, E.; Evers, A.W.M.; Solomon, A.J. Ethical considerations in the treatment of multiple sclerosis fatigue. *Mult. Scler. Relat. Disord.* **2021**, *54*, 103129. [CrossRef]

53. Nourbakhsh, B.; Revirajan, N.; Morris, B.; Cordano, C.; Creasman, J.; Manguinao, M.; Krysko, K.; Rutatangwa, A.; Auvray, C.; Aljarallah, S.; et al. Safety and efficacy of amantadine, modafinil, and methylphenidate for fatigue in multiple sclerosis: A randomised, placebo-controlled, crossover, double-blind trial. *Lancet Neurol.* **2021**, *20*, 38–48. [CrossRef] [PubMed]
54. Brown, J.N.; Howard, C.A.; Kemp, D.W. Modafinil for the Treatment of Multiple Sclerosis-Related Fatigue. *Ann. Pharmacother.* **2010**, *44*, 1098–1103. [CrossRef] [PubMed]
55. Cocco, E.; Fadda, P. Treatment of multiple sclerosis fatigue with the synthetic psychoactive drug modafinil. *Exp. Neurol.* **2022**, *347*, 113906. [CrossRef] [PubMed]
56. Benedict, R.H.; Priore, R.L.; Miller, C.; Munschauer, F.; Jacobs, L. Personality disorder in multiple sclerosis correlates with cognitive impairment. *J. Neuropsychiatry Clin. Neurosci.* **2001**, *13*, 70–76. [CrossRef]
57. Uca, A.U.; Uguz, F.; Kozak, H.H.; Turgut, K.; Tekin, G.; Altas, M.; Akpinar, Z. Personality disorders in pateints with multiple sclerosis: Prevalence and association with depressive and anxiety disorders and clinical features. *Neurol. Asia* **2016**, *21*, 55–61.
58. McKay, K.A.; Tremlett, H.; Fisk, J.D.; Zhang, T.; Patten, S.B.; Kastrukoff, L.; Campbell, T.; Marrie, R.A.; For the CIHR Team in the Epidemiology and Impact of Comorbidity on Multiple Sclerosis. Psychiatric comorbidity is associated with disability progression in multiple sclerosis. *Neurology* **2018**, *90*, e1316–e1323. [CrossRef]
59. Bruce, J.M.; Lynch, S.G. Personality traits in multiple sclerosis: Association with mood and anxiety disorders. *J. Psychosom. Res.* **2011**, *70*, 479–485. [CrossRef]
60. Afshar, H.; Roohafza, H.R.; Keshteli, A.H.; Mazaheri, M.; Feizi, A.; Adibi, P. The association of personality traits and coping styles according to stress level. *J. Res. Med. Sci.* **2015**, *20*, 353–358.
61. O'Brien, T.B.; DeLongis, A. The interactional context of problem-, emotion-, and relationship-focused coping: The role of the big five personality factors. *J. Pers.* **1996**, *64*, 775–813. [CrossRef]
62. Mroczek, D.K.; Almeida, D.M. The Effect of Daily Stress, Personality, and Age on Daily Negative Affect. *J. Pers.* **2004**, *72*, 355–378. [CrossRef] [PubMed]
63. Sutin, A.R.; Zonderman, A.B.; Ferrucci, L.; Terracciano, A. Personality Traits and Chronic Disease: Implications for Adult Personality Development. *Journals Gerontol. Ser. B* **2013**, *68*, 912–920. [CrossRef] [PubMed]
64. Concerto, C.; Rodolico, A.; Avanzato, C.; Fusar-Poli, L.; Signorelli, M.S.; Battaglia, F.; Aguglia, E. Autistic Traits and Attention-Deficit Hyperactivity Disorder Symptoms Predict the Severity of Internet Gaming Disorder in an Italian Adult Population. *Brain Sci.* **2021**, *11*, 774. [CrossRef]
65. Smirni, D.; Smirni, P.; Lavanco, G.; Caci, B. Premorbid Personality Traits as Risk Factors for Behavioral Addictions: A Systematic Review of a Vulnerability Hypothesis. *Children* **2023**, *10*, 467. [CrossRef]
66. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders: DSM-5*; American Psychiatric Association: Washington, DC, USA, 2013.
67. Hampson, S.E. Personality Processes: Mechanisms by Which Personality Traits "Get Outside the Skin". *Annu. Rev. Psychol.* **2012**, *63*, 315–339. [CrossRef] [PubMed]
68. Matthews, G. Traits, cognitive processes and adaptation: An elegy for Hans Eysenck's personality theory. *Personal. Individ. Differ.* **2016**, *103*, 61–67. [CrossRef]
69. Eysenck, H.J. A reply to Costa and McCrae. P or A and C—The role of theory. *Personal. Individ. Differ.* **1992**, *13*, 867–868. [CrossRef]
70. Davis, R.D. Millon: Essentials of his science, theory, classification, assessment, and therapy. *J. Personal. Assess.* **1999**, *72*, 330–352. [CrossRef]
71. Strack, S. Introduction. *J. Personal. Assess.* **1999**, *72*, 323–329. [CrossRef]
72. Bajraktarov, S.; Gudeva-Nikovska, D.; Manuå¡Eva, N.; Arsova, S. Personality Characteristics as Predictive Factors for the Occurrence of Depressive Disorder. *Open Access Maced. J. Med. Sci.* **2017**, *5*, 48–53. [CrossRef]
73. McCrae, R.R.; John, O.P. An Introduction to the Five-Factor Model and Its Applications. *J. Pers.* **1992**, *60*, 175–215. [CrossRef] [PubMed]
74. Maggio, M.G.; Cuzzola, M.F.; Latella, D.; Impellizzeri, F.; Todaro, A.; Rao, G.; Manuli, A.; Calabrò, R.S. How personality traits affect functional outcomes in patients with multiple sclerosis: A scoping review on a poorly understood topic. *Mult. Scler. Relat. Disord.* **2020**, *46*, 102560. [CrossRef]
75. Kendler, K.S.; Kuhn, J.; Prescott, C.A. The Interrelationship of Neuroticism, Sex, and Stressful Life Events in the Prediction of Episodes of Major Depression. *Am. J. Psychiatry* **2004**, *161*, 631–636. [CrossRef]
76. Kever, A.; Walker, E.L.; Riley, C.S.; Heyman, R.A.; Xia, Z.; Leavitt, V.M. Association of personality traits with physical function, cognition, and mood in multiple sclerosis. *Mult. Scler. Relat. Disord.* **2022**, *59*, 103648. [CrossRef] [PubMed]
77. Besharat, M.A.; Pourhosein, R.; Rostami, R.; Bazzazian, S. Perfectionism and fatigue in multiple sclerosis. *Psychol. Health* **2011**, *26*, 419–432. [CrossRef]
78. Fernández-Muñoz, J.J.; Morón-Verdasco, A.; Cigarán-Méndez, M.; Muñoz-Hellín, E.; Pérez-De-Heredia-Torres, M.; Fernández-De-Las-Peñas, C. Disability, quality of life, personality, cognitive and psychological variables associated with fatigue in patients with multiple sclerosis. *Acta Neurol. Scand.* **2015**, *132*, 118–124. [CrossRef] [PubMed]
79. Incerti, C.C.; Argento, O.; Pisani, V.; Mannu, R.; Magistrale, G.; Di Battista, G.; Caltagirone, C.; Nocentini, U. A Preliminary Investigation of Abnormal Personality Traits in MS Using the MCMI-III. *Appl. Neuropsychol. Adult* **2015**, *22*, 452–458. [CrossRef]
80. Matesic, I.; Marcinko, I. Identifying the relevant determinants of MS related fatigue: The role of the clinical indicators of disease and personality. *Mult. Scler. Relat. Disord.* **2020**, *42*, 102054. [CrossRef]

81. Merkelbach, S.; König, J.; Sittinger, H. Personality traits in multiple sclerosis (MS) patients with and without fatigue experience. *Acta Neurol. Scand.* **2003**, *107*, 195–201. [CrossRef]
82. Penner, I.-K.; Bechtel, N.; Raselli, C.; Stöcklin, M.; Opwis, K.; Kappos, L.; Calabrese, P. Fatigue in multiple sclerosis: Relation to depression, physical impairment, personality and action control. *Mult. Scler. J.* **2007**, *13*, 1161–1167. [CrossRef]
83. Sindermann, C.; Saliger, J.; Nielsen, J.; Karbe, H.; Markett, S.; Stavrou, M.; Montag, C. Personality and Primary Emotional Traits: Disentangling Multiple Sclerosis Related Fatigue and Depression. *Arch. Clin. Neuropsychol.* **2018**, *33*, 552–561. [CrossRef]
84. Spiegelberg, N.; Breuer, S.; Nielsen, J.; Saliger, J.; Montag, C.; Karbe, H.; Markett, S. Cognitive Fatigue Predicts Cognitive Failure in Multiple Sclerosis Patients and Healthy Controls: A Case-Control Study. *Arch. Clin. Neuropsychol.* **2021**, *36*, 908–917. [CrossRef] [PubMed]
85. Strober, L.B. Personality in multiple sclerosis (MS): Impact on health, psychological well-being, coping, and overall quality of life. *Psychol. Health Med.* **2017**, *22*, 152–161. [CrossRef]
86. van der Werf, S.P.; Evers, A.; Jongen, P.J.; Bleijenberg, G. The role of helplessness as mediator between neurological disability, emotional instability, experienced fatigue and depression in patients with multiple sclerosis. *Mult. Scler. J.* **2003**, *9*, 89–94. [CrossRef]
87. Fisk, J.D.; Ritvo, P.G.; Ross, L.; Haase, D.A.; Marrie, T.J.; Schlech, W.F. Measuring the functional impact of fatigue: Initial validation of the Fatigue Impact Scale. *Clin. Infect. Dis.* **1994**, *18* (Suppl. 1), S79–S83. [CrossRef]
88. Téllez, N.; Río, J.; Tintoré, M.; Nos, C.; Galán, I.; Montalban, X. Does the Modified Fatigue Impact Scale offer a more comprehensive assessment of fatigue in MS? *Mult. Scler.* **2005**, *11*, 198–202. [CrossRef]
89. Krupp, L.B.; LaRocca, N.G.; Muir-Nash, J.; Steinberg, A.D. The fatigue severity scale. Application to patients with multiple sclerosis and systemic lupus erythematosus. *Arch. Neurol.* **1989**, *46*, 1121–1123. [CrossRef]
90. Wessely, S.; Powell, R. Fatigue syndromes: A comparison of chronic "postviral" fatigue with neuromuscular and affective disorders. *J. Neurol. Neurosurg. Psychiatry* **1989**, *52*, 940–948. [CrossRef] [PubMed]
91. Beurskens, A.J.; Bültmann, U.; Kant, I.; Vercoulen, J.H.; Bleijenberg, G.; Swaen, G.M. Fatigue among working people: Validity of a questionnaire measure. *Occup. Environ. Med.* **2000**, *57*, 353–357. [CrossRef]
92. Penner, I.; Raselli, C.; Stöcklin, M.; Opwis, K.; Kappos, L.; Calabrese, P. The Fatigue Scale for Motor and Cognitive Functions (FSMC): Validation of a new instrument to assess multiple sclerosis-related fatigue. *Mult. Scler. J.* **2009**, *15*, 1509–1517. [CrossRef] [PubMed]
93. Costa, P.; McCrae, R. Normal Personality Assessment in Clinical Practice: The NEO Personality Inventory. *Psychol. Assess.* **1992**, *4*, 5–13. [CrossRef]
94. Caruso, J.C. Reliability Generalization of the Neo Personality Scales. *Educ. Psychol. Meas.* **2000**, *60*, 236–254. [CrossRef]
95. Costa, P.T., Jr.; McCrae, R.R. *The SAGE Handbook of Personality Theory and Assessment: Volume 2—Personality Measurement and Testing*; SAGE Publications Ltd.: London, UK, 2008; Available online: https://sk.sagepub.com/reference/hdbk_personalitytheory2 (accessed on 16 April 2023).
96. Goldberg, L.R.; Johnson, J.A.; Eber, H.W.; Hogan, R.; Ashton, M.C.; Cloninger, C.R.; Gough, H.G. The international personality item pool and the future of public-domain personality measures. *J. Res. Pers.* **2006**, *40*, 84–96. [CrossRef]
97. Denollet, J. DS14: Standard Assessment of Negative Affectivity, Social Inhibition, and Type D Personality. *Psychosom. Med.* **2005**, *67*, 89–97. [CrossRef]
98. Frost, R.O.; Marten, P.; Lahart, C.; Rosenblate, R. The dimensions of perfectionism. *Cogn. Ther. Res.* **1990**, *14*, 449–468. [CrossRef]
99. Terry-Short, L.A.; Owens, G.; Slade, P.; Dewey, M.E. Positive and negative perfectionism. *Personal. Individ. Differ.* **1995**, *18*, 663–668. [CrossRef]
100. Millon, T.; Davis, R.D. The MCMI–III: Present and future directions. *J. Pers. Assess.* **1997**, *68*, 69–85. [CrossRef] [PubMed]
101. Cloninger, C.R.; Svrakic, D.M.; Przybeck, T.R. A psychobiological model of temperament and character. *Arch. Gen. Psychiatry* **1993**, *50*, 975–990. [CrossRef]
102. Cloninger, C.R.; Svrakic, D.M.; Bayon, C.; Przybeck, T.R. *Measurement of Psychopathology as Variants of Personality*; American Psychiatric Association: Washington, DC, USA, 1999.
103. Fahrenberg, J.; Hampel, R.; Selg, H. *Das Freiburger Persönlichkeitsinventar: FPI; Revidierte Fassung FPI-R und Teilweise Geänderte Fassung FPI-A1; Handanweisung*; Verlag für Psychologie Hogrefe: Göttingen, Germany, 1989.
104. Eysenck, H.J. Dimensions of personality: 16, 5 or 3?—Criteria for a taxonomic paradigm. *Personal. Individ. Differ.* **1991**, *12*, 773–790. [CrossRef]
105. McCrae, R.R.; Costa, P.T. Adding Liebe und Arbeit: The Full Five-Factor Model and Well-Being. *Pers. Soc. Psychol. Bull.* **1991**, *17*, 227–232. [CrossRef]
106. Miller, J.D.; Lynam, D.R.; Vize, C.; Crowe, M.; Sleep, C.; Maples-Keller, J.L.; Few, L.R.; Campbell, W.K. Vulnerable Narcissism Is (Mostly) a Disorder of Neuroticism. *J. Pers.* **2018**, *86*, 186–199. [CrossRef] [PubMed]
107. Allroggen, M.; Rehmann, P.; Schürch, E.; Morf, C.C.; Kölch, M. The Relationship between Narcissism and Personality Traits of the Five-Factor-Model in Adolescents and Young Adults. *Z. Kinder Jugendpsychiatrie Psychother.* **2018**, *46*, 516–522. [CrossRef]
108. Mols, F.; Denollet, J. Type D personality in the general population: A systematic review of health status, mechanisms of disease, and work-related problems. *Health Qual. Life Outcomes* **2010**, *8*, 9. [CrossRef] [PubMed]
109. Boyle, L.L.M.D.; Lyness, J.M.M.D.; Duberstein, P.R.P.; Karuza, J.P.; King, D.A.P.; Messing, S.M.S.; Tu, X. Trait Neuroticism, Depression, and Cognitive Function in Older Primary Care Patients. *Am. J. Geriatr. Psychiatry* **2010**, *18*, 305–312. [CrossRef] [PubMed]

110. Weger, M.; Sandi, C. High anxiety trait: A vulnerable phenotype for stress-induced depression. *Neurosci. Biobehav. Rev.* **2018**, *87*, 27–37. [CrossRef]
111. Estrada-López, M.; Reguera-García, M.M.; Rivera, F.J.P.; Molina, A.J. Physical disability and personality traits in multiple sclerosis. *Mult. Scler. Relat. Disord.* **2020**, *37*, 101465. [CrossRef]
112. Tarasiuk, J.; Kapica-Topczewska, K.; Czarnowska, A.; Chorąży, M.; Kochanowicz, J.; Kułakowska, A. Co-occurrence of Fatigue and Depression in People with Multiple Sclerosis: A Mini-Review. *Front. Neurol.* **2021**, *12*, 817256. [CrossRef]
113. Otte, C.; Gold, S.M.; Penninx, B.W.; Pariante, C.M.; Etkin, A.; Fava, M.; Mohr, D.C.; Schatzberg, A.F. Major depressive disorder. *Nat. Rev. Dis. Prim.* **2016**, *2*, 16065. [CrossRef]
114. Baquero, M.; Martín, N. Depressive symptoms in neurodegenerative diseases. *World J. Clin. Cases* **2015**, *3*, 682–693. [CrossRef]
115. Thielscher, C.; Thielscher, S.; Kostev, K. The risk of developing depression when suffering from neurological diseases. *Ger. Med. Sci.* **2013**, *11*, Doc02. [CrossRef]
116. Flachenecker, P.; Kümpfel, T.; Kallmann, B.; Gottschalk, M.; Grauer, O.; Rieckmann, P.; Trenkwalder, C.; Toyka, K.V. Fatigue in multiple sclerosis: A comparison of different rating scales and correlation to clinical parameters. *Mult. Scler. J.* **2002**, *8*, 523–526. [CrossRef] [PubMed]
117. Zuckerman, M.; Kuhlman, D.M.; Joireman, J.; Teta, P.; Kraft, M. A comparison of three structural models for personality: The big three, the big five, and the alternative five. *J. Personal. Soc. Psychol.* **1993**, *65*, 757. [CrossRef]
118. Di Fabio, A.; Smith, M.M.; Saklofske, D.H. Perfectionism and a Healthy Attitude toward Oneself: Could Humor Be a Resource? *Int. J. Environ. Res. Public Health* **2019**, *17*, 201. [CrossRef]
119. Mofield, E.; Peters, M.P.; Chakraborti-Ghosh, S. Perfectionism, Coping, and Underachievement in Gifted Adolescents: Avoidance vs. Approach Orientations. *Educ. Sci.* **2016**, *6*, 21. [CrossRef]
120. Slade, P.; Owens, G. A Dual Process Model of Perfectionism Based on Reinforcement Theory. *Behav. Modif.* **1998**, *22*, 372–390. [CrossRef]
121. Smith, M.M.; Arnett, P.A. Perfectionism and physical disability predict depression in multiple sclerosis. *J. Psychosom. Res.* **2013**, *75*, 187–189. [CrossRef]
122. Stephan, Y.; Sutin, A.R.; Luchetti, M.; Canada, B.; Terracciano, A. Personality and fatigue: Meta-analysis of seven prospective studies. *Sci. Rep.* **2022**, *12*, 9156. [CrossRef]
123. Henriques-Calado, J.; Duarte-Silva, M.E.; Keong, A.; Sacoto, C.; Junqueira, D. Personality Traits and Personality Disorders in Older Women: An Explorative Study between Normal Development and Psychopathology. *Health Care Women Int.* **2014**, *35*, 1303–1314. [CrossRef]
124. Delva, M.; Delva, I.; Pinchuk, V.; Kryvchun, A.; Purdenko, T. Prevalence and predictors of fatigue in patients with episodic migraine. *Wiadomości Lek.* **2022**, *75 Pt 2*, 1970–1974. [CrossRef]