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Wonink, Henderyke A.; Kruithof, Willeke J.; Goedee, H. Stephan; Beelen, Anita

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ORIGINAL ARTICLE

Chronic inflammatory neuropathies and their impact on activities and participation

Henderyke A. Wonink[1,2] | Willeke J. Kruithof[3,4] | H. Stephan Goedee[5] | Anita Beelen[3,4]

[1]Physical Therapy Sciences, Program in Clinical Health Sciences, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands

[2]Center for Rehabilitation, University Medical Center Groningen, Groningen, The Netherlands

[3]Department of Rehabilitation, Physical Therapy Science and Sports, UMC Utrecht Brain Center, University Medical Center Utrecht, Utrecht, The Netherlands

[4]Center of Excellence for Rehabilitation Medicine, UMC Utrecht Brain Center, University Medical Center Utrecht, and De Hoogstraat Rehabilitation, Utrecht, The Netherlands

[5]Department of Neurology, University Medical Center Utrecht, Utrecht, The Netherlands

Correspondence
Anita Beelen, Department of Rehabilitation, Physical Therapy Science and Sports, UMC Utrecht Brain Center, University Medical Center Utrecht, Utrecht, The Netherlands.
Email: j.a.j.beelen@umcutrecht.nl

Abstract

Background: Chronic inflammatory demyelinating polyneuropathy (CIDP) and multifocal motor neuropathy (MMN) are inflammatory neuropathies that can lead to considerable limitations in daily activities and in social participation. However, systematic evaluation of these self-reported limitations is lacking in the currently available studies. Understanding the impact of these diagnoses on patients' life is important to optimize management strategies.

Aim: To systematically assess the self-reported limitations in activities and participation and determine associated factors.

Methods: A survey study was conducted in 2021 in a cohort of patients with CIDP ($n=257$) and MMN ($n=148$) from a university hospital. The survey included the Rasch-built Overall Disability Scale and the Utrecht Scale for Evaluation of Rehabilitation-Participation, questions addressing personal and disease-related factors and treatment. Multivariate linear regression analysis was used to determine associations with disease-related and personal factors.

Results: A total of 147 CIDP and 103 MMN patients responded. Limitations in activities were reported by 70.7% CIDP and 52.2% MMN patients with moderate to severe limitations in 22.4% and 5.9% patients, respectively. Participation restrictions were reported by 50% of CIDP and 40% of MMN patients, nevertheless satisfaction with participation was high. Fatigue, pain and resilience were independently associated with limitations in activities and satisfaction with participation in CIDP patients.

Conclusions: Activity limitations and restrictions in participation are common in CIDP patients and to a lesser extent in MMN patients. Fatigue, pain and resilience independently contributed to perceived limitations in CIDP patients. Referral to a rehabilitation physician is warranted to address these limitations appropriately.

KEYWORDS
activity, CIDP, inflammatory neuropathy, MMN, participation

H. Stephan Goedee and Anita Beelen contributed equally.

INTRODUCTION

Chronic inflammatory demyelinating polyneuropathy (CIDP) and multifocal motor neuropathy (MMN) are the most common chronic inflammatory neuropathies that are amenable to immune-modulating treatment strategies. CIDP and MMN can lead to considerable impairment of daily activities, limitations at work and social participation [1–3]. Despite optimized immune-modulating strategies, symptoms such as muscle weakness often persist and may even progress over time [4–7]. Axonal loss on electrodiagnostic studies and delayed treatment initiation are important determinants of long-term outcome, such as degree of residual weakness and level of disability [7–9]. Chronic fatigue and pain are other common limiting factors in chronic inflammatory neuropathies [10–13].

Current sets of clinical outcome measures such as the Inflammatory Neuropathy Cause and Treatment (INCAT) disability scale, handgrip strength and manual muscle strength examination are mainly aimed at evaluating treatment efficacy [14]. Although these are essential in optimizing routine management of individual patients in the outpatient clinic and the design of treatment trials, they lack evaluation of limitations of activities experienced by patients [15, 16]. At present the Rasch-built Overall Disability Scales for inflammatory neuropathies and MMN (I-RODS and MMN-RODS) are the only questionnaires used to evaluate possible limitations in activity and social participation [17, 18]. In contrast, systematic evaluation of self-reported limitations is lacking in the currently available studies. The latter is highly warranted for optimizing rehabilitation strategies, as routine neurologic treatment strategies often fail to address limitations in activity and social participation appropriately.

Detailed insight into perceived limitations in activities and participation of patients with chronic inflammatory neuropathies may help to raise awareness among clinicians of the impact on daily life and resulting care needs. They could also help to optimize management strategies by providing tailored care, including self-management strategies, increase efficacy of strategies aimed at compensating limitations, as well as other rehabilitation interventions. Therefore, we systematically assessed the self-reported limitations in activities and participation using a survey in a large cohort of patients with chronic inflammatory neuropathies.

METHODS

Study design

We performed a cross-sectional study using an extensive standardized survey send to patients with MMN and CIDP, seen between January 2017 and March 2021 at the neuromuscular outpatient clinic of the University Medical Center Utrecht (UMCU), a tertiary neuromuscular expert center in The Netherlands. The study protocol was reviewed and approved by our local Institutional Medical Research Ethics Committee. All participants provided informed consent.

Patients

All adult patients with a diagnosis of CIDP or MMN according to the relevant diagnostic consensus criteria [19–21] seen at our outpatient clinic were invited to participate. We sent them the study information and subsequently a personal hyperlink to an online survey (Castor Electronic Data Capture) by e-mail (April 2021, with a reminder in August 2021) or postal mail when their e-mail address was unknown/invalid or a paper version was preferred.

Standardized survey

We constructed an extensive standardized survey, after careful selection of published validated generic and disease-specific questionnaires of activities and participation, assessment scales for pain and fatigue, and other relevant personal and disease-related factors that could influence performing activities and participation. We then discussed the selected set in an expert panel that included treating physicians and patients to verify that the proposed survey contained all relevant aspects of the impact of CIDP/MMN on daily life and to ensure feasibility. The survey consisted of six validated questionnaires to evaluate limitations in activities, restrictions in and satisfaction with participation, self-reported disease severity, average pain intensity in the last week, fatigue and resilience. In addition, we addressed personal and disease-related factors.

We used the Inflammatory Rasch-built Overall Disability Scale (I-RODS) and the Multifocal Motor Neuropathy Rasch-built Overall Disability Scale (MMN-RODS) supplemented with questions addressing lower limb function from the I-RODS (range 0–100, most severe limitation in all activities to no limitation in any activity), to assess limitations in activities for patients with CIDP and MMN, respectively [17, 18]. In addition, we asked for limb dominance and most-affected upper limb, sensory impairment and cramps, and use of assistive devices. We also deployed the Utrecht Scale for Evaluation of Rehabilitation-Participation (USER-P) to measure participation in patients with physical disability [22, 23]. USER-P assesses three aspects of participation (i.e., frequency, restrictions and satisfaction) and covers vocational activities (i.e., paid work, unpaid work, study, housekeeping), leisure activities (indoors and outdoors) and social activities including relationships. Two subscales were used: USER-P Restrictions and Satisfaction. The Restrictions subscale consists of 11 items asking about restrictions in vocational, leisure and social activities as a consequence of CIDP/MMN. Items are rated on a scale from 0 (not possible) to 3 (without difficulty) or 'not applicable'. The Satisfaction subscale consists of 10 items, rating satisfaction on 10 aspects of participation with a scale ranging from 0 (very dissatisfied) to 4 (very satisfied) or 'not applicable' for the items "work/housekeeping" and "partner relationship". Subscale sum scores were all converted to scores on a 0–100 scale with higher scores indicating fewer restrictions and higher satisfaction. Optional open-comment fields were available for each item on both questionnaires, to allow more detailed explanations for

any score. To exclude confounding due to the impact of COVID-19 restrictions, all participants were asked if their answers on the USER-P were influenced by the COVID-19 pandemic. We assessed self-reported disease severity (INCAT disability scale), average pain intensity in the last week (Numeric Pain Rating Scale, NPRS), fatigue (modified Fatigue Severity Scale, mFSS) and resilience (10-item Connor–Davison Resilience Scale, CD-RISC-10). The INCAT disability scale ranges from 0 (no functional impairment) to 10 (inability to make any purposeful movement with either arms or legs) [24]. The NPRS ranges from 0 (no pain at all) to 10 (the worst imaginable pain) [25]. The mFSS is a linearly weighted scale with seven statements concerning the severity of fatigue and its effect on a person's activities and lifestyle. Each statement is scored on a four-point scale from 0 (disagree) to 3 (agree). The total mFSS score ranges from 0 (no signs of fatigue) to 21 (most disabling fatigue) [26]. The CD-RISC consists of 10 statements reflecting the ability to tolerate experiences such as painful feelings, pressure, illness, change or failure. Participants were asked to rate their amount of agreement (0 = "Not true at all" to 4 = "True nearly all the time") to the statements over the past month. A sum score is obtained (range 0–40) with 40 as the highest level of resilience [27]. Age, gender, comorbidity, disease duration, current disease activity ([1] cured, [2] remission, [3] stable active disease, [4] improving, [5] unstable active disease) based on the CIDP Disease Activity Status (CDAS) [28] and immune-modulating strategies (type) were retrieved from the electronic medical records. Finally, we also asked for details on family setting and involvement of other (than a neurologist) healthcare professionals (including rehabilitation physician, physical therapist and occupational therapist).

Statistical analysis

One author (HAW) checked the missing values, and actively contacted participants with incomplete survey responses. We used Little's Missing Completely at Random (MCAR) test to exclude bias in type of missing data [29]. Subsequently, we used descriptive statistics and for univariate and multivariate analyses only used complete cases.

In the absence of validated cut-off points to classify the extent of the experienced limitations in activities and participation, we used the following cut-offs:

(i) RODS score: ≤50 = moderate to severe limitations, 51–79 = mild limitations and ≥80 = few/no limitations.
(ii) USER-P Restriction and Satisfaction scales were dichotomized to quantify the presence of experienced restrictions and dissatisfaction in different domains of participation: 'with assistance', 'with difficulty' and 'not possible' were defined as 'restrictions' and 'without difficulty' and 'not applicable' as 'no restrictions'; 'very dissatisfied', 'dissatisfied' and 'neutral' were defined as 'dissatisfaction' and 'satisfied' and 'very satisfied' as 'satisfaction'.

We also explored whether involvement of other healthcare professionals (other than a neurologist) in the past and present in the treatment of CIDP or MMN was related to limitations, restrictions and satisfaction.

We used bivariate analysis by Pearson's R for outcomes on I-RODS, MMN-RODS, USER-P Restrictions and USER-P Satisfaction scales to evaluate possible associations between the self-reported limitations in activities and participation as dependent variables and potential determinants as independent variables (continuous). Student's *t*-test was used for categorical variables. We used one-way ANOVA analysis to determine possible association between CDAS classification and limitations in activity. We dichotomized pain as an independent variable due to skewed distribution and defined the following cut-offs: NPRS ≤2 = mild pain and NPRS ≥3 = moderate to severe pain. Multicollinearity was checked by performing Pearson correlations between all determinants (correlation coefficient ≥0.7 indicated moderate to strong correlations). We used a threshold ($p \leq 0.20$) in univariate analysis to select items for multivariate analysis. Disease severity measured with the INCAT disability scale was not included in the multivariate regression analysis because of the strong correlation with I-RODS, indicating that the content of the INCAT disability scale exhibited considerable overlap. Multivariate linear regression analysis with backward stepwise selection was used to evaluate the relationship between potential determinants with self-reported limitations in activities and participation ($p \geq 0.10$ was considered as not statistically significant). Assumptions regarding heteroscedasticity and normality were examined with residual plots and QQ plots [30]. We used SPSS Statistics version 27 (IBM Corp.) for the analysis.

RESULTS

We enrolled 250 patients (147 CIDP and 103 MMN) in our study (62% response rate). The number of total missing values was below 5% and Little's MCAR test showed missing data was MCAR for all variables. Patient characteristics are summarized in Table 1. Approximately one-third of the CIDP and MMN patients did not report pain in the last week (NPRS score 0). Experience of fatigue varied considerably, and most patients showed high resilience.

Limitations in activities

The majority of CIDP patients perceived limitations in activities (median I-RODS score 63.0, P25–P75: 51–83), 70.7% reported mild limitations in performing activities and 22.4% moderate to severe. We found that only 7.5% of CIDP patients experience no limitations in performing activities (Figure 1). Mainly mobility-related activities (e.g., running, dancing, standing for hours, and carrying and putting down a heavy object) were rated as 'impossible to perform' or 'perform with difficulty'. In contrast, the least impaired activities were related to domains of self-care (e.g.,

TABLE 1 Characteristics of the participants.

Characteristic	CIDP ($n=147$)	MMN ($n=103$)
Sex, female *n* (%)	44 (29.9)	24 (23.3)
Age (years), median; range	63.7; 19.8–88.2	60.5; 36.0–88.7
Duration since first complaints (years), median; range	7; 1–35	11; 2–51
INCAT disability score, median (P25–P75)		
Total	3 (1–5)	3 (2–4)
Upper extremity	2 (0–2)	2 (2–3)
Lower extremity	1 (1–2)	1 (0–1)
Average pain in the last week (NPRS), *n*		
NPRS ≤2	76[a]	29[b]
Fatigue (mFSS), mean ± SD, range	11.9 ± 6.3[c]; 0–21	9.1 ± 6.3; 0–21
Resilience (CD-RISC-10), mean ± SD, range	28.4 ± 7.4; 7–40	30.4 ± 6.7; 16–40
Current immune-modulating strategies, *n* (%)		
None	48 (32.7)	5 (4.9)
Immunoglobulins	81 (55.1)	97 (94.2)
Steroids	11 (7.5)	0
Plasma exchange	1 (0.7)	0
Unknown	6 (4.1)	1 (1.0)
Current medical situation based on CDAS, *n* (%)		
Stable active disease	93 (63.3)	75 (72.8)
Unstable active disease	35 (23.7)	24 (23.3)
Remission	12 (8.2)	1 (1.0)
Unknown	7 (4.8)	3 (2.9)
Improving	0	0
Cured	0	0
Comorbidity, *n* (%)	$n=138$	$n=99$
None	73 (49.7)	58 (56.3)
Cardiovascular-respiratory system	48	20
Muscular-skeletal-integumentary system	13	8
Neuropsychiatric system	10	4
Other	31	23

Note: Some variants of CIDP (e.g., distal CIDP and sensory CIDP) commonly lack response to immune-modulating strategies, have mild progression and therefore are often not considered for standard immune-modulating treatment. Also, individual cases did not respond to routine treatment strategies but were not considered eligible for more aggressive immune-modulating treatment despite an unstable disease.

Abbreviations: CDAS, CIDP Disease Activity Status; CD-RISC-10, 10-item Connor–Davidson Resilience Scale; CIDP, chronic inflammatory demyelinating polyneuropathy; INCAT, Inflammatory Neuropathy Cause and Treatment; mFSS, modified Fatigue Severity Scale; MMN, multifocal motor neuropathy; NPRS Numeric Pain Rating Scale; P25, 25th percentile; P75, 75th percentile; SD, standard deviation.

[a]$n=142$.

[b]$n=98$.

[c]$n=141$.

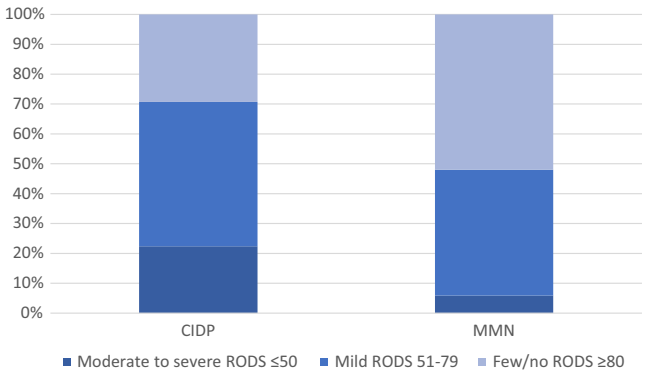

FIGURE 1 Distribution of the degree of perceived limitations in activities measured with the Inflammatory Rasch-built Overall Disability Scale (I-RODS) or Multifocal Motor Neuropathy Rasch-built Overall Disability Scale (MMN-RODS). CIDP, chronic inflammatory demyelinating polyneuropathy; MMN, multifocal motor neuropathy.

sitting on a toilet, brushing teeth and eating; Table 2). Half of the CIDP patients used an assistive device (including walking aids, ankle-foot orthoses, bathroom seat and wheelchair). More than three-quarters of CIDP patients reported sensory deficits, leading to impairment of performing activities in half of these patients. Almost two-thirds of CIDP patients reported cramps, of which half indicated that these muscle cramps limited their activities. CIDP patients with moderate to severe limitations were on average slightly older and had longer disease duration compared to patients with mild/no limitations. Presence of comorbidity was comparable in both groups of limitations in CIDP.

Interestingly, we found that 52% of MMN patients exclusively reported few or no limitations in performing activities, with a median score of 78.8 (P25–P75: 69.2–90.1; Figure 1). Severe to moderate limitations were only seen in 5.9% of MMN patients. Most frequent activities rated as 'impossible to perform' or 'perform with difficulty' were related to fine hand use (e.g., clipping fingernails, tying laces, picking up a small object and peeling an apple/orange; Table 3). Qualitative data showed that one-third of the MMN patients used a supportive device (e.g., wrist braces and adapted cutlery).

Open comments on I-RODS, MMN-RODS and USER-P revealed that CIDP and MMN patients performed activities differently than before disease, including use of tricks or a supportive device. Some participants reported that performing activities demanded more time than before and required more attention and concentration.

Participation

In contrast to the high number of CIDP patients experiencing limitations in activities, fewer restrictions in participation were reported (USER-P Restrictions scale median 79.1, P25–P75: 63.5–96.7). Approximately half of the CIDP patients reported relatively few restrictions, and these mainly concerned physical exercise,

TABLE 2 Frequencies of activities of chronic inflammatory demyelinating polyneuropathy patients ($n=147$) measured with the Inflammatory Rasch-built Overall Disability Scale (I-RODS).

Activity	Perform with difficulty or impossible to perform (*n* (%))
Mobility	
Stand for hours	118 (80.3)
Bend and pick up an object	79 (51.0)
Carry and put down a heavy object	90 (61.2)
Move a chair	30 (20.4)
Turn a key in a lock	45 (30.6)
Read a newspaper/book	32 (21.9)
Catch an object	59 (40.1)
Walk one flight of stairs	79 (53.7)
Run	124 (84.9)
Walk outdoors <1 km	78 (53.1)
Walking around obstacles	73 (49.7)
Go to the general practitioner	35 (24.0)
Travel by public transport	69 (47.6)
Dance	110 (75.3)
Self-care	
Wash upper body	29 (19.7)
Wash lower body	41 (27.9)
Take a shower	39 (26.5)
Brush your teeth	13 (8.8)
Sit on a toilet	11 (7.5)
Dress upper body	37 (25.2)
Eat	17 (11.6)
Domestic life	
Do the shopping	62 (42.5)
Make a sandwich	24 (16.4)
Do the dishes	48 (33.1)

TABLE 3 Frequencies of activities of multifocal motor neuropathy patients ($n=103$) measured with the Multifocal Motor Neuropathy Rasch-built Overall Disability Scale (MMN-RODS).

Activity	Perform with difficulty or impossible to perform (*n* (%))
Mobility	
Pick up a small object	55 (53.4)
Turn a key in a lock	41 (39.8)
Handle small object	52 (51.0)
Get money from cashpoint	25 (24.3)
Use a phone	24 (23.3)
Read a newspaper/book	17 (16.5)
Write	52 (50.5)
Work on computer	24 (23.3)
Open and close a door	8 (7.8)
Throw an object	33 (32.0)
Self-care	
Brush your teeth	14 (13.6)
Clip fingernails	67 (65.7)
Clean after toilet	17 (16.5)
Dress upper body	21 (20.4)
Button shirt/blouse	64 (62.7)
Tie laces	48 (47.1)
Zip your trousers	27 (26.2)
Eat	17 (16.5)
Use knife/fork	39 (37.9)
Drink out of mug/glass	22 (21.4)
Domestic life	
Prepare a meal	27 (26.2)
Peel an apple/orange	53 (52.0)
Slice vegetables	34 (33.0)
Fold laundry	27 (26.2)
Do the bed	28 (27.2)

housekeeping, outdoor activities and going out (all >50%). We found that all leisure and social activities were performed twice a week in CIDP patients (22%–97%).

Despite the fact that about half of the MMN patients indicated that the COVID-19 pandemic limited their participation, the vast majority of MMN patients experienced almost no restrictions in the different domains of participation (median 90.0, P25–P75: 75.6–96.7). We found a score ≥80 points on the USER-P Restrictions scale in 60.7% of MMN patients. The most commonly perceived restrictions concerned housekeeping, work (in employed patients), physical exercise, and leisure activities indoors (all >38%).

Satisfaction with participation, for patients with mild to moderate restrictions, was 59.0 ± 16.4 for CIDP patients and 65.7 ± 13.8 for MMN patients, compared with 77.2 ± 15.4 and 79.0 ± 17.4 for CIDP and MMN patients with few or no restrictions. We found that dissatisfaction was mainly (but not only) expressed by the patients that experienced the most restrictions (Figure S1). For CIDP and MMN patients, satisfaction was highest in relationships with partner, family and friends or acquaintances. Detailed information regarding the different items of the USER-P and on the association between these subscales can be found in Supplemental data (Figure S2).

Treatment

We found that 67.3% of CIDP and 95.1% of MMN patients were on immune-modulating treatment. The main treatment strategy in both groups was immunoglobulin treatment (55.1% CIDP, 94.2% MMN). Almost one-third of CIDP patients with moderate to severe limitations ($n=33$) and up to half of CIDP patients experiencing few or no limitations ($n=43$) did not have immune-modulating treatment. Intriguingly, at present no other healthcare professional (other than a neurologist) was involved in the treatment in almost

TABLE 4 Involvement of healthcare professionals in chronic inflammatory demyelinating polyneuropathy and multifocal motor neuropathy patients.

Healthcare professional	CIDP (*n* = 140)	MMN (*n* = 99)
Involved at the current moment, *n* (%)		
None	92 (65.7)	77 (77.8)
Physical therapist	31 (22.1)	16 (16.2)
Occupational therapist	8 (5.47)	7 (7.1)
Social worker or nurse specialist in PC	4 (2.9)	1 (1.0)
Psychologist	3 (2.1)	1 (1.0)
Rehabilitation physician	14 (10.0)	6 (6.1)
Orthopedic shoe technician	9 (6.4)	3 (3.0)
Orthopedic instrument manufacturer	6 (4.3)	2 (2.0)
Podiatrist	7 (5.0)	1 (1.0)
Other	11 (7.9)	3 (3.0)
Involved in the past, *n* (%)		
None	85 (60.7)	70 (70.7)
Physical therapist	40 (28.6)	22 (22.2)
Occupational therapist	20 (14.3)	14 (14.1)
Social worker or nurse specialist in PC	12 (8.6)	2 (2.0)
Psychologist	12 (8.6)	7 (7.1)
Rehabilitation physician	32 (22.8)	15 (15.2)
Orthopedic shoe technician	11 (7.9)	4 (4.0)
Orthopedic instrument manufacturer	11 (7.9)	6 (6.1)
Podiatrist	12 (8.6)	3 (3.0)
Other	8 (5.7)	6 (6.1)

Abbreviations: CIDP, chronic inflammatory demyelinating polyneuropathy; MMN, multifocal motor neuropathy; PC, primary care.

two-third of CIDP and 80% of MMN patients. In more than half of the CIDP patients with moderate to severe limitations in activities ($n = 33$) no other healthcare professional was involved (past and present). Involvement of other healthcare professionals is described in Table 4. Also, we found that activity limitations did not significantly differ between the groups based on CDAS.

Associated factors with disease-related and personal factors

Based on univariate analyses on CIDP data, age, pain, fatigue and resilience were included in the multivariate regression analysis for limitations in activities. For restrictions in participation, assumptions were not met because of skewed distribution. Disease severity, pain, fatigue and resilience were included in the multivariate analysis for dissatisfaction with participation. Univariate correlations matrices are displayed in supplemental data (Tables S1 and S2). Multivariate testing (Table 5) showed that fatigue, moderate to severe pain, higher age and more resilience were significantly associated with more limitations in activities (adjusted R^2 51%). Fatigue, high resilience and moderate to severe pain were significantly associated with dissatisfaction with participation (adjusted R^2 40%). Due to skewed distribution, no further analyses were performed for MMN-RODS and USER-P Restrictions and Satisfaction scales in MMN patients.

TABLE 5 Multivariate linear regression analysis of the Inflammatory Rasch-built Overall Disability Scale and Utrecht Scale for Evaluation of Revalidation-Participation satisfaction scales for chronic inflammatory demyelinating polyneuropathy patients.

Variable	I-RODS Multivariate (standardized β)	USER-P satisfaction Multivariate (standardized β)
Age	−0.246**	–
Sex	–	–
Disease duration	NS	–
Disease severity	–	NS
Pain (0 = NPRS 0–2, 1 = NPRS 3–10)	−0.291**	−0.222**
Fatigue	−0.435**	−0.336**
Resilience	0.149*	0.312*
Adjusted R^2	0.510	0.402

Note: *$p \leq 0.05$, **$p \leq 0.01$. Dash indicates that the determinant is not included in multiple regression analysis, based on the univariate linear regression analyses.

Abbreviations: CIDP, chronic inflammatory demyelinating polyneuropathy; I-RODS, Inflammatory Rasch-built Overall Disability Scale; NPRS, Numeric Pain Rating Scale, NS, not significant; USER-P, Utrecht Scale for Evaluation of Revalidation-Participation.

DISCUSSION

Our study showed that the limitations as regards activities and participation in CIDP and MMN patients are different and may warrant distinct rehabilitation strategies. We found that patients with CIDP experience mild to severe limitations in activities and participation, mainly related to mobility with restrictions in physical exercise, household and outdoor activities. In contrast, our MMN patients experienced fewer restrictions, often related to fine motor skills of the hand and physical exercise, household and indoor leisure activities. Importantly, we also found that the degree of reported restrictions did not correspond with the level of experienced satisfaction, indicating that other factors such as resilience may ameliorate or even amplify experienced disease burden. We also found that fatigue, pain and higher age were associated with more limitations and less satisfaction, while higher resilience is associated with fewer limitations and higher satisfaction in CIDP patients. Taken together, our

results suggest that rehabilitation strategies may apply to a wider range of restrictions and should not only be reserved for CIDP and MMN patients with more severe disabilities.

The degree of limitations in activity in our sample corresponds to previous studies that exclusively used RODS scores [7, 31, 32]. In line with earlier studies, we found that MMN not only affects the upper limb, but also results in significant limitations in activities related to standing and walking, indicating a more widespread loss of muscle function in both upper and lower limbs [3, 33]. Compared to other slow progressive neuromuscular diseases (NMD), CIDP and MMN patients experience fewer participation restrictions [34–37]. This may be explained by the fact that in contrast to most NMD, effective medical treatment strategies to decrease disease activity are available for CIDP and MMN.

Fatigue and pain are common symptoms in neuropathies and NMD and can be very disabling, resulting in significant impairment of activities and participation, corresponding with our findings [10–13, 19, 38]. Pain in CIDP may be caused by degenerative changes in musculoskeletal structures related to muscle weakness, altered gait and muscle activation patterns, and associated mechanical foot collapse [19]. The underlying mechanisms of fatigue in CIDP and MMN are complex and still largely unknown and likely include a combination of factors, such as personal factors, changes in peripheral nervous system and individual characteristics of central nervous system processing [10]. Despite this lack of our understanding of involved mechanisms, rehabilitation strategies may also address and help to ameliorate their impact. Exercise programs in NMD have been shown to have promising results in reducing fatigue, especially individualized programs, and could also be effective in CIDP and MMN patients, in addition to abolishing known contributing factors to fatigue [10, 38–40].

We found that one-third of CIDP patients who reported mild to severe limitations did not receive drug treatment. Furthermore, no rehabilitation physician was involved in fewer than half of the CIDP patients who reported mild to severe limitations in activities. Previous studies showed that a majority of CIDP patients have moderate disabilities with physical and functional impairments and a few with severe disabilities at long term [7, 41]. Early initiation of appropriate treatment may prevent axonal loss, which has been shown to be an important determinant of long-term prognosis [7, 42, 43]. Our study shows that despite optimal immune-modulating strategies, significant limitations in activities and participation are far from uncommon. Consequently, tailored care with referral to a rehabilitation physician warrants more frequent consideration (not only limited to CDAS class 1 or 2, where there is no role for immunotherapy) to address these limitations in the appropriate context, including consideration of relevant factors such as fatigue, pain and resilience [38].

Our study has several limitations. By using a standardized set of questionnaires on limitations in activity and participation we may not have captured the full impact of the disease on activities and participation. However, we added optional comment fields in all the questionnaires which were used frequently by enrolled patients and have provided additional insight into the impact. Apart from resilience our survey did not contain validated questions on psychological functioning such as anxiety or depression that may impact perceived limitations and satisfaction. Therefore, underestimation of the neuropsychiatric prevalence rates in our study cannot be ruled out, but as participation and resilience levels were high we expect this to only have a modest impact. Not all of our eligible patients responded, resulting in possible loss of data in a subset of patients. However, given the high response rates in our survey and the fact that participants presented the full range of disease severity and variable disease durations, we think that significant reporting bias is unlikely. As our survey was conducted between April and August 2021, restrictions of the COVID-19 pandemic may have affected our results addressing participation. We therefore asked all participants whether their answers on the USER-P were possibly influenced by the COVID-19 pandemic. Half of the participants did mention this, but median scores on the USER-P Restrictions and Satisfaction scales were nearly the same, suggesting that these effects were only mild. Diversity in immune-modulating strategies in our study may have impacted functional outcomes, but we found that despite optimal treatment a significant number of patients experienced substantial limitations in activities and participation. We therefore think that our results accurately represent the routine clinical population and therefore are unlikely to be biased by specific treatment modalities.

Our study indicates that the perceived impact of CIDP/MMN on participation and satisfaction with daily life is significant and, importantly, may not be routinely addressed with treatment strategies in neurologic outpatient settings. Referral to a rehabilitation physician is warranted to address these limitations appropriately. Moreover, other determinants of these limitations such as fatigue and pain and resilience are amenable to rehabilitation treatment. Future research should be aimed at developing an improved and practical set of functional outcome measures, which can be easily implemented in routine clinical evaluation to capture the impact of functional changes in daily life. This could complement the current management strategies that are primarily aimed at evaluating treatment efficacy and disease activity and help to identify patients that may benefit from early referral to rehabilitation physicians in the routine clinical setting.

CONCLUSIONS

Our study shows a diverse range of reported limitations in activities and participation in CIDP patients. In contrast, MMN patients experience fewer limitations, although some patients did report moderate to severe limitations. Importantly, the degree of reported limitations does not necessarily correspond with experienced satisfaction. Despite optimal immune-modulating strategies, limitations in activities and participation remain present. Therefore, a multidisciplinary approach, that at the very least includes rehabilitation physicians, seems appropriate to address these issues, including important determinants such as fatigue, pain and resilience.

CONFLICT OF INTEREST STATEMENT

The authors report no conflicts of interest as regards the content of this article. HA Wonink, WJ Kruithof and A Beelen report no disclosures. HS Goedee has received research grants from Prinses Beatrix Spierfonds and speaker fees from Shire/Takeda, all paid to the author's institution.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Henderyke A. Wonink https://orcid.org/0000-0001-9873-7526
H. Stephan Goedee https://orcid.org/0000-0001-9591-1672
Anita Beelen https://orcid.org/0000-0002-1269-0710

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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