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Citation for published version (APA):

Van Heugten, C., Meuleman, S., Hellebrekers, D., Kruitwagen-van Reenen, E., & Visser-Meily, J. (2018). Participation and the Role of Neuropsychological Functioning in Myotonic Dystrophy Type 1. *Journal of neuromuscular diseases*, 5(2), 205-214. <https://doi.org/10.3233/JND-170246>

Document status and date:

Published: 29/05/2018

DOI:

[10.3233/JND-170246](https://doi.org/10.3233/JND-170246)

Document Version:

Publisher's PDF, also known as Version of record

Document license:

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Research Report

Participation and the Role of Neuropsychological Functioning in Myotonic Dystrophy Type 1

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Abstract.

Background: Myotonic Dystrophy type 1 (DM1) is primarily a neuromuscular disease but can also have neuropsychological consequences (i.e. cognitive, emotional and behavioural) which can influence daily living and societal participation. Not much is known about the level of participation of DM1 patients and their relatives and the factors influencing participation. This information can guide the development of rehabilitation programs and identify those at risk of long-term participation problems.

Objective: To investigate the level of participation of DM1 patients and their partners and the determinants.

Methods: Cross-sectional study using the Utrecht Scale for Evaluation of Rehabilitation-Participation. Determinants were demographic, disease related, and neuropsychological characteristics. Spearman correlations and backward multiple regression analyses were performed.

Results: Of the 66 DM1 participants, 54% reported severe fatigue and 47% apathy. Experienced participation restrictions were most prevalent in housekeeping (74%), sports (68%) and outdoor activities (55%). Participants were relatively satisfied with their level of participation, but dissatisfaction occurred mostly in housekeeping (58%), outdoor activities (55%), and sports (54%). Age and apathy were significant predictors of frequency of ($R^2 = 10.4$) and restrictions in participation in the multivariate model ($R^2 = 14.4$). Emotional functioning was the only significant predictor of satisfaction with participation ($R^2 = 23.8$).

Conclusions: A considerable number of DM1 patients have Central Nervous System-related problems such as fatigue and apathy in addition to neuromuscular restrictions. Risk factors for lower participation are age, apathy, and emotional problems. Physical as well as neuropsychological rehabilitation programs are recommended.

Keywords: Activities of daily living, social participation, myotonic dystrophy, neuromuscular diseases, apathy

INTRODUCTION

Myotonic Dystrophy type 1 (DM1) is a slowly progressive neuromuscular disease with an autosomal dominant transmission. It is the most common neuromuscular disease in adults, with a global incidence of 1 in 8000 individuals [1, 2]. DM1 is characterized

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primarily by myotonia and progressive muscle weakness, but also affects the ocular, cardiac, respiratory, gastrointestinal and the central nervous system, which essentially means this is a multi-systemic disorder. Involvement of the central nervous system (CNS) may lead to neuropsychological consequences such as cognitive, emotional and behavioral deficits.

In adult-onset DM1 involvement of the CNS is associated with hypersomnia and fatigue, as well as visuoconstructive impairment, attention deficits, reduced initiative and apathy [3]. Impairments in executive functioning (i.e. initiative, planning, organization and flexibility) are especially prominent suggesting the involvement of the frontal lobes [4]. Some characteristics of the cognitive deficits in DM1 patients are related to specific structural cerebral changes [5]. In the course of five years, cognitive decline is also seen in adult DM1 patients which is related to earlier onset and longer duration of the disease [6]. A recent study in which a nine year follow up was conducted suggests an earlier and more accelerated normal cognitive aging process in DM 1 patients [7]. The presence of depression can also reflect the involvement of the CNS, but some authors have suggested that depressed mood reflects an emotional reactive adjustment disorder rather than structural brain damage [8]. The high prevalence of other CNS-related symptoms such as apathy (almost 40%), suggests a central cause rather than an adjustment process [9].

These neuropsychological consequences can have a negative influence on the patients' daily living, participation in society, and quality of life. A recent study found that both physical and mental health related quality of life (HRQOL) were impaired in DM1 patients [10]. Many different factors including demographic, disease-related and neurological factors contribute to this reduced level of HRQOL. In another study [11] only physical HRQOL was reduced which was not only related to disease related characteristics such as daytime sleepiness and fatigue, but also to psychological distress, unemployment, and dissatisfaction with social participation. More recently, a study [12] showed that cognitive deficits and fatigue both negatively impact the quality of life of juvenile and adult DM1 patients. No study, however, has investigated the contribution of the neuropsychological related to brain involvement to the level of participation in society. From a clinical perspective, it is important to establish whether any factors that would be responsive to treatment, contribute to reduced daily functioning, as that would

mean that not only physical, but also neuropsychological rehabilitation programs could be effective in this patient group.

The need for assistance has been found to influence the well-being of patients more than the symptoms of the disease [13], and this may also impact caregiver burden and partner well-being. Patients' lack of initiative and avoidant behavior also influences the well-being of their partners [13, 14]. This suggests that rehabilitation programs should involve psychosocial interventions for both patients and partners. However, as there is only one quantitative study in which both patients and partners were investigated, further evidence is needed.

The primary aim of the present study was therefore to describe the level of participation of patients with DM1 and of their caregivers. The second aim was to determine whether demographic, disease-related and neuropsychological characteristics were related to participation of the patients and finally, which of these factors were related to caregiver functioning (i.e. burden and emotional functioning).

METHODS

Participants

Patients who visited the DM outpatient clinic at the University Medical Centre Utrecht, the rehabilitation centers Revant in Breda, Het Roessingh in Enschede and VieCuri in Venlo (the Netherlands) from March 2011 to October 2012 were eligible for participation in the study. Inclusion criteria were a diagnosis of the classic form of DM1, as confirmed by a neurologist, over 18 years of age, and living independently. If a caregiver was present, they were also asked to participate. Partners were included if they were married or living together with the patient. If the patient did not have a partner, a relative, who knew the patient well, such as a parent, sibling or adult child was asked to participate.

Procedure

Patients and caregivers were recruited during a regular outpatient visit to one of the participating centers. Their rehabilitation physician and/or specialized DM nurse informed the patient and caregiver about the study, both orally and in writing. Patients and their partners/caregivers were asked to complete one set of questionnaires (see Measures) and gave permission to use data from their medical

file. The rehabilitation physician who performed a physical examination filled in the Muscular Impairment Rating Scale (MIRS). All other variables were collected via the questionnaires. Participants either completed the questionnaires during their outpatient visit, or took them home and returned them using the freepost envelope provided. The study was conducted in accordance with guidelines on human experimentation and approved by the Medical Ethics Committee of the UMC Utrecht and the rehabilitation centers which is in accord with the Helsinki Declaration of 1975. All patients and caregivers provided a signed consent form at the start of the study.

Measures

Outcome: Participation

Participation was measured using the Utrecht Scale for Evaluation of Rehabilitation-Participation (USER-P) [15]. The USER-P is a self-report measure, consisting of three participation domains (frequency, restrictions, satisfaction), with a total of 32 items. The following domains of participation are measured: vocational activities (i.e. work, education and housekeeping) and leisure and social activities (i.e. of sports and physical exercise, going out, making day trips, leisure activities at home, visiting family or friends, receiving visits from family or friends, and contacts by computer or telephone). The sum score of each domain ranges from 0 to 100. The higher the sum score, the better the level of participation (higher frequency, fewer restrictions, higher satisfaction). To quantify the presence of restrictions and dissatisfaction in different domains of participation, the item scores of the USER-Participation Restriction and Satisfaction scales were dichotomized. The Restriction scale, 'with assistance', 'with difficulty', and 'not possible' were defined as 'restriction', and 'without difficulty' and 'not applicable' were defined as 'no restriction'. For the Satisfaction scale, 'very dissatisfied', 'dissatisfied', and 'neutral' were defined as 'dissatisfaction', and 'satisfied' and 'very satisfied' were defined as 'satisfaction'. The USER-P has previously shown satisfactory validity and reliability [15].

Determinants

Demographic characteristics

The level of education was recorded using the Dutch classification system ranging from 1 (did not

finish primary school) to 7 (university education), which was dichotomized as low (0–5) and high (6–7). Marital status was identified using five categories: 'married/living together', 'single', 'divorced', 'widow/widower' and 'otherwise'. Employment status was measured by using a closed question: "Are you currently in paid employment and for how many hours?"

Disease characteristics

Age-of-onset of DM1 was taken from the medical case notes. Muscle strength was assessed by a rehabilitation physician using the Muscular Impairment Rating Scale (MIRS), a 5-point scale focusses on proximal muscle weakness where 1 is no muscular impairment, 2 minimal signs, 3 weaknesses present (with or without weakness of the elbow extensors), 4 mild-to-moderate weaknesses and 5 severe proximal weaknesses [16]. Mild muscular impairment was defined as MIRS grades 1–3 and severe muscular impairment as MIRS grades 4–5. Studies in persons with DM support the validity and reliability of the scale [16].

Daytime sleepiness was measured using the Epworth Sleepiness Scale (ESS), an 8-item questionnaire, which asks about daytime sleepiness over the previous 4 weeks. Each item is rated on a scale of 0–3, leading to a total score range of 0–24. A score above 10 indicates the presence of excessive daytime sleepiness [16], and is considered to be sufficiently reliable [17, 18].

Fatigue was measured using the Fatigue Severity Scale (FSS) [19], a 9-item questionnaire, asking about fatigue over the previous 7 days. Each item is rated on a Likert scale ranging from 1 (strongly disagree) to 7 (strongly agree). A higher total score represents higher levels of fatigue. A score equal to or above 4 indicates a moderate to high impact of fatigue on daily living. The scale has a high reliability [19].

Neuropsychological characteristics

Subjective cognitive functioning was measured by the Cognitive Failure Questionnaire (CFQ). This questionnaire contains 25 items about the frequency of everyday cognitive failure. Scores range between 0–100, with higher scores indicating more problems with cognitive functioning [20]. A score higher than 43.5 indicates the presence of cognitive failures.

The Apathy Evaluation Scale (AES) was used to assess the presence of apathy or the lack of initiative. This is an 18-item scale, scored from 1 (not at all characteristic) to 4 (very characteristic), with total scores

ranging from 18 to 72, higher scores indicating more apathy. A score of 34 or higher indicates a clinically relevant level of apathy [21].

Anxiety and depression were evaluated in both patients and spouses using the Dutch Hospital Anxiety and Depression Scale (HADS) [22] which is a 14-item questionnaire divided into two separate scales. Each subscale contains seven items asking about the person's feelings over the last week. Each question is rated from 0 (no symptoms) to 4 (maximum distress). The total score ranges from 0 to 56, and 0 to 28 for each subscale. A subscale score above 8 indicates the presence of a probable clinically relevant level of depression or anxiety.

Patients rated their own cognitive complaints (CFQ), apathy (AES) and emotional functioning (HADS). Caregivers reported on the cognitive complaints (CFQ) and apathy (AES) of the patient and on their own emotional functioning (HADS).

Caregiver burden

Caregiver burden was measured using the Caregiver Strain Index (CSI) [23]. The CSI is a 13-item questionnaire of closed questions with a score range from 0–13, completed by the spouse. Seven or more positive answers indicate a high burden level.

Statistical analyses

IBM SPSS Statistics version 22 was used for statistical analysis. Descriptive statistics were used to describe the sample in terms of demographic characteristics, disease and neuropsychological characteristics. Continuous data were checked for normality.

Bivariate correlations between the demographic, disease and neuropsychological determinants and USER-P patient, HADS-patient, HADS-partner and Caregiver Strain Index scores were tested using Spearman correlations. Because the present study was exploratory, backward multiple regression analyses were chosen to examine associations between the determinants and USER-P as primary outcome measure for the patients. Similar analyses were performed to investigate determinants of caregiver burden (CSI) and emotional functioning (HADS-partner). In the first step the significant variables from the bivariate correlational analyses were entered; in the final step the significant predictors were retained in the regression model. A p-level of <0.05 was used to indicate statistical significance.

RESULTS

Patient and partner characteristics

From March 2011 to October 2012, 87 patients with DM1 were invited to visit the participating outpatient clinics. Twenty-one patients were excluded: eight did not respond or declined participation, six were living in a nursing home and thus did not live independently (inclusion criterion), six were treated outside the area in another center, and one had died. Sixty-six patients were included in this study. Fifty-five caregivers of patients returned the questionnaire, 32 partners and 23 relatives. The characteristics of these participants are displayed in Table 1.

About half of patients (54.5%) and half of their partners (50%) were men, and about 60% of patients were married or living together. The mean age of the patients was 47 (12.7). The partners and relatives were somewhat older ($M = 51.2$, $SD = 10.5$). Nearly 70% of both patients and partners were categorized as having 'low level education', and 60% of the patients did not have a paid job.

Eighty-seven percent of the patients showed minimal signs of paresis as measured by the MIRS scale. More than half of the patients scored above the cut-off point of the FSS, indicating severe fatigue. About one third of the patients (29%) scored above the cut-off point of the ESS, indicating clinically relevant daytime sleepiness.

Thirteen percent of the patients had problems in cognitive functioning on the CFQ and almost half of the patients had a clinically relevant level of apathy (AES). Subjective cognitive complaints of patients perceived by caregivers were lower than those experienced by patients themselves ($M = 30$ $SD = 13$ versus Partners $M = 28.6$, $SD = 13.2$ and Relatives $M = 31$, $SD = 10.8$). Caregivers also rated the presence of apathy as frequently occurring (44–48%). HADS scores showed that one in five patients and partners had depressive symptoms (18.2% and 21.9%, respectively), and more than a third had high anxiety levels (30.8% and 37.5%, respectively). Only a minority of the partners (15.6%) experienced high caregiver burden.

Participation (USER-Participation)

The mean Frequency score was 31.0 ($SD 11.8$) for patients and 39.6 ($SD 8.0$) for partners. The mean Restriction score was 73.3 ($SD 19.9$) for patients and 91.8 ($SD 12.5$) for partners. Most restric-

Table 1
Characteristics of patients with Myotonic Dystrophy type 1 and their partners or relatives

	Patients (n = 66)	Partners (n = 32)	Relatives (n = 23) ^a
Demographic characteristics			
Gender, male n (%)	36(54.5)	16 (50)	5 (22)
Mean age in years (SD)	47(12.7)	51.2(10.5)	52.8(17.5)
Marital status (%)			
Married/living together	61.5	100	
Living alone	18.5		
Other	20		
Educational level at least high school (n, %)	26.6	37.5	26.1
Employment status (%)			
Full time paid employment	13.8	–	–
Part time paid employment	26.2		
No paid job	60	–	–
Disease characteristics patient			
Mean illness duration in years (SD)	21(10.8)	n/a–	n/a–
Muscular Impairment Rating Scale (n = 47)			
Mild paresis, 1–3(%)	87.2		
Severe paresis, 4–5(%)	12.8		
Fatigue severity scale (n = 59)			
Mean (SD)	3.9(1.3)		
Fatigue score >4(%)	54.2		
Epworth Sleeping Scale (n = 50)			
Mean (SD)	8.1 (4.3)		
Excessive daytime sleepiness score >10 (%)	28.8		
Neuropsychological characteristics			
Cognitive complaints, CFQ (n)	61	29	21
Mean (SD)	30(13)	28.6(13.2) ^b	31(10.8) ^b
Cognitive failures score >43.5 (%)	13.1	9.4	8.7
Behavioral complaints AES (n)	58	29	22
Mean (SD)	34.2(7.8)	35(10.8) ^b	36.4 (9.9) ^b
Apathy score >34 (%)	46.6	43.8	47.8
Emotional complaints ^c , HADS (n)	65	31	
Mean Anxiety (SD)	5.6 (3.2)	6.5(2.8)	
Anxiety subscore >7 (%)	30.8	37.5	
Mean Depression (SD)	4.6(3.3)	5.0(3.4)	
Depression subscore >7 (%)	18.2	21.9	
Caregiver functioning			
Caregiver burden, CSI			
Mean (SD)		4.2(3.2)	
High burden score >6 (%)		15.6	

^aRelatives were defined as brother, sister, parent, child, friend or mentor. ^bPartner or relatives scores for patient.

^cPatient and partner scores for themselves. MIRS = Muscular Impairment Rating Scale; FSS = Fatigue Severity Scale; ESS = Epworth Sleepiness Scale; CFQ = Cognitive Failure Questionnaire; AES = Apathy Evaluation Scale, CSI = Caregiver Strain Index, HADS = Hospital Anxiety and Depression Scale.

tions were experienced by patients in housekeeping (74.2%), sports/leisure activities (67.7%) and activities outside the home environment (54.5%). For partners restrictions were most often experienced in the relationship with their partner (45.2%). The percentages of patients and partners experiencing restrictions and dissatisfaction are shown in Table 2.

The mean Satisfaction score was 64.5 (SD 13.3) for patients and 71.8 (SD 12.5) for partners.

Patients were least satisfied with housekeeping (57.8%), sports/leisure activities (54.0%) and activities outside the home environment (65.0%). Partners

were least satisfied with going out (46.0%) and day trips and other outdoor activities (46.0%).

Determinants of patient participation

Table 3 shows the bivariate relationships between the demographic, disease, and neuropsychological characteristics and the subscales of the USER-P. Age and AES scores were significantly and negatively correlated with frequency of participation in social activities (USER-P frequency). Age, ESS, FSS, AES, and HADS correlated significantly with USER-P Restrictions and FSS, AES and

Table 2
Participation – restrictions and satisfaction

USER-P items	Patient (n = 66)*		Partner (n = 32)*	
	N	%	N	%
% patients/partners experiencing restrictions				
Paid job, voluntary work or education	65	47.7	31	9.7
Housekeeping		74.2		21.9
Outdoor mobility		45.5		9.4
Sports/physical activities	65	67.7		21.9
Going out	63	39.7		21.9
Day trips and other outdoor activities		54.5		28.1
Leisure activities at home		16.7		18.8
Relationship with partner	65	24.6		45.2
Visiting family and friends	65	29.2		21.9
Receive visitors at home		15.2		12.5
Contacting people by telephone or computer		10.6		6.3
% patients/partners unsatisfied				
Paid job, voluntary work or education	37	19.7	29	15.6
Housekeeping	64	57.8		34.4
Outdoor mobility	65	35.4		6.3
Sports/physical activities	63	54.0		28.1
Going out	63	52.4		40.6
Day trips and other outdoor activities	62	54.0		40.6
Leisure activities at home		18.2		18.8
Relationship with partner	45	13.6		21.9
Relationship with family		13.6		15.6
Contact with friends and acquaintances	65	26.2		21.9

*unless otherwise specified. Bold % numbers indicate: restrictions >50% or unsatisfied >50%. USER-P = Utrecht Scale for Evaluation of Rehabilitation-Participation.

Table 3
Bivariate analyses of patient characteristics and patients' USER-Participation subscale scores and patient mood

Determinant	N	USER-P Frequency	USER-P Restrictions	USER-P satisfaction	HADS patient
Demographic characteristics					
Age	66	-0.391**	-0.544**	-0.209	0.208
Gender	66	-0.009	0.154	0.034	0.125
Marital status	65	-0.104	-0.038	-0.051	-0.035
Education	64	0.163	-0.021	-0.067	-0.233
Disease characteristics					
MIRS	47	-0.260	-0.243	-0.235	0.146
ESS	59	0.107	0.274	0.159	0.143
FSS	59	-0.223	-0.336**	-0.391**	0.429**
Neuropsychological characteristics					
CFQ	61	-0.047	-0.121	-0.210	0.486**
AES	58	-0.332**	-0.329*	-0.275*	0.447**
HADS	65	-0.242	-0.287*	-0.511**	–

NOTE: Correlation coefficient is Spearman's rho. **Correlation is significant at the 0.01 level (2-tailed).

*Correlation is significant at the 0.05 level (2-tailed). Frequency, participation and satisfaction with participation are subscales of the Utrecht Scale for Evaluation of Rehabilitation-Participation. Higher scores on the subscales indicate good levels of participation (higher frequency, less restrictions, higher satisfaction). MIRS = Muscular Impairment Rating Scale, ESS = Epworth Sleepiness Scale, FSS = Fatigue Severity Scale, AES = Apathy Evaluation Scale; HADS = Hospital Anxiety and Depression Scale.

HADS showed significant relationships to USER-P Satisfaction.

Multivariate linear regression analyses showed that age and AES were significantly associated with USER-P frequency and with USER-P restrictions in

the final regression model, explaining 10.4% and 14.4% of the total variance. In the multivariate analysis with the USER-P satisfaction HADS was the only significant predictor in the final model, explaining 23.8% of the total variance (see Table 4).

Table 4
Results of the multivariate linear regression analyses with USER-P as outcome and its determinants

Determinants	USER-P Frequency β	USER-P Restrictions β	USER-P Satisfaction β
Age	-0.34*	-0.53*	
AES	-0.40*	-0.31*	
HADS			-0.57*
Explained variance	10.4%	14.4%	23.8%

USER-P = Utrecht Scale for Evaluation of Rehabilitation-Participation; AES = Apathy Evaluation Scale; HADS = Hospital Anxiety and Depression Scale. * = $p < 0.05$.

Determinants of partners' burden and emotional functioning

Table 5 shows the correlations between patient and partner characteristics, and partners' caregiver burden (CSI) and emotional functioning (HADS-partner). The level of restrictions as experienced by the patient was significantly and negatively correlated with caregiver burden. Partner mood was significantly and positively correlated with caregiver burden, indicating that those partners with more symptoms of depression or anxiety experienced higher caregiver burden. There were no significant

correlations between any of the patient and partner characteristics and the HADS-partner.

DISCUSSION

DM1 is a multi-systemic disorder in which the neuromuscular problems are most prominent, but the present study shows that CNS-related symptoms such as apathy, depression and anxiety are involved in the disease process as well. Half of all patients reported fatigue and apathy, although the majority (87.2%) had only mild paresis. In addition, one-third experienced anxiety, and some (respectively 30% and 18.2%) also had cognitive and depressive complaints. These CNS-related symptoms can lead to restrictions in many areas of daily functioning such as work, housekeeping, sports and leisure activities and other activities outside the home environment. Partners experienced most restrictions in their relationship with their partner with DM1. Age and apathy were associated with frequency of and restrictions in participation, but did not explain much variance in the model. Emotional functioning was associated with satisfaction in participation, explaining a quarter of the variance. The restrictions in participation of the patient and the level of emotional functioning of the partner were associated with caregiver burden. Caregiver well-being has been shown to be influenced by patient characteristics before [13, 14].

Gagnon et al. [24] also showed disrupted participation in DM1 patients as measured with the Life Habits Measure ($n = 200$, 121 women). Disrupted participation was defined as the amount of help needed to perform most life habits. Forty-five to 61% of the patients showed disrupted participation in all four domains being mobility, housing, employment and recreation, similar to the domains of the USER-P. Fatigue, strength, family support and public services were independent predictors. Similar to our results, predictors of participation are both personal and environmental factors. The level of participation of DM1 patients is lower than that of their partners,

Table 5
Bivariate correlations of patient and partner characteristics, and CSI and HADS of the partner

Determinant	N	CSI	HADS partner
Patient			
Demographic characteristics			
Age	32	0.026	0.71
Gender	32	0.079	-0.087
Education	21	-0.113	-0.311
Disease characteristics			
MIRS	22	0.105	0.150
ESS	29	0.139	-0.061
FSS	30	0.224	-0.075
Neuropsychological characteristics			
CFQ	29	0.182	0.257
AES	28	0.252	0.219
HADS	32	0.045	0.185
Participation restrictions			
USER-P	32	-0.388*	-0.203
Partner			
Demographic characteristics			
Age	32	-0.032	0.088
Gender	32	-0.174	-0.022
Psychosocial characteristics			
HADS	31	0.563**	-

NOTE: Correlation coefficient is Spearman's rho. **Correlation is significant at the 0.01 level (2-tailed). *Correlation is significant at the 0.05 level (2-tailed). MIRS = Muscular Impairment Rating Scale, ESS = Epworth Sleepiness Scale, FSS = Fatigue Severity Scale, HADS = Hospital Anxiety and Depression Scale, CFQ = Cognitive Failure Questionnaire; AES = Apathy Evaluation Scale; CSI = Caregiver Strain Index, USER-P = Utrecht Scale for Evaluation of Rehabilitation-Participation.

but comparable to other patients who have received rehabilitation [15]. The frequency of and satisfaction with participation is lower than in patients with spinal cord injury [2]. The neuropsychological problems in DM1 patients may cause this difference. The experienced restrictions by DM1 patients in this study are higher than those experienced by stroke patients 6 months after their stroke and being discharged home from hospital [26]. These findings, combined with the contribution of neuropsychological characteristics to the level of participation, suggest that central neural mechanisms may play an important role in addition to neuromuscular mechanisms in DMI.

Moreover, the disease characteristics (i.e. motor functioning, sleep and fatigue) did not contribute significantly to the level of participation. In their recent review Gourdon and Meola [27] also state that central nervous system alterations are a common element of this multisystemic disease thereby recognizing myotonic dystrophies as brain diseases.

Involvement of the central nervous system is further strengthened by the finding that many DM1 patients report levels of fatigue comparable to levels of fatigue experienced by stroke patients [28]. The percentage of DM1 patients reporting apathy (47%) is much higher than in the stroke population during the first year post stroke (27%) [29]. Depressive symptoms occur somewhat less than in stroke patients two months post stroke [30], and feelings of anxiety are higher [31]. Subjective cognitive complaints were, however, not experienced often and the mean score on the CFQ was lower than in stroke patients and comparable to controls [32]. From clinical experience we know that DM type 1 patients do not experience many problems subjectively despite the level of objective functioning. This could also be one of the reasons why they often do not comply to motor exercises. A discrepancy is seen between self-awareness of motor functioning and objective measurements. This may also explain the low level of cognitive complaints.

Although most chronic diseases are accompanied by fatigue, depressive symptoms and anxiety, the presence of cognitive consequences and apathy in DM1 suggest additional involvement of the central nervous system. However, the relationships between these factors were not examined in our study but should also be considered in order to understand the underlying mechanisms and causality. Fatigue and sleep dysfunction, for instance, may lead to cognitive problems and depressive symptoms without specific brain involvement in the disease process.

This study presents some unique data that adds to our understanding of DM1 as a multisystemic disease, but it does have some limitations. In comparison to the study of Gagnon et al. [24] ($n=200$) we have a limited sample size. The cross-sectional design of the study does not permit statements about causal relationships. Future studies should explore the longitudinal relationship between the developments of apathy, fatigue, mood disorders and the level of participation. We only included one type of DM and the sample showed variation in illness duration. Additionally, we measured sleepiness with the Epworth Sleepiness scale while recently it was shown that the Fatigue and Daytime Sleepiness Scale (FDSS) is more reliable in this patient group [33]. We measured cognitive functioning only in terms of subjective cognitive functioning and did not perform objective cognitive testing nor did we measure the level of awareness of the patients. The subjective nature of complaints may have influenced the experience of participation. Objective cognitive testing and measures of awareness should be considered in future studies. Finally, the group of relatives was rather heterogeneous involving brothers, sisters, parents and adult children who could be living with patient or not, which may have caused bias in the scores on the questionnaires in this subgroup. However, we also studied partners as a separate homogeneous group allowing stronger conclusions.

A considerable proportion (47%) of our sample experienced clinically significant apathy, as indicated as a score of 34 or higher on the AES. Given that patients may have declined to participate because of high levels of apathy, the high prevalence of apathy in this sample may be an underestimate of levels of apathy in patients with DM1. Further large scale prospective studies are necessary to confirm these findings.

The results of this study suggest that rehabilitation programs for DM1 should not solely focus on the more obvious neuromuscular symptoms, but attention may also need to be paid to any neuropsychological symptoms. Information on the brain-related aspects of the disease may be offered to both patients and their caregivers; as this may help reduce emotional problems in patients and partners/caregivers. Future studies should assess whether rehabilitation for neuropsychological symptoms is beneficial in patients with DM1. Currently an RCT is being conducted in which cognitive behavioural therapy is combined with graded exercises and compared to standard care for DM 1 patients, but results have not

been reported yet [34]. Recently a study on childhood phenotype of MD 1 patients showed that participation restrictions were present and related to problems in many different areas of functioning [35]. The authors also recommend an interdisciplinary approach. In two other studies by the same research group an integrated care program involving health, social and community services is recommended based on the correlates of health-related quality of life in DM 1 patients [36]; a more holistic approach is needed in which all relevant stakeholders are involved [37]. Other medical conditions in which a mere physical rehabilitation approach has successfully been augmented with psychological interventions is in the field of cardiac rehabilitation where stress, anxiety and depression play a major role in the outcome of treatment [38].

Although not a determinant, 50% of the patients report fatigue. The occupational therapists could help the patients increase their level of participation and manage their daily routines by applying energy management principles to reduce fatigue. Further, we suggest the high prevalence of clinically relevant apathy in these patients may require a proactive role of the rehabilitation professional. Specific rehabilitation interventions can be developed on the basis of these findings.

From the present study we can conclude that DM1 is a complex disease that affects not only physical functioning but many domains of cognitive functioning and mood in patients, and may also affect caregivers' mood and experienced burden of caregiving. Risk factors for lower participation identified in this study were age, apathy and emotional problems. Targeted rehabilitation programmes should be considered.

ACKNOWLEDGMENTS

No financial or material support was received for the study in this paper.

We would like to thank all participating rehabilitation centers and hospitals: University Medical Center Utrecht, Revant Rehabilitation (Breda), Het Roessingh Rehabilitation (Enschede), Vie Curi Rehabilitation (Venlo). In particular, we would like to thank J.W. Meijer, R. van Vliet and W. Wetzelaer. We would like to thank R. de Gooijer for participating and C. Vrinten for providing useful comments on an earlier draft of the manuscript.

CONFLICT OF INTEREST STATEMENT

None of the authors report any conflicts of interest.

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