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### **Vitality, perceived social support and disease activity determine the performance of social roles in recently diagnosed multiple sclerosis: a longitudinal analysis.**

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ORIGINAL REPORT

VITALITY, PERCEIVED SOCIAL SUPPORT AND DISEASE ACTIVITY DETERMINE THE PERFORMANCE OF SOCIAL ROLES IN RECENTLY DIAGNOSED MULTIPLE SCLEROSIS: A LONGITUDINAL ANALYSIS

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**Objective:** The aim of this study was to identify the principal determinants that are longitudinally associated with the performance of social roles in the first 3 years following a diagnosis of multiple sclerosis.

**Design:** Inception cohort with 5 measurements over 3 years.

**Patients:** A total of 156 patients recently diagnosed with multiple sclerosis.

**Method:** Performance of social roles was measured using the 2 role functioning and the social sub-scales of the Medical Outcome Study Short Form 36. Potential determinants ( $n = 43$ ) were divided into the following clusters: patient and disease characteristics ( $n = 12$ ), psychosocial characteristics ( $n = 10$ ), basic functions ( $n = 18$ ) and basic activities ( $n = 3$ ). Multivariate longitudinal regression analyses were performed with generalized estimating equations. A backwards selection procedure for every cluster per outcome reduced the large number of potential determinants. In order to determine whether longitudinal associations are present the selected determinants were entered into an overall regression model.

**Results:** Twenty-three candidate determinants were selected. Vitality, measured with the SF36 sub-scale vitality, the T2-weighted supratentorial lesion load and the perceived amount of social support, measured with the Social Support List Discrepancies, were longitudinally associated with the performance of social roles in 2 or 3 of the models.

**Conclusion:** Vitality, the perceived amount of social support, and disease activity, i.e. the T2-weighted supratentorial lesion load, determine the performance of social roles in the early stages of multiple sclerosis.

**Key words:** multiple sclerosis, prognosis, social support, fatigue, disability evaluation.

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INTRODUCTION

Multiple sclerosis (MS) is characterized by variable neurological symptomatology, which differs not only between patients,

but also within patients over time. This makes it difficult to predict the clinical course of the disease, which poses an important problem for clinicians treating patients with MS. Reviews of the studies that examined determinants of the clinical course showed that a progressive disease course, higher age at time of diagnosis, less than one year between relapses, and impairments of pyramidal or cerebellar tracts are associated with an unfavourable disease course, whereas an exacerbation as first sign of MS, a high recovery rate after the first exacerbation and afferent or monoregional symptoms are associated with a more favourable disease course (1–4). Most studies have focused on neurological and locomotor function using the Expanded Disability Status Scale (EDSS) (5) as outcome and the neurological deficits or magnetic resonance imaging (MRI) parameters as determinants.

We were also interested in how patients with MS perform their social roles in the early stages of the disease. We used the International Classification of Functioning, Disability and Health (ICF) as a framework to study and explain the consequences of MS for the patient (6). The ICF describes how patients live with their disease and therefore looks beyond mortality and disease. It is a classification of functioning that describes body functions and structures, activities and participation. Performance of social roles, i.e. participation, is mainly represented in the ICF chapters on interpersonal interactions and relationships, major life areas, and community, social and civic life (7).

Another frequently used framework to study the consequences of disease is the Health-Related Quality of Life framework (HR-QoL) (8, 9). The Medical Outcome Study Short Form 36 (SF36) (10) is an example of a well-known frequently used HR-QoL measure. Although the ICF and HR-QoL frameworks represent different perspectives from which to look at functioning and health, it is possible to link items of HR-QoL measures to ICF constructs (11).

Most studies of the social consequences of MS have been cross-sectional (12–17). In the first 3 years after the diagnosis MS has been made, when for most patients mobility and mental health are relatively mildly affected, about 40% of the patients report considerable limitations in the performance of social

roles (18). For the whole group this percentage did not change in the first 3 years of the disease, but individual changes in the performance of social roles did occur.

The aim of this study was to identify the principal determinants that are longitudinally associated with the performance of social roles in the first 3 years after the diagnosis of MS.

## METHODS

### Patients and design

The inclusion criteria were: diagnosis according to the Poser-criteria for definite MS less than 6 months previously (19); age range 16–55 years; written informed consent. Patients with other neurological disorders, systemic or malignant neoplastic diseases besides MS were excluded. All consecutive potentially eligible patients visiting the 5 participating outpatient clinics of neurology departments were asked to participate. One of the members of the research team regularly reminded the neurologists to ask all potentially eligible patients. A total of 174 patients fulfilled the inclusion criteria and were asked to participate. Eighteen declined to participate. A cohort of 156 diagnosed patients was recruited (in 1998–2000) and prospectively followed for 3 years. Measurements took place at inclusion (between time of diagnosis and 6 months later), after 6 months, and after 1, 2 and 3 years. In case of a relapse, measurements were postponed for a few weeks until the relapse had subsided. Patients received a set of postal questionnaires that took them approximately 45 min to complete. Subsequently, they were visited at home in order to minimize dropouts. During this 2-hour home-visit the questionnaires were checked for completeness, and the other tests were performed. Three well-trained physical therapists and one well-trained physician performed the scoring.

### Outcome measures

We used the SF36 (10) sub-scales role physical (SF36rp), role emotional (SF36re) and social functioning (SF36sf) to measure the performance of social roles. Validity and reliability have been extensively studied and found to be good (10).

### Determinants

Forty-three potential determinants, divided over 4 clusters that were based on the ICF (6), were identified using a literature search. Almost all determinants were measured on each point in time. MRI data were only available at the baseline measurement. Scores on the questionnaires and cognitive tests were linearly transformed into a 0–10 scale.

The cluster “patient and disease characteristics” contains the following determinants: age (per 10 years), gender, co-morbidity measured with the Cumulative Illness Rating Scale (range 0=no co-morbidity to 10=maximal co-morbidity score) (20), whether the disease starts with an exacerbation (non-relapse onset (NRO) vs relapse onset (RO)), the self-reported number of exacerbations in the previous period, time since first symptoms (logarithmically transformed), first neurological symptom (pyramidal, cerebellar, brainstem, sensory, bowel or bladder, optical; analysed as 5 dummy variables), T1-hypointense and T2-weighted (supra- and infratentorial) lesion loads in cm<sup>3</sup> (MRI) (21), and number of lesions in the spinal cord (MRI) (22).

The cluster “psychosocial characteristics” contains 10 determinants. Locus of Control is measured with the sub-scales internal, physician and chance of the Multidimensional Health Locus of Control Scale (23); sub-scale scores range from 0 = lowest to 10 = highest locus of control score. Personality traits were measured with the sub-scales psychoticism, extraversion and neuroticism of the Eysenck Personality Questionnaire (24); sub-scale scores range from 0=lowest to 10=highest score on the personality trait. Two methods to measure social support were used. The *amount* of social support, i.e. a measure of the *quantity* of supportive interactions, was measured with the

Social Support List Interactions (25); scores range from 0 = no support to 10 = maximal social support. The *perceived amount* of social support, i.e. a measure of the *extent* to which the available supportive interactions cover the patient's need for social support, was measured with the Social Support List Discrepancies (25); scores range from 0 = needs are not covered at all to 10 = needs are completely covered. We also assessed whether the patient had a partner, and whether the patient had children.

The cluster “basic functions” consists of 18 determinants. The involvement of the different neurological systems was measured with the Functional System (FS) scores, ranging from 0=no impairment to 5 or 6 = maximal impairment) of the EDSS (5): the FS optical, the FS brainstem, the FS cerebellar, the FS bowel and bladder, the FS pyramidal, the FS sensory, the FS mental and the FS other. Cognitive function was measured with the Brief Repeatable Battery of cognitive tests for MS (26), which includes the sub-scales Consistent Long Term Retrieval and Long Term Storage of the Selective Reminding Test measuring verbal learning and memory, the 10/36 Spatial Recall Test measuring visuospatial learning and delayed recall, the Symbol Digit Modalities Test measuring sustained attention and concentration, the Paced Auditory Serial Addition Test measuring sustained attention and information processing speed, and the Word List Generation measuring verbal fluency; the scores range from 0 = worst possible to 10 best possible score. Fatigue was measured with the Fatigue Severity Scale (27), which measures the patient's perceived level of fatigue in a variety of situations; scores range from 0 = lowest possible to 10 = highest possible fatigue score. Vitality, i.e. the presence of energy and the absence of fatigue, was measured with the SF36 sub-scale vitality; (10) scores range from 0 = lowest to 10 = maximal vitality score. Pain was assessed with the SF36 sub-scale bodily pain; (10) scores range from 0 = minimal to 10 = maximal pain score. Because we used the ICF as framework, which classifies pain and vitality as body functions, we think it is justified to use these variables as independent variables in a regression analysis, even though they are, like the outcome measures, a sub-scale of the SF36.

Finally, a cluster “basic abilities” was created that consists of 3 determinants. Dexterity was measured with the Action Research Arm test (28), and the Nine Hole Peg Test (29). Ambulation was assessed with the 10-m Timed Walk Test (30). Because we measured patients at home, we had to find a suitable 10-m stretch in or around the house of the patient. At subsequent measurements we used the same stretch.

### Analysis

Because the scores on the SF36 sub-scales are skewed, we had to dichotomize them. We used data of an age-matched Dutch reference population (10) to determine the cut-off for each sub-scale. We calculated the mean –1.96 standard deviation (SD) with these reference data for each sub-scale. SF36 sub-scale scores in our data that were worse than this cut-off were classified as aberrant.

Statistical analyses were performed using *binomial* generalized estimating equations (GEE) (31) from the Statistical Package for Interactive Data Analysis version 6.05 from the Statistical Computing Laboratory, because for dichotomous outcomes GEE results are more stable than Hierarchical Linear Modelling (32). Time was modelled as a continuous variable expressed in years in every regression model. The analysis was performed in 3 steps:

- Step 1. A backwards selection procedure for every cluster per outcome was used to reduce the large number of potential determinants. Because statistical modelling in small data sets is susceptible to bias (33), we used in this step a liberal *p*-value of 0.10.
- Step 2. The determinants identified in step 1 were entered into an overall regression model, and reduced using a backwards selection procedure with a significance level of 0.05. Results of the final regression models are presented as odds ratios (OR), because we were interested in the strength of the relationship of the determinant with the outcome. In this step it is important to construct models with determinants that are significantly associated with the outcomes.
- Step 3. Because these ORs contain information about the between-

subject differences (cross-sectional relationship at each time point) as well as information about the within-subject changes (longitudinal relationship, i.e. is a change in the determinant for a patient associated with a change in the outcome for that same patient) (34), autoregressive models were created to disentangle the relative contribution of the between-subject differences and the within-subject changes to the ORs. For this purpose, the outcome of the previous measurement was added as determinant to the regression models obtained in step 2. The power of the autoregression models is lower than the power of the standard models, which means that the confidence intervals may be wider and may occasionally be not significant any longer. However, because the aim of this step in the analysis is to determine whether associations can be attributed to within- or between-subject changes, we focus on the interpretation of changes in the ORs and not on the level of significance. When the ORs of the standard and autoregressive models are roughly similar, the effect can be attributed to within-subject changes (longitudinal relationship). When the ORs are closer to 1 (no effect) in the autoregressive model as compared with the standard model, the effect can be attributed to between-subject differences (cross-sectional relationship). Thus, 6 regression models were created (a standard and an autoregressive model for 3 outcome measures).

RESULTS

Patients

We included 128 patients in the RO group: mean age 36.25 years (SD 9.24), 87 (68%) women, median symptom duration 2.12 (interquartile range (IQR) 0.71–4.70) years, median disease duration 0.26 (IQR 0.15–0.41) years, median number of exacerbations 2 (IQR 2–3), and median EDSS 2.0 (IQR 2.0–3.0); and 28 patients in the NRO group: mean age 43.74 years (SD 8.64), 14 (50%) women, median symptom duration 2.38 (IQR 1.15–3.60) years, median disease duration 0.23 (IQR 0.14–0.33) years, and median EDSS 3.0 (IQR 2.5–4.0). At time of diagnosis 8 patients (5%) in the RO group had a secondary progressive disease type with a long time since first

symptoms (median 7.50 (IQR 3.35–14.51)). Looking carefully at their history, it became clear that for all of these patients there was a delay in making the diagnosis, either caused by the patient or the physician. At the baseline measurement, 6% of the patients and, at the last measurement, 30% of the patients with RO were receiving disease-modifying drugs.

Most characteristics comply with the expected pattern: more women than men in the RO group, more men than women in the NRO group, and more severe EDSS scores in the NRO group. Seven patients were lost to follow-up (3 after one year, one after 2 years and 3 after 3 years). Of the 149 patients with a complete 3-year follow-up 15 measurements were missing.

Table I shows the median (IQR) and the percentage of patients with aberrant scores of the outcomes SF36rp, SF36re and SF36sf for the RO and NRO group at each measurement. In a healthy reference population 5% has aberrant scores. Our population clearly showed more problems with regard to performance of social roles as measured with the SF36rp, SF36re and SF36sf. The most pronounced deviation was found for the sub-scale SF36rp, followed by SF36sf and SF36re.

Reduction of determinants

In the first step of the analysis, where we analysed the determinants for every cluster per outcome measure separately (using a *p*-value <0.10), the list of 43 potential determinants was reduced to a list of 11–13 determinants for each outcome (Table II). In total, 23 determinants were associated with one or more of the outcome measures.

Construction of standard models

Results of the second step in the analysis, the construction of the standard models, can be found in Table III. The OR is the ratio of the probability that the patient does not deviate from the norm to

Table I. Performance of social roles of recently diagnosed patients with multiple sclerosis (n = 156). Median (interquartile range; IQR) scores and percentage (%) of patients with aberrant scores at each measurement

		Baseline	6 months	1 year	2 years	3 years
<i>SF36 role physical</i>						
RO (n=128)	Median (IQR)	50 (0–100)	75 (0–100)	75 (18.8–100)	75 (6.3–100)	75 (0–100)
	% aberrant	37.5	35.5	36.1	31.0	33.9
NRO (n=28)	Median (IQR)	25 (0–75)	25 (0–93.8)	25 (0–100)	25 (0–81.3)	25 (25–75)
	% aberrant	42.9	42.9	46.2	46.2	30.4
<i>SF36 role emotional</i>						
RO (n=128)	Median (IQR)	100 (33.3–100)	100 (66.7–100)	100 (66.7–100)	100 (66.7–100)	100 (66.7–100)
	% aberrant	13.3	14.5	9.8	15.3	12.1
NRO (n=28)	Median (IQR)	100 (41.7–100)	100 (41.7–100)	100 (58.3–100)	100 (66.7–100)	100 (100–100)
	% aberrant	7.1	10.7	15.4	3.8	8.7
<i>SF36 social functioning</i>						
RO (n=128)	Median (IQR)	75 (62.5–100)	87.5 (62.5–100)	87.5 (62.5–100)	87.5 (62.5–100)	75 (62.5–100)
	% aberrant	11.7	10.5	12.3	12.7	15.3
NRO (n=28)	Median (IQR)	87.5 (62.5–100)	75 (40.6–100)	62.5 (46.9–87.5)	62.5 (62.5–87.5)	62.5 (62.5–87.5)
	% aberrant	17.9	28.6	23.1	11.5	4.3

SF36: Medical Outcome Study Short Form 36; RO: relapse onset; NRO: non-relapse onset; % aberrant: % of patients with aberrant SF36 sub-scale scores. Because the scores on the SF36 sub-scales are skewed, we had to dichotomize them. Data of an age-matched Dutch reference population were used to determine the cut-off for each sub-scale. The mean -1.96 standard deviation was calculated with these reference data for each sub-scale. SF36 sub-scale scores in our data that were worse than this cut-off were classified as aberrant.

Table II. Candidate determinants for final regression models

Determinants per cluster	SF36rp	SF36re	SF36sf
<i>Patient and disease characteristics</i>			
Co-morbidity	+		+
Self-reported number of exacerbations	+		+
Gender		+	
MRI: T2-weighted supratentorial lesion load	+	+	
<i>Psychosocial characteristics</i>			
Locus of control: internal			+
Locus of control: physician		+	
Personality trait: neuroticism	+	+	+
Personality trait: psychoticism		+	
Social support: amount of social support	+		
Social support: perceived social support	+	+	+
<i>Basic functions</i>			
Cognition: sustained attention and concentration			+
Cognition: verbal learning and memory: CLTR		+	
Cognition: verbal learning and memory: LTS		+	
Cognition: visuospatial learning delayed recall		+	
Fatigue	+		
Functional systems: cerebellar			+
Functional systems: mental	+	+	+
Functional systems: optical		+	
Functional systems: pyramidal			+
Pain	+		
Vitality	+	+	+
<i>Basic abilities</i>			
Dexterity: ARA			+
Dexterity: NHPT	+	+	

SF36rp: Medical Outcome Study Short Form 36 sub-scale role physical; SF36re: SF36 sub-scale role emotional; SF36sf: SF36 sub-scale social functioning; CLTR: Consistent Long Term Retrieval; LTS: Long Term Storage; ARA: Action Research Arm Test; NHPT: Nine Hole Peg Test; MRI: magnetic resonance imaging.  
+ *p*-value < 0.10 in stepwise backwards selection procedure per cluster per outcome.

the probability that he does in reference to a score of zero on the determinant. Because we standardized most of the scales of the determinants, the ORs in Table III can be compared with each other in order to determine which determinant has the strongest association with the outcome of interest. An OR > 1 indicates that a patient with a higher score on the determinant is *more* likely to have a normal performance of social roles, while an OR < 1 indicates that a patient with a higher score on the determinant is *less* likely to have a normal performance of social roles. When the increase in the score of the determinant is more than one point, the OR can be calculated. First, the OR from Table III is converted to the original logistic coefficient by taking the natural log (ln). This logistic coefficient is then multiplied by the score on the determinant, and finally e is raised to the power of this coefficient. In formula:  $e^{(\text{score} \times \ln[\text{OR in Table III]})}$ .

Vitality, measured with the SF36vt, is associated with all outcome measures (ORs 1.63–2.25), indicating that patients reporting more vitality have higher odds to have a normal performance of social roles. Besides this being a consistent

association, it is also the strongest association among the determinants studied.

The T2-weighted supratentorial lesion load (ORs 0.71 and 0.78) and the *perceived amount* of social support (ORs 1.19 and 1.31), i.e. the extent to which the available supportive interactions cover the patient's need for social support, are associated with 2 outcome measures, indicating that patients who have a higher T2-weighted supratentorial lesion load have lower odds and that patients who perceive more social support have higher odds to have a normal performance of social roles.

The other determinants are associated with only one of the social roles. Fatigue (OR 0.81), exacerbations (OR 0.79) and the *amount* of social support (OR 0.71), i.e. the quantity of supportive interactions, are associated with the outcome role physical, indicating that more fatigued patients, patients who have experienced more exacerbations and patients having a large amount of social support are less likely to have normal role physical functioning. Gender (OR 0.16), verbal learning and memory (OR 1.26), psychoticism (OR 0.66), neuroticism (OR 0.78), and locus of control physician (OR 1.45) are associated with the outcome role emotional, indicating that male patients, patients who have better verbal learning and memory and patients who rely more heavily on their physician are more likely to have normal role emotional functioning, and patients who have higher psychoticism and neuroticism scores are less likely to have normal role emotional functioning. The functional system score cerebellar (OR 0.70) is associated with the outcome social functioning, indicating that patients with more cerebellar symptoms are less likely to have normal social functioning.

#### Construction of autoregressive models

In step 3, the construction of the autoregressive models, most odds ratios are similar to the odds ratios in the standard models, indicating that the association can be attributed to *within-subject changes* (longitudinal relationship). However, the association of the perceived amount of social support with the outcome role physical is somewhat reduced, indicating that this association is based on both between-subject differences (cross-sectional relationship) and within-subject changes (longitudinal relationship).

## DISCUSSION

The most important determinants associated with the performance of social roles as measured with the SF36rp, SF36re and SF36sf are vitality, the *perceived amount* of social support, and the T2-weighted supratentorial lesion load. The associations are based on within-subject changes, which means that a change in the determinant for a particular patient in the 3-year study period is associated with a change in the outcome for that same patient.

Until now, studies that looked for determinants associated with the performance of social roles have predominantly been cross-sectional (15–17). An important strength of our study is its longitudinal design and analysis, and the simultaneous assessment of an extensive set of determinants, each measuring

Table III. Determinants of the performance of social roles in recently diagnosed patients with multiple sclerosis. Odds ratios (95% CI) for standard and autoregression models.

Determinant	SF36rp		SF36re		SF36sf	
	Standard	Auto-regression	Standard	Auto-regression	Standard	Auto-regression
Vitality*	1.84 (1.58–2.15)	1.92 (1.65–2.24)	1.63 (1.24– 2.15)	1.80 (1.37– 2.37)	2.25 (1.85– 2.73)	2.16 (1.74– 2.68)
Perceived social support*	1.19 (1.02–1.39)	1.08 (0.91– 1.29)			1.31 (1.16– 1.47)	1.25 (1.11– 1.4)
T2-weighted supratentorial lesion load (cm <sup>3</sup> )	0.78 (0.62–0.99)	0.82 (0.65– 1.04)	0.71 (0.57– 0.88)	0.54 (0.43– 0.67)		
Self-reported number of exacerbations	0.79 (0.66–0.95)	0.65 (0.46– 0.93)				
Amount of social support*	0.71 (0.58–0.88)	0.77 (0.61– 0.98)				
Fatigue*	0.81 (0.71–0.93)	0.86 (0.74– 1.01)				
Gender†			0.16 (0.06– 0.44)	0.11 (0.05– 0.25)		
Verbal learning and memory*			1.26 (1.01– 1.56)	1.19 (0.88– 1.59)		
Functional systems: cerebellar‡					0.70 (0.51– 0.97)	0.76 (0.51– 1.11)
Psychoticism*			0.66 (0.46– 0.96)	0.72 (0.53– 0.98)		
Neuroticism*			0.78 (0.69– 0.88)	0.79 (0.72– 0.88)		
Locus of control physician*			1.45 (1.14– 1.83)	1.25 (0.98– 1.58)		

Outcomes are dichotomized using the mean -1.96 standard deviation of a healthy Dutch reference population; for all outcomes 1= normal social functioning and 0 = aberrant social functioning. SF36rp = Medical Outcome Study Short Form 36 sub-scale Role Physical; SF36re = SF36 sub-scale Role Emotional; SF36sf = SF36 sub-scale Social Functioning.

\*Scaled from 0 to 10.

†Female is reference category.

‡Scaled from 0 to 6.

a distinct construct, and outcome measures, which cover different aspects of the performance of social roles. This enables a direct comparison of the adjusted association of several determinants with the outcome measures. In this way, the most important determinants are selected, and it becomes clear which determinants are redundant. Furthermore, it is possible to use longitudinal data analysis techniques, which enable investigation of the contribution of between-subject differences (cross-sectional relationship) and within-subject changes (longitudinal relationship) to the regression coefficients.

A possible weakness is the use of multiple raters. Due to the 6-year study period 3 physical therapists had to be trained by the research physician (VdG) to perform the measurements, probably at the risk of reducing reliability of the measurements. For the measures that require skilled raters, such as the cognitive tests and the scoring of the functional systems of the EDSS, an intensive training was given, and new raters were supervised until they were adequately able to perform the measurements.

Another possible weakness is the relatively small sample size of 156 patients. Modelling in small samples might influence the selection of variables. Simulation experiments have shown that stepwise methods have limited power to select important determinants, and, on the other hand, carry the risk that one or more (almost) random determinants are selected, since multiple comparisons are made (33). Furthermore, the estimate of the regression coefficient might be biased (33). In order to minimize these effects, we used longitudinal regression analysis (GEE) to describe the longitudinal relationships. GEE has the important advantage that all available data are used, which increases the power to detect subtle relationships. Furthermore, we used a more liberal *p*-value of 0.10 for the initial selection of candidate determinants.

Ideally, in a longitudinal study the treatment of the patients should either be standardized or withheld. Of course, this cannot be justified in patients with a chronic progressive disease like MS, for which effective therapy was available and became available during the study (35, 36). Disease-modifying drugs reduce the rate of relapse by approximately 30%, but they have not yet convincingly been shown to reduce disability progression, and certainly not in such a short study period of 3 years. Therefore, we think that our results are still very useful.

This study shows some consistent findings across the different aspects of the performance of social roles, which suggests that the determinants vitality, the *perceived amount* of social support and the T2-weighted supratentorial lesion load might play a role in the development of problems with regard to the performance of social roles. Previously, we have studied the initial course of daily functioning in the same cohort (18). We showed that the differences regarding the performance of social roles between the RO and NRO groups were not significant, and that inclusion of the 8 secondary progressive patients did not confound our results. Also, we studied the course of mental health. We expected that mental health was greatly reduced in the first period after the diagnosis has been made, and that it would gradually recover. However, we found that mental health was relatively unaffected, which indicates that mental health cannot explain the reduced performance of social roles.

However, the results of this study should be interpreted with caution, because causal inferences cannot be made. From a clinical point of view it can easily be understood that diminished vitality, i.e. a lack of energy, leads to problems with regard to the performance of social roles. Patients might have problems to continue sports or leisure activities, skip social activities with family or friends, or are no longer able to work a full day (37). It is surprising that vitality was selected in all

models, while fatigue, measured with the FSS, was selected in the role physical model only. The items of the vitality sub-scale of the SF36 address feelings of fatigue or energy levels, while the items of the FS address fatigue in the context of the consequences of this fatigue for functioning. This conceptual difference in the assessment of fatigue is reflected in the correlation of 0.71 between the FS and the vitality sub-scale of the SF36. Although our binomial GEE models were stable, this correlation may have led to some competition as to which determinant was selected in the final model (collinearity).

Although the relationship between an increase in T2-weighted supratentorial lesion load and more problems with regard to the performance of social roles is also imaginable, the precise mechanism is less obvious. A higher T2-weighted supratentorial lesion load might be an indicator of cognitive dysfunction (38), or might indicate that there has been more disease activity (accumulated pathological changes). In our sample, however, there was no association of T2-weighted supratentorial lesion load with time since first symptoms, which indicates that T2-weighted lesion load is not an indicator of time since first symptoms.

The interpretation of the associations with the 2 social support scales is complex, and further complicated by the fact that the associations of both scales point in opposite directions. The correlation between both scales is low ( $\rho = 0.44$ ), indicating that they measure different constructs, and contribute independently to the results of the analyses. The association with the *perceived amount* of social support can be interpreted in 2 ways. It might be that a patient, who experiences a lack of social support is less inclined to participate in social activities. However, the relationship might also be interpreted in the opposite direction: a patient, who shows social dysfunction for any reason, experiences this as a lack of social support. The interpretation of the finding that patients who report a greater *amount* of social support have higher odds of problems with regard to the performance of social role should probably be that problems with regard to the performance of social roles lead to an accumulation of supportive interactions, and thus an increase in the *amount* of social support. Finally, an overall interpretation of social support might be that a low *perceived amount* of social support leads to a compensatory increase in the *amount* of social support, which is, unfortunately, not sufficient to normalize the performance of social roles.

Future studies should focus on further clarification of the possible causal relationship between vitality, the *perceived amount* of social support and the T2-weighted supratentorial lesion load, and the performance of social roles. It would be very interesting to design trials that study the effect of interventions that are developed to influence the above mentioned determinants. Trials showing that these interventions lead to improved performance of social roles would provide strong evidence for a causal relationship.

But first, more longitudinal studies are needed to build a broader evidence base. Our results might aid the selection of determinants for these studies. Since we realize that the 3-year follow-up of this cohort is relatively short, we intend to extend the follow-up. This would enable a description of the course

of the performance of social roles during the later stages of the disease and a study of the determinants associated with the performance of social roles in these later stages. Patients in our incidence cohort are currently only relatively mildly disabled, which will certainly change with longer disease duration. This will probably have consequences for the relative importance of the determinants we have studied.

Clinicians caring for patients with MS will be confronted with patients who are limited in their performance of social roles. Interventions to reduce the development of new lesions are available and implemented in clinical practice. Our results indicate that vitality and the *perceived amount* of social support might also be important factors to improve in these patients. Isolated interventions to improve vitality, such as amantadine (37), energy conservation techniques (39) and aerobic training (40), are available, but evidence regarding their efficacy is not conclusive. Different interventions to improve the *perceived amount* of social support are also available, but again the evidence is not conclusive (41). Furthermore, as argued above, it has not been shown that these interventions lead to improved performance of social roles. However, it has been shown that outpatient as well as home-based multidisciplinary rehabilitation programmes can lead to improvements in the performance of social roles (42–44). These studies looked at the rehabilitation programme as a whole and did not focus on specific elements in these programmes. It is very likely, though, that these programmes contained elements addressing vitality and the *perceived amount* of social support.

In conclusion, vitality, the perceived amount of social support, and disease activity, i.e. the T2-weighted supratentorial lesion load, determine the performance of social roles in the early stages of MS.

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