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Everyday cognitive failure and depressive symptoms predict fatigue in sarcoidosis: A prospective follow-up study

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ABSTRACT

Background: Fatigue is a major and disabling problem in sarcoidosis. Knowledge concerning correlates of the development of fatigue and possible interrelationships is lacking.
Objective: A conceptual model of fatigue was developed and tested.
Methods: Sarcoidosis outpatients (n = 292) of Maastricht University Medical Center completed questionnaires regarding trait anxiety, depressive symptoms, cognitive failure, dyspnea, social support, and small fiber neuropathy (SFN) at baseline. Fatigue was assessed at 6 and 12 months. Sex, age, and time since diagnosis were taken from medical records. Pathways were estimated by means of path analyses in AMOS.
Results: Everyday cognitive failure, depressive symptoms, symptoms suggestive of SFN, and dyspnea were positive predictors of fatigue. Fit indices of the model were good.
Conclusions: The model validly explains variation in fatigue. Everyday cognitive failure and depressive symptoms were the most important predictors of fatigue. In addition to physical functioning, cognitive and psychological aspects should be included in the management of sarcoidosis patients.

1. Introduction

The clinical manifestation, natural history, and prognosis of sarcoidosis are highly variable, and its course is often unpredictable [1]. Clinical manifestations vary with the organs involved [1,2]. While the lungs are affected in approximately 90% of patients with sarcoidosis, the disease frequently also involves lymph nodes, skin, and eyes. Interpretation of the severity of sarcoidosis can be complicated by its heterogeneity. Apart from lung-related symptoms, patients may suffer from a wide range of rather nonspecific symptoms [2–4]. Sarcoidosis-related complaints, including fatigue, general and muscle weakness, exercise limitation, pain, depressive symptoms, and cognitive failure may become chronic and persist even after all other signs of disease activity have disappeared [5–7].

Fatigue is the most frequently described and devastating symptom in sarcoidosis and is globally recognized as a disabling problem [3]. The reported prevalence varies from 60% to 90% of sarcoidosis patients, and up to 25% of fatigued sarcoidosis patients report extreme fatigue [3]. It affects patients' quality of life (QoL), i.e. their social life, and physical as well as psychological capacities [8–14]. Strookappe et al. showed that exercise capacity partly predicts patients' fatigue scores [15]. In their study, fatigue was not explained by lung function test results, inflammatory markers, or other clinical parameters.

The etiology of sarcoidosis is poorly understood and is likely to be multifactorial, encompassing active inflammation, cytokine release, depression, sleep disturbance, and/or small fiber neuropathy (SFN) [3,4,16]. Furthermore, fatigue can be caused by systemic treatments used to treat sarcoidosis, such as corticosteroids [6,17].

The diagnosis of sarcoidosis-associated fatigue requires extensive evaluation to identify and treat potentially reversible causes [3,12]. Its etiology may involve granuloma formation and cytokine release. However, despite effective treatment of the sarcoidosis activity, many

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patients continue to experience fatigue, causing limitations [3,16,18].

Symptoms of fatigue and dyspnea induce exercise limitation, and fatigue also leads to physical inactivity. Although less recognized than exertional dyspnea, it is a very common and frustrating physical symptom in patients with sarcoidosis. Decreased physical activity can induce general deconditioning, which in turn contributes to increased perceived physical fatigue and a sense of dyspnea, lack of energy, or exhaustion [19,20]. Additionally, other symptoms reported by patients with sarcoidosis, including everyday cognitive deficits [12], depressive symptoms [21], anxiety, and symptoms associated with SFN [22], are also related to fatigue. Comorbidities associated with sarcoidosis, including depression, anxiety, hypothyroidism, and altered sleep patterns, all contribute to fatigue [6,23,24].

It is important to examine the potential factors that sustain fatigue in sarcoidosis. This may be accomplished by understanding clinical, psychological, and social predictors of fatigue in these patients. The knowledge concerning correlates of the development of fatigue and possible interrelationships is still incomplete, and previous research has mainly had a cross-sectional design [22] and studied the variables individually, instead of simultaneously. Therefore, the aim of the present study was to test a conceptual model of fatigue that includes physical and psychological symptoms.

2. Material and methods

2.1. Development model of fatigue

A conceptual model of fatigue, based on the model of Taylor and Aspinwall [25], was developed and tested. This conceptual model is represented in Fig. 1. Clinical variables were not incorporated in this model, because previous studies showed no consistent significant relationships between the fatigue assessment scale (FAS) and medical data widely used in sarcoidosis [22]. Time since diagnosis, sex, and age were incorporated into this model to control for background variation. Trait anxiety was expected to predict stressors, social support, and fatigue.

2.2. Study design and subjects

All sarcoidosis outpatients (n = 588) of the ILD Care Center of the Department of Respiratory Medicine of the Maastricht University Medical Center, a tertiary referral center in the Netherlands, were asked to participate. Patients were diagnosed with sarcoidosis based on consistent clinical features and bronchoalveolar lavage fluid analysis results, according to the guidelines of the World Association of Sarcoidosis and Other Granulomatous Disorders [1]. The exclusion criteria were poor command of the Dutch language (n = 3) and relevant co-morbidity, such as malignancy (n = 7), dementia (n = 1), and a history of psychiatric illness (n = 2). Thirteen patients were found to be non-eligible and 133 patients refused to participate. The remaining 348 patients participated at baseline. After 12 months, 292 patients remained in the study.

2.3. Procedure

The patients received information about the study by e-mail and were asked to return an informed consent form if they were willing to participate. Patients who agreed to participate received the first set of questionnaires and were asked to return the completed set to the hospital in an enclosed envelope. After 6 and 12 months, patients received another set of questionnaires with an envelope. The most common reason for not completing the set of questionnaires was 'insufficient time'. The data were collected by the ILD care team. The Medical Ethics Committee of MUMC+ (MEC 07-4-015) approved the study protocol, and written informed consent was obtained from all patients.

2.4. Measurements

2.4.1. External resources and background variables

The following variables were taken as exogenous: gender (0 = male, 1 = female), age, and time since diagnosis.

2.4.2. Personal resource

At baseline the patients completed the State and Trait Anxiety Inventory (STAI) [26] to measure trait anxiety. Trait anxiety concerns differences between individuals in their disposition to respond to stressful situations with varying amounts of stress. The trait scale consists of 20 statements and asks people to describe how they generally feel. The psychometric characteristics of the Dutch version of this questionnaire are well established and considered good. High trait anxiety was defined as a score above 40, based on Dutch norm scores [26].

2.4.3. Questionnaires (stressors)

At baseline, the patients completed the Center for Epidemiological Studies-Depression Scale (CES-D) [27], the Small Fiber Neuropathy Screenings List (SFNSL) [28], and the Cognitive Failure Questionnaire (CFQ) [29]. In addition, patients were asked to determine their Borg Dyspnea Index (BDI) [30]. The CES-D [27] is a 20-item scale designed to measure the presence and degree of depressive symptoms. Scores of 16 or above are indicative of a depressive disorder. Reliability and

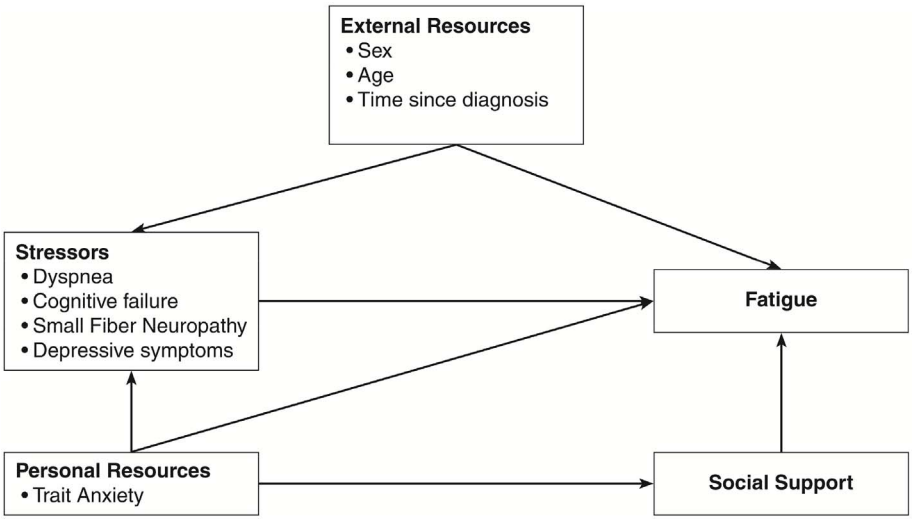

Fig. 1. Initial conceptual model of fatigue in sarcoidosis.[a]
[a] Error terms are omitted from this figure. All predictors were measured at baseline, and fatigue at 12 months follow-up.