

# Cognitive inefficiency in sarcoidosis

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## Introduction

In many areas of human suffering, patients often present with symptoms that are in excess of objective physical evidence. The clinical course of sarcoidosis is highly variable and virtually every organ can be involved.<sup>1</sup> Patients with pulmonary sarcoidosis may present with symptoms related directly to the chest such as coughing and dyspnoea on exertion. Non-specific symptoms, especially fatigue and pain, have an important impact on the quality of life (QOL) of sarcoidosis patients too.<sup>2</sup> These symptoms are disabling for the patient and may become chronic. Symptoms involving cognitive complaints such as memory loss, concentration problems, and other mental problems are often recalled by patients suffering from sarcoidosis. However, till now no studies were performed to assess this problem extensively.

## Aim

The aim of this study was to compare cognitive inefficiency scores, as assessed by the Cognitive Failures Questionnaire (CFQ), between patients with sarcoidosis and healthy controls. Moreover, the relationship of cognitive inefficiency to fatigue, measures of depressive symptoms (mood) and other clinical parameters was examined.

## Methods

The study included 347 sarcoidosis patients from the MUMC, the Netherlands. They completed the CFQ, the fatigue assessment scale (FAS) and the Centre for Epidemiological Studies-Depression Scale (CES-D). The control group consisted of 1358 healthy volunteers, who completed the CFQ.

### Cognitive Failures Questionnaire (CFQ)

The CFQ was developed by Broadbent et al.<sup>3</sup> It was designed specifically to assess examples of everyday cognitive errors of attention, perception, memory, and motor functioning. The questionnaire consists of 25 items measuring the frequency of everyday cognitive failures or lapses. These concern failures of memory, attention, action, and perception. Participants indicate on a five-point scale how.<sup>3</sup> The total possible CFQ score ranged from 0 to 100, with higher scores indicating more cognitive failures.

### Fatigue Assessment Scale (FAS)

The FAS is a 10-item questionnaire to assess fatigue.<sup>2</sup> The response scale is a 5-point scale (1 never to 5 always); scores on the FAS can range from 10 to 50.<sup>2</sup> The cut-off score of the FAS is 22. A score below 22 indicates no fatigue, whereas a score of 22 or higher indicates fatigue. ([www.ildcare.eu/pages/artsen\\_informatie\\_fasen.html](http://www.ildcare.eu/pages/artsen_informatie_fasen.html))

### Center for Epidemiological Studies-Depression Scale (CES-D)

The CES-D assesses the presence and severity of depressive symptoms. It is a 20-item self-administered measure of depressive symptomatology. It assesses both negative and positive affect which, have been grouped into four factors: depressed affect, positive affect, somatic, and interpersonal relations. Overall scores range from 0-60 with higher scores indicating more depressive symptoms. A score of 16 is most commonly used to screen for depression.<sup>4</sup>

### Small Fiber Neuropathy Screening List (SFNSL)

The SFNSL is a 21-item self-administered measure of symptomatology related to small fiber neuropathy (SFN). The response scale is a 5-point scale (1 never to 5 always); scores on the SFNSL can range from 0 to 84. The cut-off score of the SFNSL is 11. A score below 11 indicates no SFN, a score of 11-48 indicates probably or highly likely (>37) SFN, a score ≥48 is indicative of SFN.<sup>5</sup> ([www.ildcare.eu/pages/artsen\\_informatie\\_fasen.html](http://www.ildcare.eu/pages/artsen_informatie_fasen.html))

### Statistical analysis

The influence of demographic characteristics, clinical characteristics (such as duration and severity of sarcoidosis) and of fatigue and depression on CFQ-scores, was evaluated by categorizing the participants into subgroups according to the variables that were considered as potential determinants of higher cognitive failure. Differences between subgroups were tested for statistical significance using the Student's t-test for independent samples.

**Table 1.** Demographic characteristics of sarcoidosis patients (cases) and controls.

	cases	controls
number	347	1358
gender f/m	154/193	672/687
age, yrs±SD (range)	48.3±11.0 (20-79)	51.4±16.3 (24-83)
CFQ total score	36.4±16.1	31.8±11.0*

CFQ= Cognitive Failures Questionnaire; \* p<0.0001

**Table 2.** Summary of the clinical characteristics of the studied sarcoidosis population.

	cases
time since diagnosis, yrs (range)	5.0±7.5 (0-41)
DLCO, % of predicted values	81.8±18.1
FVC, % of predicted values	98.8±19.8
Chest X-ray stage: 0/II/III/IV %*	28.7/18.0/29.9/13.2/10.2
treatment, no/yes %*	41.8/58.2
FAS	29.2±8.4
CES-D	13.9±9.0
SFNSL	42.9±7.3

Data are expressed as mean±SD or percentages, if appropriate\*.

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## Results

The demographic characteristics of the cases and healthy controls are summarized in table 1 and the most relevant clinical data of the studied sarcoidosis population in table 2. The mean CFQ-score was significantly higher in sarcoidosis patients (36.4±16.1) compared to the controls (31.8±11.1; p<0.0001). The mean difference between the groups was 4.56 (95% CI: 3.11-6.00). After adjustment for differences in age and gender distribution, the CFQ score remained higher in the sarcoidosis group with a mean difference of 4.68 (95% CI: 3.23-6.14).

After categorizing participants into two subgroups with a low CFQ score (<43) versus a high CFQ score (≥43), 31.4% of the sarcoidosis patients (n=109; 55.1±8.4) compared to 14.0% (n=190; 50.1±5.9) of the controls had a high CFQ-score (p<0.0001).

Within the sarcoidosis group, the CFQ score correlated positively with fatigue (r=0.483; p<0.0001; figure 1) and depression (r=0.489; p<0.0001), but not with clinical characteristics, such as disease severity and treatment.

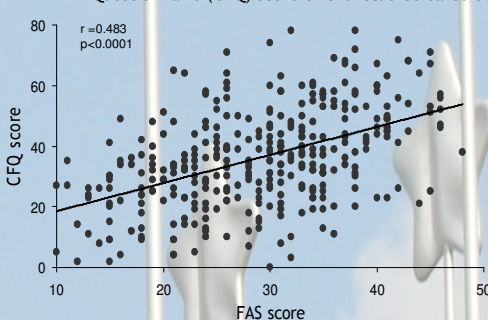
In Table 3, participants are categorized into subgroups (group I and group II) according to the variables that were considered as potential determinants of higher cognitive failure. The mean CFQ scores between the subgroups was compared using the Student's t-test for independent samples. Females scored higher on the CFQ than males (p<0.0001). No significant difference was found between patients with a time since diagnosis of ≤2 years compared to those with a disease duration of more than 2 years. Furthermore, lung function parameters, chest X ray stages, sex and age did not reveal differences in the CFQ scores (table 3).

Patients suffering from fatigue (FAS ≥22), depressive symptoms (CES-D >16) or substantial symptoms indicative of SFN and autonomic dysfunction (SFNSL score >37) demonstrated high CFQ scores as well (p<0.0001).

**Table 3.** Comparison of CFQ scores of subgroups within the sarcoidosis population using clinical data indicating disease severity and psychological characteristics.

	number	Group I	Group II	Δ (I vs I)	p-value
gender m/f	193/154	33.5±15.1	40.0±16.5	6.5 (3.2-9.9)	<0.0001
age, yrs <50/≥50	205/142	37.8±17.0	34.5±14.4	-3.3 (-6.7-0.2)	0.06
disease duration, yrs ≤2/>2	184/163	35.4±15.4	37.9±16.7	2.5 (-0.9-5.9)	0.15
DLCO ≥80%/<80%	189/158	35.9±15.9	37.4±16.5	1.5 (-2.2-5.2)	0.42
FVC ≥80%/<80%	295/52	37.1±16.0	42.5±16.6	4.5 (-0.4-9.5)	0.07
Chest X-ray stage 0-II/III-IV	156/191	37.4±17.0	35.5±15.0	1.9 (-5.3-1.5)	0.27
treatment no/yes	145/202	37.7±16.7	35.4±15.6	-2.3 (-5.7-1.2)	0.19
FAS <22/≥22	80/267	26.1±13.4	39.5±16.6	13.4 (9.6-17.2)	<0.0001
CES-D ≤16/>16	216/131	31.8±15.1	43.6±14.4	11.8 (8.3-15.3)	<0.0001
SFNSL ≤37/>37	150/197	31.0±14.8	40.5±15.9	9.5 (6.1-12.9)	<0.0001

**Figure 1.** Fatigue Assessment Scale (FAS) score versus Cognitive Failures Questionnaire (CFQ) score of the studied sarcoidosis population.



## Conclusion

Cognitive inefficiency, as assessed by the CFQ, occurs more often in patients with sarcoidosis than in healthy volunteers.

A high CFQ score (>43) occurred in about 31% of the sarcoidosis patients.

Therefore, cognitive inefficiency appears to be a substantial problem and seems to be related to fatigue and depression.

These results emphasize the need for further research and a necessity to integrate knowledge about neuropsychological deficits in sarcoidosis into clinical management.

## References

- Iannuzzi MC, Rybicki BA, Teirstein AS. Sarcoidosis. *N Engl J Med* 2007;357:2153-65.
- De Vries J, Rothkrantz-Kos S, van Diejen-Visser MP, Drent M. The relationship between fatigue and clinical parameters in pulmonary sarcoidosis. *Sarcoidosis Vasc Diffuse Lung Dis* 2004;21:127-36.
- Broadbent DE, Cooper PF, FilzGerald P, Parkes KR. The cognitive failures questionnaire and its correlates. *Br J Clin Psychology* 1982;21:1-16.
- Radloff LS. The CES-D scale: A self-report depression scale for research in the general population. *Applied Psychol Meas* 1977;1:385-401.
- Holtsma E. Small fiber neuropathy. A novel finding in sarcoidosis. Thesis 2005. ISBN: 90-9018868-1.