

**Fatigue in CIDP:
A comparison between active and remission
disease states**

Chronic inflammatory demyelinating polyneuropathy (CIDP)

Prevalence¹⁻⁴

- Estimates of prevalence range from 1.0 to 8.9 per 100,000 individuals
- Most common in adults aged 40–60 years

Clinical features and symptoms⁵

- Typically symmetrical proximal and distal muscle weakness and numbness, hyporeflexia or areflexia
- Evolving >2 months, progressive or relapsing pattern
- Symptoms include fatigue, pain, depression

Diagnosis and treatment⁶

- EFNS/PNS guidelines, electrophysiology and CSF analysis mandatory
- Immunoglobulin, corticosteroids, plasma exchange

CSF: cerebrospinal fluid; EFNS/PNS: European Federation of Neurological Societies/Peripheral Nerve Society

1. Lunn MP *et al.* J Neurol Neurosurg Psychiatry. 1999;66(5):677–680.
2. McLeod JG *et al.* Ann Neurol. 1999;46(6):910–913.
3. Laughlin RS *et al.* Neurology. 2009;73(1):39–45.
4. Robertson EE, Donofrio PD. Curr Treat Options Neurol. 2010;12(2):84–94.
5. Rajabally YA *et al.* Neurodegener Dis Manag. 2015;5(3):257–268.
6. Van den Bergh PY *et al.* Eur J Neurol. 2010;17(3):356–363.

|||| CIDP: Fatigue

- Fatigue is common in immune-mediated polyneuropathies
 - It affects up to 65% of patients with CIDP¹
 - The majority of patients experience severe fatigue²
 - 80% of patients consider fatigue one of their three most disabling symptoms²
 - Fatigue correlates negatively with quality of life – most notably, with general health and physical functioning²
- Despite the significant impact of fatigue, the underlying cause in patients with CIDP remains poorly understood

Importantly, the occurrence of fatigue across different disease activity states in CIDP has not been examined and is unknown

CIDP: chronic inflammatory demyelinating neuropathy

1. Rajabally YA *et al.* Neurodegener Dis Manag. 2015;5(3):257–268.
2. Merkies IS *et al.* Neurology. 1999;53(8):1648–1654.

STUDY OBJECTIVE

To explore fatigue, sleepiness, sleep quality, and depression in patients with active CIDP and patients with CIDP in drug-free remission

Definitions

Sleepiness

- A propensity to fall asleep from presumed impairment of the normal arousal mechanism

Fatigue

- Overwhelming sense of lack of energy or feeling of exhaustion, with impaired physical or cognitive function

Both

- Complex, heterogeneous phenomena which often co-exist as a consequence of poor sleep or medical illness

Study design

- **Study design:**

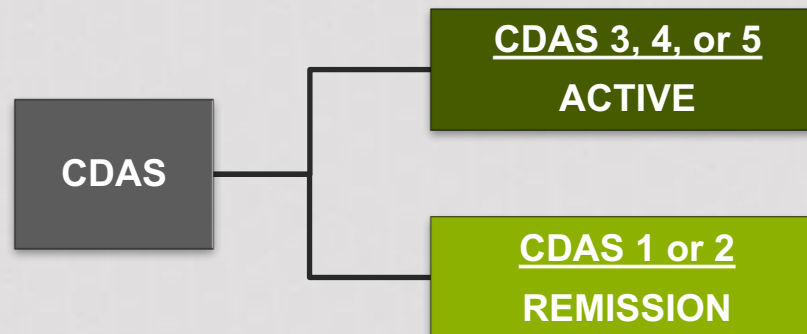
- Cross-sectional¹

- **Study population:**

- 46 patients with CIDP, seen between January 2015 and June 2016¹
- All patients satisfied the EFNS/PNS CIDP diagnostic criteria²

- **Stratification:**

- Patients stratified according to CIDP Disease Activity Status (CDAS):¹



CIDP Disease Activity Status (CDAS)³

1. **Cure:** ≥ 5 years off treatment
2. **Remission:** < 5 years off treatment
3. **Stable active disease:** ≥ 1 year on treatment
4. **Improvement:** 3 months to 1 year on treatment
5. **Unstable active disease:** abnormal examination with progressive or relapsing course

CDAS: CIDP Disease Activity Status; CIDP: Chronic Inflammatory Demyelinating Neuropathy; EFNS/PNS: European Federation of Neurological Societies/Peripheral Nerve Society

1. Gable K, Attarian H, Allen JA. PNS INC 2016 meeting, June 21–24, 2016. Glasgow, Scotland.
2. Van den Bergh PY *et al.* Eur J Neurol. 2010;17(3):356–363.
3. Gorson KC *et al.* J Periph Nerv Syst. 2010;15:326–333.

|||| Evaluations

- **Physical impairment:**
 - Jamar grip strength, Medical Research Council (MRC) sum scale, Timed Up and Go walk (TUG)
- **Disability:**
 - Rasch-built Overall Disability Scale (R-ODS), Overall Neuropathy Limitations Scale (ONLS)
- **Pain:**
 - Visual Analogue Scale (VAS) for pain
- **Sleepiness and sleep quality:**
 - Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI)
- **Fatigue:**
 - Rasch-built 7-item modified Fatigue Severity Scale (FSS)
- **Depression:**
 - Beck Depression Inventory (BDI)

|||| Sleep, fatigue, and depression scales

Scale	Description	Standardized reference data
Epworth Sleepiness Scale (ESS)	Self-rated questionnaire to assess daytime sleepiness in various situations	<i>Normal:</i> 0–7 <i>Average:</i> 8–9 <i>Excessive:</i> 10–15 <i>Severe:</i> 16–24
Pittsburgh Sleep Quality Index (PSQI)	Self-rated questionnaire to assess sleep quality and disturbances	<i>Poor:</i> >6
Fatigue Severity Scale (FSS)	Self-reported scale for assessment of daytime fatigue and impact on daily function	
Beck Depression Inventory (BDI)	Self-reported inventory to measure the presence and severity of depression	<i>Minimal:</i> 0–13 <i>Mild:</i> 14–19 <i>Moderate:</i> 20–28 <i>Severe:</i> 29–63

Patient disposition and demographics



- Demographic data were similar in both groups:

	Active (N=27)	Remission (N=19)	P-value
Age, mean (SD), years	51.4 (10.7)	46.9 (13.3)	0.21
Male (%)	70	53	0.35
Weight, mean (SD), kg	84.3 (18.1)	83.8 (17.5)	0.91
BMI, mean (SD)	27.1 (5.5)	27.8 (5.3)	0.65
Symptom duration, mean (SD), months	93.3 (73.2)	93.8 (66.7)	0.98
Time since diagnosis, mean (SD), months	82.3 (69.5)	84.7 (62.4)	0.90
Time in remission, mean, range (SD), months	N/A	18.6, 6–54 (15.6)	N/A

CDAS: CIDP Disease Activity Status; N/A: not applicable; SD: standard deviation.

Co-morbidities

	Active (N=27)	Remission (N=19)	P-value
Known secondary autoimmune disease (%)	15	0	0.13
Known depression (%)	15	16	0.99
Sedating medications (%)	48	42	0.76

- Although non-neurological autoimmune disease was not seen in the remission group, no statistically significant differences in pre-existing depression, non-neurological autoimmune disease, or sedating medications were observed

Outcomes I: Physical impairment, disability & pain

- Disability (R-ODS, ONLS) and strength impairment (MRC sum scale, grip strength, TUG) were generally more prevalent in the active group than the remission group

Outcome	Active (N=27)	Remission (N=19)	P-value
Grip strength, mean (SD), kg	27.6 (17.0)	31.9 (14.9)	0.39
MRC sum scale (0–80), mean (SD)	70.7 (12.3)	78.3 (1.8)	0.01
TUG, mean (SD), seconds	10.8 (5.5)	8.1 (2.8)	0.07
R-ODS, mean (SD)	60.0 (20.3)	72.9 (19.7)	0.04
ONLS, mean (SD)	3.9 (1.9)	2.5 (1.4)	0.01
Pain (VAS), mean (SD)	2.4 (2.5)	2.7 (2.8)	0.63

Outcomes II: Sleep, fatigue & depression

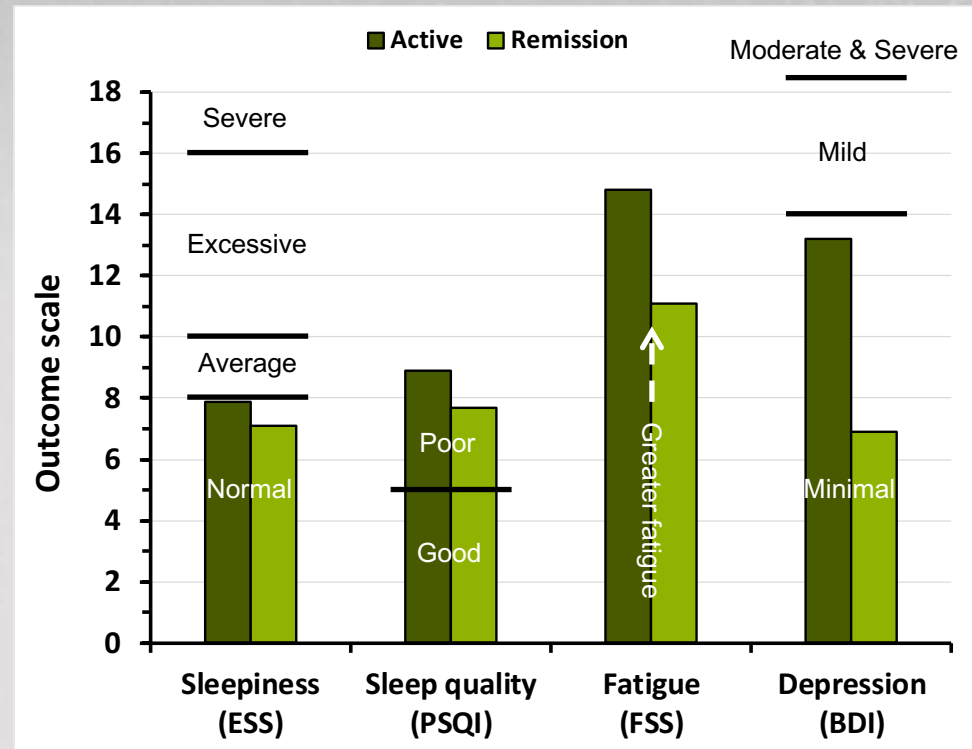
- Depression was more severe in the active group than the remission group
- Fatigue was more severe in those with active disease, although the difference did not reach statistical significance
- Sleepiness and sleep quality were similar in both groups

Outcome	Active (N=27)	Remission (N=19)	P-value
Sleepiness (ESS), mean (SD)	7.9 (4.4)	7.1 (5.4)	0.58
Sleep quality (PSQI), mean (SD)	8.9 (4.1)	7.7 (4.4)	0.35
Fatigue (FSS), mean (SD)	14.8 (7.7)	11.1 (7.8)	0.12
Depression (BDI), mean (SD)	13.2 (10.1)	6.9 (5.0)	0.02

BDI: Beck Depression Inventory; ESS: Epworth Sleepiness Scale; FSS: Fatigue Severity Scale; PSQI: Pittsburgh Sleep Quality Index; SD: standard deviation.

Outcomes II: Sleep, fatigue & depression (continued)

- Compared to standardized normative data:
 - Sleepiness would be considered “normal” and sleep quality “poor” in both groups
 - Although BDI scores were higher (worse) in the active group, in both groups depression would be considered “minimal”
 - Fatigue scores were <15 in both groups



Conclusions I

- Fatigue, but not sleepiness, is a common problem in patients with CIDP regardless of the disease state
- Like strength impairment and disability, fatigue appears to improve when CIDP is less active but also persists as a residual symptom even when the disease is in remission
- Persistent fatigue, especially in patients with chronic but stable residual motor deficits, may be one factor contributing to over-treatment of inactive CIDP

Conclusions II

- Although depression is “minimal” even in active disease, the observation that depression improves with remission suggests that this might be under recognized in active CIDP and may contribute to fatigue, disability, and quality of life
- Poor sleep quality may contribute to CIDP-associated fatigue and might be targeted for symptomatic therapy

This study is ongoing and continues to enroll patients