

AUTONOMIC NERVOUS SYSTEM DYSFUNCTION IN CHRONIC FATIGUE SYNDROME: A POPULATION-BASED STUDY

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Introduction

- Chronic Fatigue Syndrome (CFS) is characterized by disabling fatigue. A case definition for CFS was developed (1988) and revised (1994) under the leadership of the Centers for Disease Control and Prevention.
- Autonomic Nervous System (ANS) dysfunction, manifested as increased heart rate (HR) with reduced heart rate variability (HRV), and orthostatic intolerance, has been demonstrated in the awake CFS patients.
- The autonomic dysfunction described during daytime wakefulness has been demonstrated to extend to nighttime sleep.
- The cause for the syndrome is unknown and there are no validated diagnostic tests.

Objective

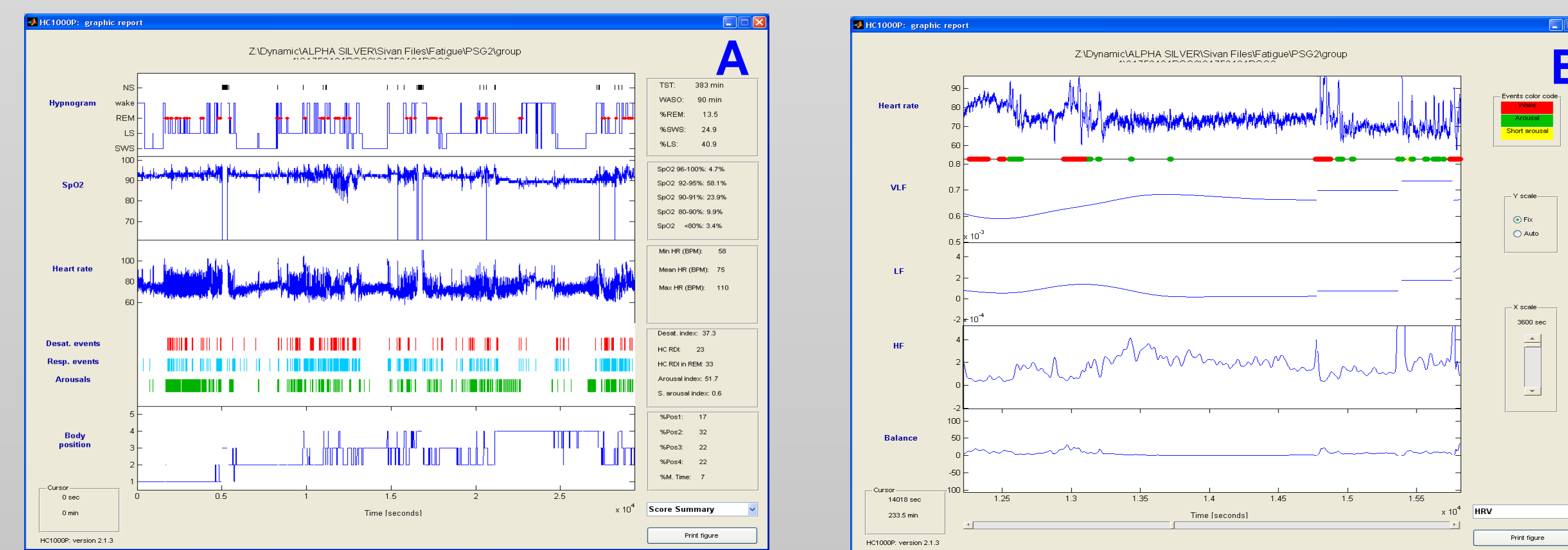
- To determine the impact of individual sleep states on ANS activity in CFS patients.
- To identify a possible etiologic link between autonomic dysfunction during sleep and daytime fatigue.

Methods

- Design: retrospective study on patients selected carefully from a cohort of 254 subjects in a CFS study performed by the CDC in Wichita, Kansas.
- Subjects: 29 in the Fatigue (F) group presenting with persistent fatigue at the time of the study and 35 normal controls (NF) were included in the study (after the exclusion of 12 subjects due to technical problems precluding ANS analysis).
- Study protocol:
 - All subjects were screened by a nurse practitioner and sleep specialist before intake
 - Whole night standard PSG followed by MSLT and second night standard PSG
- PSG and MSLT analysis for sleep architecture, cortical arousals, respiratory events and limb movements according to gold standard criteria (R&K; ASDA) were performed manually by the same expert (RPSGT).
- Autonomic arousals and autonomic function were evaluated by means of a novel technique (HC1000P) based on ECG and pulse oximetry signals developed by HypnoCore LTD.
- The autonomic function evaluation is based on time dependent analysis of HRV (after RRI computation from the recorded ECG signal). The frequency regions of interest are:

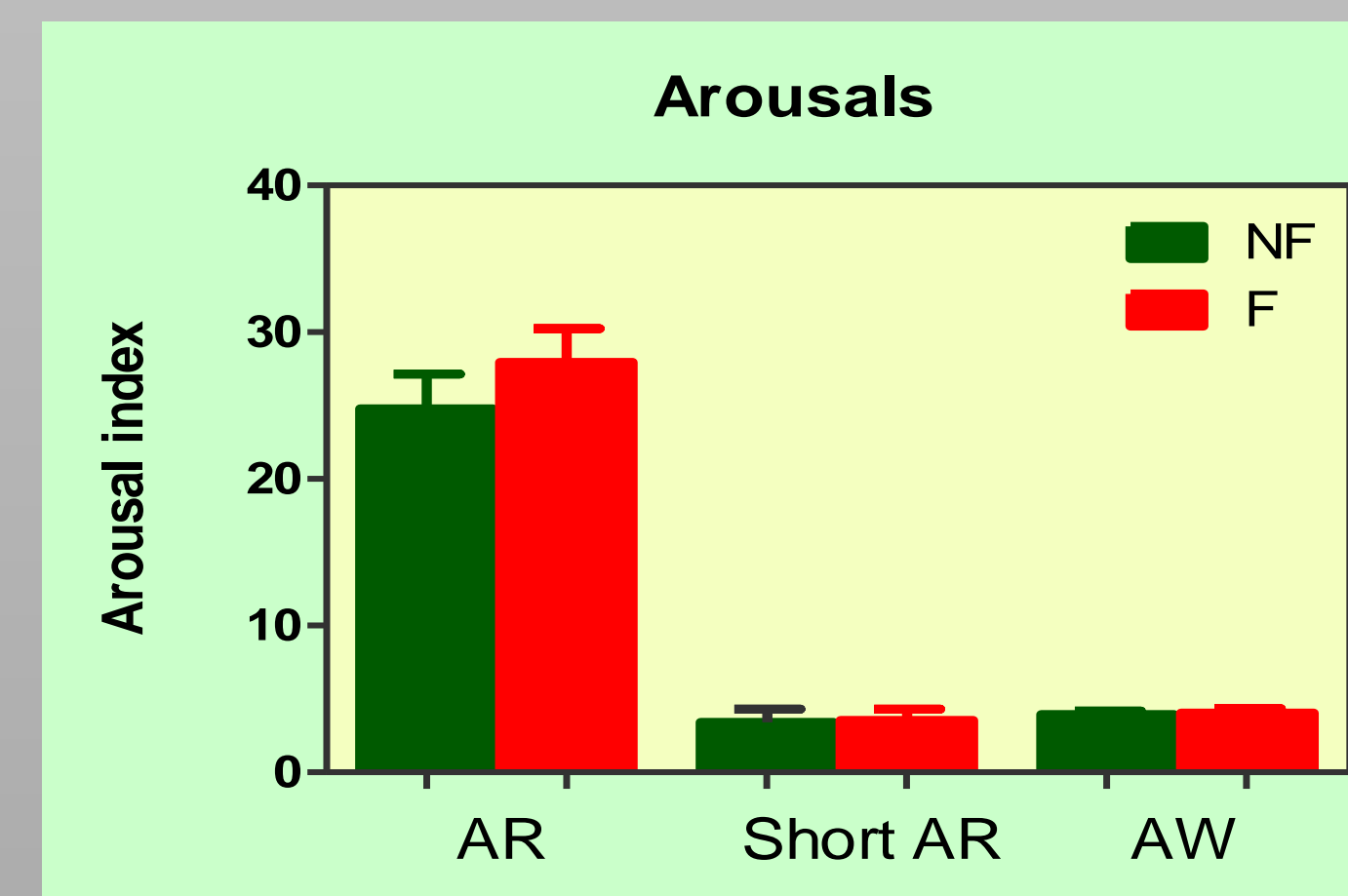
- VLF (.008-.04 Hz) - vasomotor and thermal regulation
- LF (.04-.15 Hz) - sympathetic and parasympathetic modulation at the sinus node
- HF (0.15-0.47 Hz) - mainly parasympathetic modulation at the sinus node
- ABI (LF/HF ratio) - sympatho-vagal balance

Results



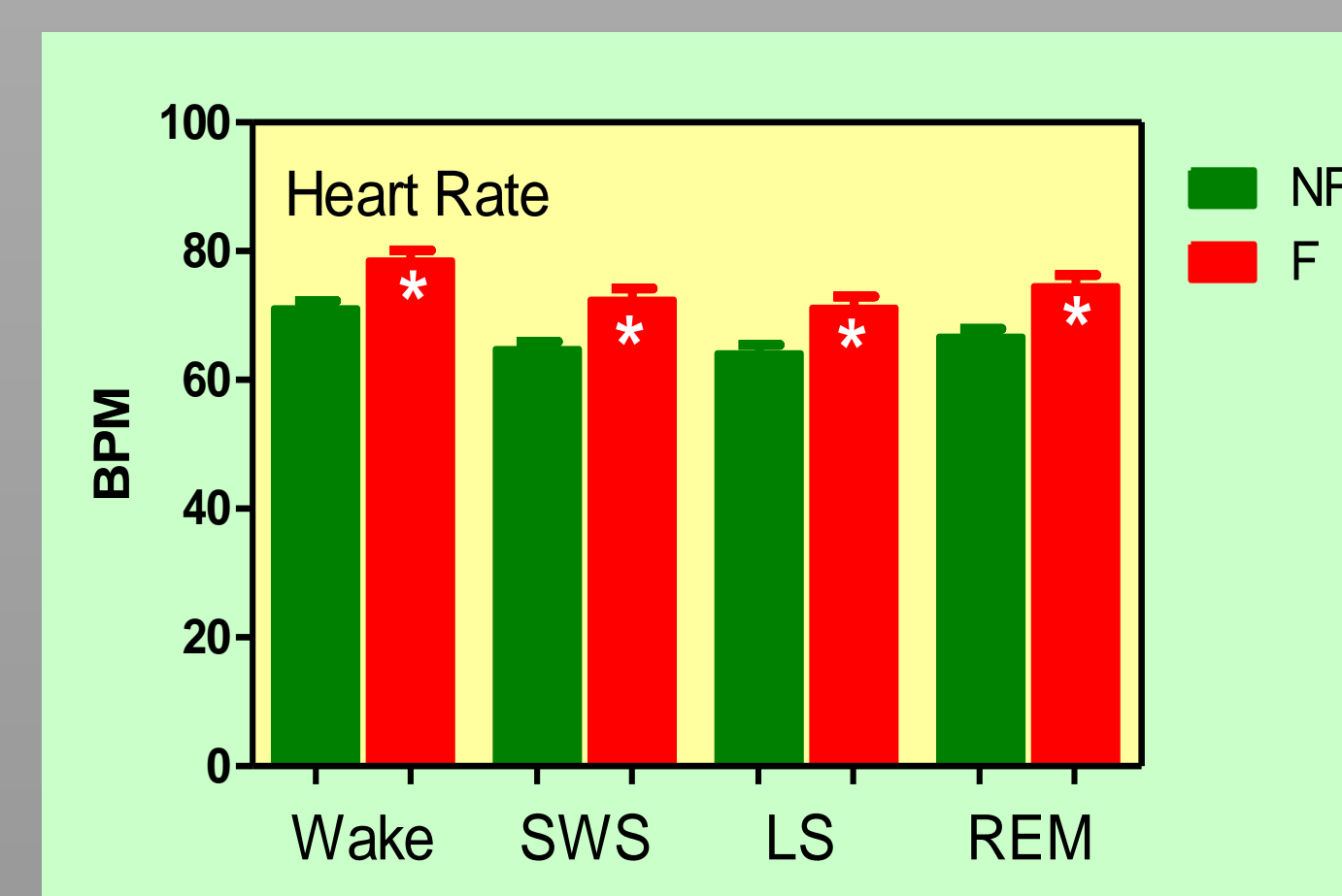
Results in a CFS patient: Frame A contains Sleep study results as provided by HC1000P; Frame B presents HR, arousals and autonomic parameters during a 3600 sec epoch.

✓ Sleep architecture and Respiratory Disturbance Index were similar in both groups.



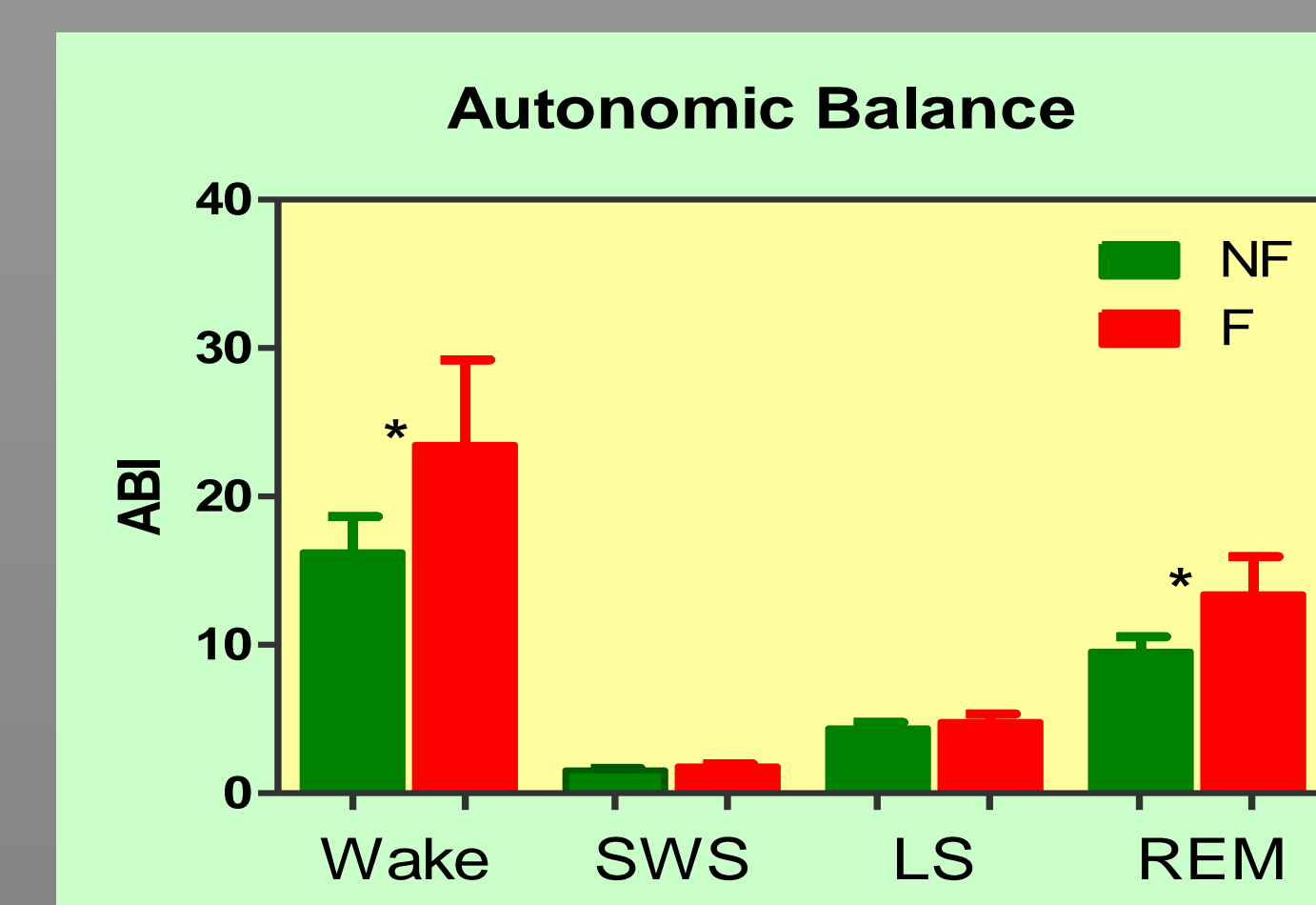
Sleep fragmentation

- ✓ No significant difference was detected in cortical arousals and awakening between groups
- ✓ Autonomic arousal index was similar in F and NF



Heart Rate

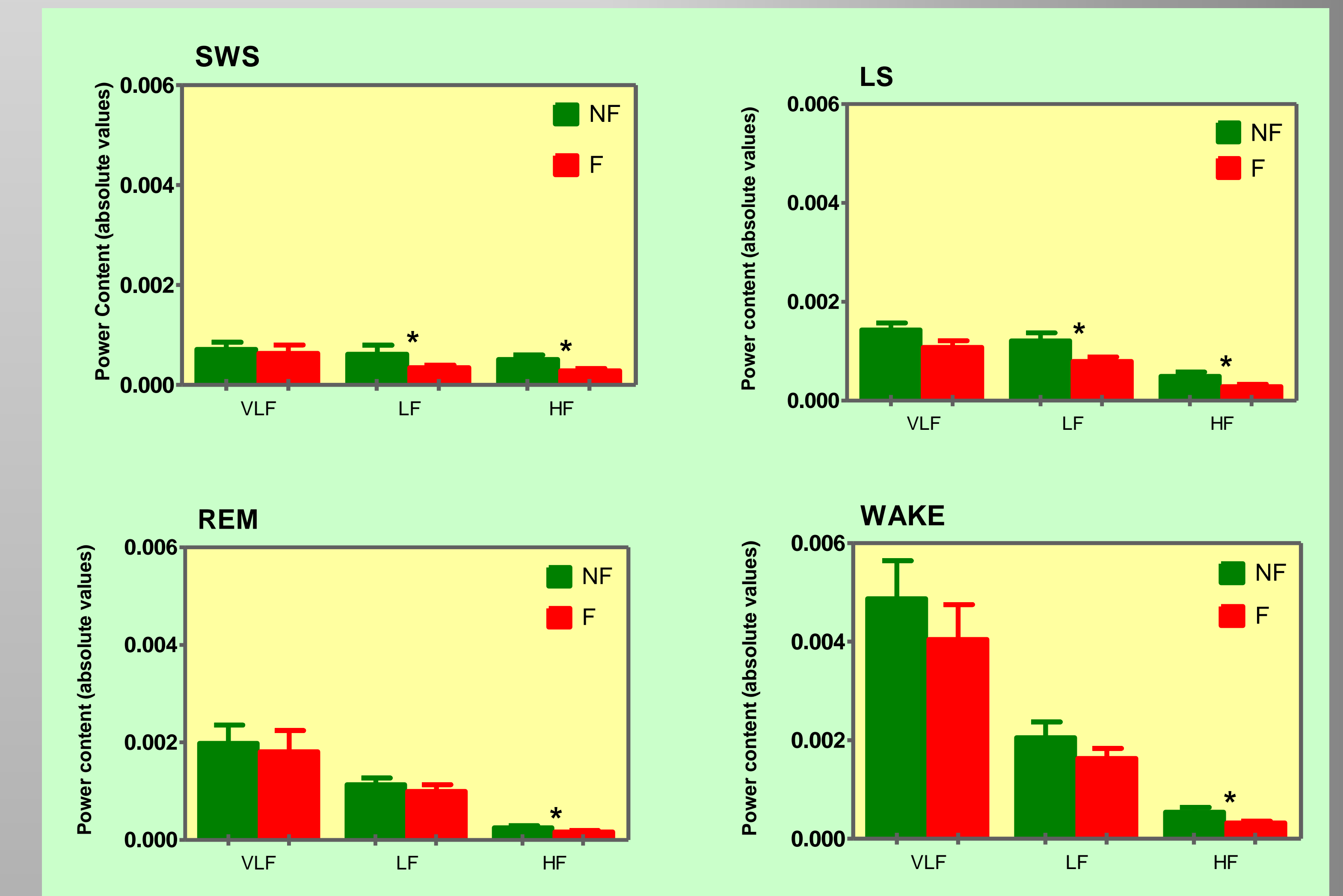
- ✓ HR was significantly higher during all sleep wake states in the F group as compared to NF (* For $p < 0.001$ by *t*-test)



Autonomic Balance

- ✓ The sympatho-vagal balance was consistently higher in F group than in the NF. This difference reached significance only during Wake and REM (* For $p < 0.05$ by *t*-test)

Autonomic Parameters during different sleep-wake states: SWS (NREM STAGES III&IV); LS (NREM STAGES I&II); REM and WAKE (before sleep onset).



- ✓ VLF and LF are high during Wakefulness and REM and lowest during SWS, with intermediate values during LS in both groups
- ✓ HF is highest during SWS and lowest during REM in both groups
- ✓ VLF, LF and HF tend to be higher in the NF group as compared to F group. The difference is significant for HF during all states, wakefulness included, whereas LF is significantly higher only during NREM sleep and VLF does not reach significance levels. (* For $p < 0.05$ by *t*-test)

Summary and Conclusions

- Employing a novel approach, we demonstrate for the first time that the increased HR in CFS is unaffected by behavioral state or circadian time (nocturnal wakefulness, LS, SWS, and REM sleep, MSLT)
- Power content in VLF, LF and HF ranges, as well as the LF/HF ratio indicated that parasympathetic modulation was significantly lower ($p < 0.05$) in CFS subjects during all states
- We establish that no difference exists in the frequency of sub cortical arousals between CFS and NF subjects
- We reaffirm our previous findings of normative values of sleep-wake architecture as well as the absence of clinically relevant levels of sleep disordered breathing in CFS
- We postulate that the unremitting fatigue, a hallmark trait of CFS, is not a manifestation of perturbed sleep, nor a primary sleep disorder. Rather, we suspect a more generalized disturbance in central autonomic function contributes to the characteristic symptoms of CFS