Two-Year Follow-Up of Impaired Range of Motion in Chronic Fatigue Syndrome

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Objective To measure changes in range of motion (ROM) over time in a cohort of 55 adolescents and young adults with chronic fatigue syndrome and to determine whether changes in ROM correlated with changes in health-related quality of life.

Study design Participants underwent a standardized examination of 11 areas of limb and spine ROM at baseline and at 3- to 6-month intervals for 2 years, resulting in a ROM score that ranged from 0 (normal throughout) to 11 (abnormal ROM in all areas tested). We measured the time until the ROM score was ≤2 (the score in healthy age-matched controls). Change in ROM was measured by subtracting the 24-month from the baseline ROM score and by summing the degrees of change in the 10 tests with continuous outcomes. Health-related quality of life was measured using the Pediatric Quality of Life Inventory 4.0 (PedsQL).

Results The mean age at enrollment was 16.5 years (range 10-23). Two-year follow-up was available for 53 (96%). The proportion with a ROM score of >2 fell gradually over 2 years, from 78% at entry to 20% at 24 months ($P < .001$). ROM scores improved from a median of 5 at entry to 2 at 24 months ($P < .001$). The change in the summed degrees of improvement in ROM correlated positively with improvement in the PedsQL physical function subscale (r = 0.30; $P < .03$).

Conclusions In association with multimodal therapy, young people with chronic fatigue syndrome experienced progressively less impairment in ROM over 2 years, correlating with improvements in the physical function subscale of the PedsQL. *(J Pediatr 2018;■■:■■-■■).*

Pediatric chronic fatigue syndrome (CFS), also known as myalgic encephalomyelitis or myalgic encephalomyelitis/CFS, is a relatively common and often disabling disorder of uncertain etiology.[1-8] The illness is characterized by profound fatigue lasting at least 6 months, a characteristic worsening of symptoms after physical or cognitive exertion (termed postexertional malaise), and other common symptoms including headache, unrefreshing sleep, lightheadedness, cognitive dysfunction, myalgias, joint pain, and less commonly sore throat and tender glands. The onset of symptoms can be abrupt, following an infectious illness such as mononucleosis,[9] or gradual. The illness is less common before adolescence,[5] and occurs 2-4 times more commonly among female individuals.[3,5-7] Pediatric CFS is strongly associated with circulatory disorders such as postural tachycardia syndrome and neurally mediated hypotension,[10-15] and with joint hypermobility or Ehlers-Danlos syndrome.[16,17]

Recent research has demonstrated a higher prevalence of restrictions in symptom-free range of motion (ROM) among individuals with CFS.[18-20] In a study of 48 adolescents and young adults with CFS and 48 healthy controls matched for sex and degree of joint hypermobility, those with CFS had a higher median number of areas with impaired ROM (5 vs 2; $P < .001$) and were more likely to have greater than 3 areas of impaired ROM (OR 6.0; 95% CI 2.1-17.3; $P < .001$).[19] Performing the ROM examination was more likely to provoke increased fatigue and other abnormal symptomatic responses in those with CFS (40 vs 4%; $P < .001$).[19] Subsequent work has shown that in response to a 15-minute passive straight leg raise maneuver, individuals with CFS develop an increased intensity of CFS symptoms immediately and for at least 24 hours afterward,[20] consistent with the hypothesis that increased sensitivity to neuromuscular mechanical strain is a mechanism of symptom provocation in the illness.[18] Because these observations are relatively new, little is known about the course of ROM abnormalities over time. The Johns Hopkins CFS Cohort Study was designed in part to assess whether these ROM impairments were static or changed over time, examine the pace of change in association with multimodal therapy and determine whether changes in ROM correlated with changes in overall function.

CFS	Chronic fatigue syndrome
PedsQL	Pediatric Quality of Life Inventory 4.0
ROM	Range of motion

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Methods

Participants

The study enrolled consecutive adolescents and young adults referred to the Johns Hopkins Children's Center Chronic Fatigue Clinic between October 2008 and December 2012. All participants satisfied the 1994 International CFS Study Group criteria for CFS.[2] Full inclusion and exclusion criteria are described elsewhere.[19] Participants were followed and treated clinically for 2 years. The study was approved by the Institutional Review Board of the Johns Hopkins Medical Institutes. Written informed consent was obtained from participants 18 years of age and over; parents of younger children provided written, informed consent, and those younger than 18 years of age also provided verbal assent.

Physical Examinations and Definitions of Abnormal Tests

All participants had a general physical examination that included the 9-point Beighton score, a commonly used, reliable measure of joint hypermobility.[21] Participants were assessed for neurodynamic dysfunction and ROM using the following maneuvers commonly used in physical therapy practice: seated slump testing, ankle dorsiflexion, passive straight leg raise, the upper limb neurodynamic test (also known as the upper limb tension test with a median nerve bias), prone knee bend, and prone press-up. Methods for performing the examination maneuvers have been described in detail elsewhere.[19] The definition of abnormal ROM for each test is shown in **Table I**. The sum of the dichotomized ROM scores (normal = 0/abnormal = 1) for prone press-up and for each limb of the other 5 measures formed a composite ROM score, with possible values ranging from 0 to 11. All testing was performed by a single experienced general pediatrician after >20 hours of training with the study physical therapist. Goniometers were used to measure ROM for all measures except the prone press-up.

Treatment

Participants returned for clinical care as indicated (more frequently in the first 6-12 months until treatment regimens were stable) as well as for repeat ROM examinations and questionnaire completion at approximately 3- to 6-month intervals for the 24 months of the study. The treatments involved multimodal therapy directed at individual symptoms and specific comorbid conditions (including orthostatic intolerance, insomnia, headaches, myalgias, pain, dysmenorrhea, inhalant allergies, and food allergies), tailored to the specific needs of each individual. When ROM impairments were observed at enrollment, we most often recommended manual physical therapy techniques, especially early in the course of treatment. However, the form of therapy was not standardized and treatment methods were at the discretion of the individual's physical therapist.

Study Measures

All participants completed the Pediatric Quality of Life Inventory 4.0 (PedsQL), a brief, multidimensional child self-report instrument for measuring health-related quality of life, available in age-appropriate formats (Child Report for ages 8-12 years, Teen Report for ages 13-18 years, or Young Adult for ages 18-24 years).[22] The 23-item assessment examines the child's health and activities, feelings, ability to get along with others (which includes social relations as well as stamina), and school functioning (which includes measures of cognition as well as attendance). The total score ranges from 0 to 100, with higher scores indicating better quality of life. Subscales of the PedsQL measure physical, emotional, social, and school functioning. This instrument is reliable, valid, and has been used widely in pediatric chronic illness populations, including CFS.[3,7,23,24]

Statistical Analyses

Normally distributed continuous data were compared using paired t tests. We used the Wilcoxon signed-rank tests for ordinal and interval level data when comparing paired changes in range of motion over 24 months for each participant. For nominal level data, paired data were analyzed using the McNemar test. Life table methods were used to analyze the time until the ROM score was ≤2, the median score for healthy individuals in the cross-sectional study at baseline. The change in ROM score between baseline and 24 months was analyzed using the Wilcoxon signed-rank test.

The change in the PedsQL total and subscale scores was obtained by subtracting the 24-month PedsQL score from the score at study entry; positive results indicate improvement in the PedsQL, and negative results worsening from baseline to 24 months. To obtain a continuous measure of change in ROM we summed the changes in ROM on the 10 tests (excluding the prone press-up, which was a categorical variable). For example, an individual with 2 degrees of improvement in seated slump testing on the left side and 2 degrees on the right, 5

Table I. The ROM score

Examination maneuvers	Definition of abnormal response	Score if abnormal Unilateral	Bilateral
Seated slump test	<170 degrees of knee extension	1	2
Ankle dorsiflexion	<95 degrees of dorsiflexion	1	2
Passive straight leg raise	Onset of stretch at <45 degrees	1	2
ULNT 1	<170 degrees of elbow extension at onset of stretch	1	2
Prone knee bend	<130 degrees of knee flexion at onset of anterior thigh stretch	1	2
Prone press-up	Examiner score of mild, moderate, or severe thoracic spine hypo-mobility	Present = 1	

ULNT, upper limb neurodynamic test.

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