Title
Anticipation of and Response to Exercise in adolescents with CFS: an experimental study

Running Head: Response to exercise in adolescents with CFS

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Conflicts of Interest
TC is the author of several self-help books on chronic fatigue for which she has received royalties. TC /KCL has received ad hoc payments for workshops carried out in long term conditions. KCL have received payments for TC's editor role in the Journal of Mental Health. KR has co-authored a book with TC called "Overcoming Chronic Fatigue in Young People" for which she receives royalties. ML has no conflicts of interest to declare.

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Abstract

Background: Using a laboratory-based exercise task, this study investigated objective exercise performance as well as expectations, anxiety and perceived task performance ratings in adolescents with CFS compared to healthy controls and illness controls.

Method: Trials of a sit-stand exercise task (SST) were undertaken (CFS: n= 61, asthma (AS): n= 31, healthy adolescents (HC): n= 78). Adolescents rated their expectations, pre- and post-task anxiety, and perceived task difficulty. Their parents independently rated their performance expectations of their child.

Results: The CFS group took significantly longer to complete the SST than the AS group (MD 3.71, 95% CI [2.41, 5.01] p <.001) and HC (MD 3.61, 95% CI [2.41, 4.81], p < .001). Adolescents with CFS had lower expectations for their performance on the exercise task than AS participants (MD -11.79, 95% CI [-22.17, -1.42] p=.022) and HC (MD -15.08, 95% CI [-23.01, -7.14] p<.001). They rated their perceived exertion as significantly greater than AS (MD 3.04, 95% CI [1.86, 4.21] p < .001) and HC (MD 2.98, 95% CI [1.99, 3.98], p < .001). The CFS group reported greater anxiety pre-task than AS (MD 14.11, 95% CI [5.57, 22.65] p<.001) and HC (MD 11.20, 95% CI [2.64, 19.75], p.=007). Parental group differences showed similar patterns to the adolescents'.

Conclusions: Lower expectations and greater anxiety regarding exercise may reflect learning from previous difficult experiences which could impact future exercise performance. Further examination of pre-exercise expectations and post-exercise appraisals could improve our understanding of the mechanisms by which fatigue is maintained.

Keywords: exercise, expectations, adolescence, chronic fatigue syndrome, case control

Highlights

- Adolescents with CFS, asthma and healthy controls undertook an exercise task.
- Those with CFS took longer to complete a laboratory-based exercise task than controls.
- They (and their parents) expected to perform worse.
- They were more anxious pre-task and rated their performance as worse afterwards.
- Pre-exercise expectations and post-exercise appraisals may be important in CFS.

Chronic fatigue syndrome (CFS) affects approximately 1-2% of adolescents (1). It is diagnosed when an adolescent has experienced unexplained, unremitting and disabling fatigue for at least 3 months (2). CFS impacts considerably on functioning, particularly on school attendance (3-5). About a third of adolescents with CFS experience co-morbid mental health problems (6).

Activity levels, including physical exercise, have been implicated in proposed maintenance cycles in CFS (7). Activity reduction, an understandable response to reduce fatigue, is thought to result in reduced exercise capacity (i.e. exercise intolerance) and functional impairment. Activity reduction and impairment may be further maintained by beliefs about the consequences of doing activity (e.g. 'If I do more, I'll feel worse', 'Activity will be difficult'). These thoughts may result in anxiety about undertaking activity such as physical exercise, further driving the avoidance of activity. In addition to activity reduction and avoidance, another common behavioural pattern in CFS is "boom and bust" (that is, overexerting oneself and subsequently being able to do very little). This behavioural pattern makes it difficult to build up strength and stamina, which requires a more consistent approach to activity. Despite the potential importance of activity and exercise capacity, there has been relatively little investigation of either objective exercise capacity or psychological factors such as thoughts and feelings before and after exercise in adolescents with CFS.

There are several reasons why people with fatigue may avoid exercise. Fatigue is often precipitated by viral illnesses or stressful events (8). Exercising during an acute illness or stressor is likely to lead to fatigue, and individuals may understandably, begin to avoid exercise based on their expectations of it. Reduced physical activity typically results in physical deconditioning; there is evidence of cardiopulmonary deconditioning in adolescents with CFS (9). This may make exercise harder physically, perpetuating avoidance of it. Through experience, physical activity may become associated with increased fatigue by classical conditioning (10-12). Furthermore, in theory, expectations may influence the experience of fatigue, creating a vicious cycle whereby the

expectation of fatigue being induced by exercise makes it more likely that an individual attends to signs of fatigue in response to exercise. These expectations may also induce anxiety in anticipation of exercise, although this has not previously been investigated in adolescents with CFS. Higher physiological arousal, which typically co-occurs with anxiety, has been shown to be associated with increased levels of fatigue in adults with CFS (13).

There is some limited evidence pertaining to potential maintenance factors, mostly based on self-report. Adolescents with CFS report that they favour rest over exercise (14) although not all adolescents with CFS fall into a pattern of inactivity; more tend towards relatively active boom and bust patterns (1, 15). Our previous work found that adolescents with CFS more strongly endorse avoidance/rest and all-or-nothing (i.e. boom and bust) behavioural patterns than adolescents with asthma (16). Furthermore, unhelpful beliefs about activity are endorsed more strongly by adolescents with CFS than adolescents with asthma (16). Both adolescents with CFS and their parents have inaccurate expectations and unrealistic perceptions of fatigue (17). Furthermore, both adolescents with CFS and their parents significantly underestimate the adolescents' current activity levels (18). Parental expectations may influence their child's activity levels, for example, by understandably advocating rest, inadvertently contributing to reduced physical fitness. These individual and systemic factors merit further exploration.

The few existing investigations which have used objective measures of exercise tolerance and capacity have shown conflicting results. Less than one third of a small sample of 20 children and adolescents with CFS were found to have reduced maximal exercise capacity (i.e. less than 2 standard deviations below normal on measures of cardiopulmonary exercise tests) on a stationary bicycle, although a significant association was found between their exercise capacity and self-reported physical activity (19). In another small study of 21 adolescents who developed CFS post infectious mononucleosis, those with CFS had reduced physical fitness compared to recovered

controls on an exercise task, but did not have reduced exercise tolerance (20). In a larger sample of 138 children and adolescents with CFS seen in specialist services, whilst not all were inactive, on average they were found to do less than half the government recommended levels of physical activity for their age (21). In this study they also showed substantially less moderate-to-vigorous physical activity than a nationally representative sample of 7 to 8-year olds, based on accelerometer data.

Although there is some evidence consistent with the possibility that physical exercise capacity and psychological responses to exercise may contribute to the perpetuation of fatigue in adolescents with CFS, more research is needed, especially using experimental designs with control groups. Additionally, there has been little attention given to the responses of parents/caregivers (henceforth referred to as 'parents' to anticipated exercise in this population. The current study investigated responses to a physical exercise test in adolescents with CFS compared to an illness control group and healthy controls. Expectations of exercise performance (adolescent and parent-rated), objective ratings of performance (time taken), and post-task ratings of perceived performance and exertion were all compared. We used a sit-to-stand task as an objective exercise test to assess exercise capacity. On the basis of the hypothesised maintenance model, we predicted that, compared to adolescents with asthma and healthy adolescents, adolescents with CFS would 1) perform worse and report greater perceived exertion on an exercise task; 2) report lower pre-task expectations of their performance (similarly for their parents) and more pre-task anxiety; 3) report poorer evaluation of their actual performance post-task.

Method

Design

This experimental study compared adolescents with CFS to adolescents with asthma and healthy adolescents. All groups completed an exercise task in a laboratory and completed self-report

measures of expectations, anxiety and fatigue before and after the task. Parents, who were in a different room and had the task described to them, also completed measures of their expectations.

Participants

Participants were aged 11-18 years. Adolescents who met the Oxford criteria for CFS (22) were recruited from two specialist CFS units (n = 62). Adolescents with asthma severe enough to be prescribed inhalers were recruited through GP surgeries (n = 31). Healthy adolescents were recruited from schools (n = 78). Those with a history of CFS or asthma were excluded from the healthy adolescent group. Those with a history of psychiatric disorder were excluded from the asthma and healthy adolescent groups. The groups did not differ on age, gender or ethnicity (Table 1). A parent attended with the adolescent in most instances (CFS: n =59, 95%, asthma: n = 24, 77%, healthy: n = 60, 77%). One CFS participant left the laboratory session without attempting the exercise task.

Procedure

Written consent was sought from adolescents and parents. Adolescents with CFS were seen at King's Health Partners chronic fatigue unit for the laboratory session. Controls were seen at the chronic fatigue unit or a GP surgery (asthma group) or school (healthy controls). The laboratory tasks were uninterrupted, undertaken in private, quiet rooms. The exercise task took place following a series of other tasks, including self-report measure completion. Most testing sessions were conducted in the afternoon. Parental ratings were completed on the same day in a separate room. The task was explained to the parent before they were asked to make their ratings.

Self-report measures:

Demographic information was collected. Additionally, the following were administered:

Fatigue – The Chalder Fatigue Questionnaire (CFQ) (23) comprises 11 items. Higher scores indicate more severe fatigue, with a total possible score of 0-33. The CFQ has good validity and reliability (24). In this study, the Cronbach's alpha was .89 (CFS), .82 (healthy controls) and .64 (asthma).

Physical Functioning - The SF36 physical functioning subscale (25) measures physical impairment in activities of daily living. This 10-item scale has a maximum score of 100. Higher scores indicate less impairment. This measure has been previously used in adolescents with CFS (26) and there is evidence of acceptable psychometric properties in this population (27). Cronbach's alpha in this study was .90 (CFS), .90 (healthy controls) and .68 (asthma).

Depression symptoms- The Children's Depression Inventory (CDI) (28) has 27 items pertaining to mood during the past fortnight. Higher scores indicate more depressive symptoms, with a maximum possible score of 54. It has favourable psychometric properties (29). Cronbach's alpha in this study was .87 (CFS), .84 (healthy controls) and .83 (asthma).

Anxiety – The State-Trait Anxiety Inventory (STAI) (30) consists of 20 state items (current anxiety intensity) and 20 trait items (general anxiety). It has acceptable validity and reliability (30). In this study, the Cronbach's alpha was > .93 (STAI-S) and > 0.94 (STAI-T).

Experimental Task:

Sit-to-Stand test (SST) – This is a test of physical functioning which encompasses functional strength, endurance and exercise capacity. The participant begins the manoeuvre seated in a chair, and is asked to complete 5 consecutive sit-to-stand manoeuvres as quickly as possible (31). The speed of completion is used as an indication of strength. This test has good reliability and validity (32). SSTs have previously been used as an outcome measure in adolescents with CFS (33). In the current

study, two trials of the 5 repetition SST were completed by participants, with time between trials to recover (approximately 30 seconds).

Expectations, anxiety and task performance ratings:

Pre-SST, participants completed pen-and paper 0-100 visual analogue scales (VAS) with labels provided at 0 and 100. Participants were asked to complete them for how they were feeling at that moment on the following scales: "How are you feeling?" (0 Not at all anxious-100 Extremely anxious), "How well do you think you're going to do on this task? 50% represents average performance" (0 Not at all well-100 Extremely well) and "How difficult do you think you're going to find this task? (0 Not at all difficult-100 Extremely difficult). Post-task, participants completed two VASs again, rating how well they did and how difficult they found the task. They also completed the Borg Rating of Perceived Exertion (RPE) Scale (34) to assess their perceived physical exertion on the exercise task. This is a scale from 6 (no exertion at all) to 20 (maximal exertion), with several anchors along the 15 points of the scale. Parents completed VASs, rating how well they thought their child would do on the task and how difficult they thought their child would find it.

Data analysis plan

Power calculations were performed a priori based on data from Coddington and Chalder (35). With a power of 80% and alpha of 0.05, the sample size estimate was 29 participants in each group. This requirement was exceeded in all groups.

Sex, ethnicity and main carer characteristics were compared between groups using Pearson's chi squared tests. All other group comparisons were undertaken using one-way ANOVAs, followed by Tukey post-hoc comparisons to assess the direction of significant effects. Where there was heterogeneity of variances, according to Levene's test, a Welch test and Games-Howell post-hoc test are reported. Significant outliers according to studentized residuals are reported and addressed for

each comparison. Where data was found to be not-normal according to Q-Q plots, we report any transformations carried out; See Table 2.

[Table 1]

Results

Group characteristics

The groups did not differ significantly on age, gender, ethnicity or family composition (Table 1). Compared to both control groups, the CFS group were significantly more fatigued, more physically impaired, and endorsed more depressive symptoms and state and trait anxiety symptoms (Table 1).

SST performance and perceived exertion

Time taken to complete the SST on trial 1 was strongly associated with time taken on trial 2 in all participant groups (CFS: $r = 0.92$, $p < .001$, asthma: $r = 0.92$, $p < .001$, healthy: $r = 0.90$, $p = .001$). SST performance on both trials was averaged for each patient to be used in analysis from this point on. CFS participants took significantly longer to complete the SST than the participants in the control groups (Table 2). Their perceived exertion on the Borg Scale was significantly higher than the other two groups.

Pre-task expectations and anxiety

Before the task, adolescents with CFS and their parents had significantly lower expectations of the adolescent's performance on the exercise task and expected that they would find it more difficult compared to the other control groups (Table 2). Adolescents with CFS also rated themselves as feeling significantly more anxious pre-task than adolescents in the other two groups (Table 2).

[Table 2]

Post-task performance ratings

Adolescents with CFS rated their performance post-task significantly more poorly than the healthy control group. There was no significant difference between CFS and the asthma group (Table 2). Adolescents in the CFS group also reported they found the exercise task significantly more difficult than health controls and asthmatic participants.

Discussion

As predicted, adolescents with CFS took longer to complete the exercise task, rated their performance more poorly post-task and reported more perceived effort than the healthy adolescents or adolescents with asthma. Pre-exercise task, adolescents with CFS and their parents had lower performance expectations and anticipated greater task difficulty than the control groups. Adolescents with CFS also had higher pre-task self-rated anxiety than adolescents in the control groups.

Our finding that exercise task performance was impaired in adolescents with CFS compared to both adolescents with asthma and healthy controls may be due to physical deconditioning in CFS. Adolescents with CFS reported greater perceived exertion than the controls, even when we controlled for the time taken on the task; thus, the same task appeared to require more effort for an adolescent with CFS. This is consistent with previous research on cardiopulmonary deconditioning (9). It may be that this deconditioning is the result of reduced daily activity in CFS (21). Our finding is also consistent with the considerable functional limitations reported by adolescents with CFS (3-5). It may be that functional limitations are the result of being less able to undertake physically demanding tasks and needing to exert more effort for the same task. Adolescents with CFS report that even basic tasks of daily living can become hard to do (36). Alternatively, our finding may be due to avoidance of maximal exercise in adolescents with CFS. Takken, Henneken (19) did not find a

reduction in maximal exercise capacity in adolescents with CFS compared to normative data. The difference in findings may be due to the sample size limitations of the latter, and due to the nature of the exercise task, as our exercise task focused on stamina and strength (i.e. exercise tolerance) rather than maximal capacity. Thus, whilst adolescents with CFS might be able to push themselves on a maximal exercise task to a comparable degree to controls, our findings and those of qualitative research (37) suggest that they may be more limited on strength and stamina and may have to work harder (i.e. exert more effort) to do physical tasks.

In adults, evidence regarding exercise capacity is mixed. Some studies suggest that people with CFS are less fit and have reduced exercise capacity (38, 39), while others found normal aerobic capacity (40)and muscle functioning compared to sedentary controls (18). In the laboratory, many adults with CFS do not achieve age-predicted maximal heart rate and also find exercise more effortful and fatiguing than healthy controls(41). In combination, the findings from these studies are more suggestive of sub-maximal exertion than physical deconditioning. It is possible that misattribution of bodily symptoms may be a contributory factor, e.g. that people with CFS attribute symptoms associated with exertion as an indication of their CFS symptoms worsening and hence are understandably reluctant to exert more effort. In adolescents, more studies are needed before conclusions about the precise roles of exercise capacity and tolerance can be drawn. However, our results suggest than perceptions may well play a role. We found that adolescents with CFS were more anxious pre-task and expected to do worse and to find the task more difficult than the controls did. It is possible that subsequent exercise performance is influenced by expectancies based on previous experiences with physical activity (42). There is evidence for associative learning in chronic pain conditions (43, 44) although this literature is primarily based on evidence from studies conducted in adult populations. It may be that the adolescents with CFS are more likely than those in the control groups to learn, through experience, that physical activity is difficult and aversive due to their fatigue and therefore have more negative expectations and greater anxiety about subsequent

exercise. But of course, it is also possible that the participants are reasonably good at predicting their performance.

Adolescents with CFS had poorer ratings of their performance than the control groups. These perceptions may further reduce their expectancies for future exercise, creating a vicious cycle whereby they further reduce their activity levels, become more deconditioned and anticipate further poor performance.

We found significant group differences in self-rated pre-task anxiety. Elevated levels of depression and anxiety are common in adolescents with CFS (6). According to cognitive behavioural models, individuals who are depressed have more negative thoughts about past events, whilst individuals who are anxious have more negative thoughts about the future (45). It may be that these negative thinking patterns that are typical of anxiety and depression affect task expectancies, and that by addressing mood problems and challenging negative thinking in those with elevated distress, reduced activity patterns might be easier to overcome. It is also possible that anxiety and negative thinking about exercise experienced by adolescents with CFS contributes to their more general anxiety and depression symptoms.

In addition, we found that parent's expectations of anticipated task difficulty and performance were considerably lower in adolescents with CFS than in either of the control groups. This is a novel finding in relation to exercise or physical activity in CFS, and importantly, may contribute to parental responses to anticipated physical activities, for example, by making it more likely that a parent may discourage an adolescent with CFS from undertaking a task and more likely that a parent may encourage rest, although we were not able to explicitly test this in the current study. However, future studies could benefit from including more extensive measures of the expectations of significant others and the responses of significant others to activities such as exercise.

Strengths and Limitations

These findings add to the existing literature by our use of an objective measure of exercise performance, in a much larger sample than previous laboratory-based studies, and included two control groups, enabling direct comparison between adolescents with CFS and peers without CFS. In addition to the laboratory-based measure, we included measures of self-rated expectations pre-task, pre-task anxiety and post-task difficulty and effort, allowing for a far more extensive consideration of the psychological factors than in previous studies. We also included parent as well as self-report, enabling consideration of systemic factors, although not all parents completed the measures. Although the reliability and validity of the sit-to-stand task is yet to be established in adolescents with CFS, there has been extensive investigation of the reliability and validity of this task in other illness populations, and it is widely accepted as a measure of exercise capacity. The VAS were specifically developed for this study, and no data is available on their reliability and validity. It is possible that participants interpreted the questions asking them to rate their anticipated task difficulty and task performance may have been particularly open to different interpretations by the participants.

As the CFS participants were recruited from specialist services, the generalisability of the findings is limited to those attending similar services. The asthma group was also smaller than the other 2 groups, which means that we had the power to detect large effects only. We did not have the power to investigate sex differences, which would be important to examine in future studies as exercise may have different connotations for males and females (46). Furthermore, we did not collect data on body composition (e.g. body mass index) or on usual physical activity levels (or sedentary behaviour) which may contribute to perceived difficulty, anxiety about performance, actual performance and ratings of perceived effort.

Research Implications

The role of physical deconditioning, exercise intolerance, anxiety and expectations for exercise and physical activity avoidance all require further research to help clarify their possible roles in the maintenance of CFS in adolescents. Exercise tolerance may be further subdivided, for example, into maximal exercise capacity, endurance, muscular strength, and it seems likely that these various aspects of exercise are differentially compromised in CFS. Therefore, to further the understanding of the nature of exercise tolerance in CFS, a range of objective measures, as well as physiological recording devices that enable continuous measurement of physiological variables such as heart rate through the exercise task should be used.

Clinical implications

It is promising that small-scale treatment studies have found that gradually increasing activity levels through exercise may be beneficial for adolescents with CFS (33, 47). However, we found that adolescents with CFS reported that they were more anxious prior to an exercise task, expected to perform more poorly, took longer to complete the task, and rated their performance as worse than controls did. These pre-exercise expectancies and post-exercise appraisals may impede progress towards increasing activity levels and may therefore be important to examine and address in treatment. Cognitive behaviour therapy (CBT) typically involves planned activity and rest, and a graded increase in activity, whilst also addressing unhelpful beliefs. Parents of participants with CFS also had poorer exercise expectations; CBT for CFS in children and adolescents recognises the importance of involving the family in treatment (26, 48, 49). Our findings indicate that addressing adolescent pre-task anxiety and both adolescents' and parents' expectations of exercise, as well as broader patterns of negative thinking associated with depression and/or anxiety where necessary, may be important to enable individuals to increase their activity levels.

Conclusion

Adolescents with CFS took longer to complete an exercise task than healthy adolescents and adolescents with asthma, which is consistent with daily physical functioning limitations reported by adolescents with CFS. Post-task, adolescents with CFS rated their performance as worse than the other groups. Beforehand, adolescents with CFS were also more anxious about the task, and both they and their parents had lower performance expectations, which may impact on adolescents' motivation or time taken to complete an exercise task. Addressing pre-exercise anxiety and performance expectations, and the possible behavioural implications of these, may be important in the understanding and treatment of CFS in adolescence.

Table 1. Participant demographic and clinical characteristics by group (mean, SD unless otherwise specified)

	CFS participants (n=62)	Asthma participants (n=31)	Healthy participants (n=78)	Group comparison
Age (mean, SD)[c]	15.06 (1.70)	15.00 (2.18)	14.58 (1.40)	F[2, 71.93] = 1.83, p = .168
Sex (number, % female)	40 (64.5)	15 (48.4)	48 (61.5)	χ^2 (2) = 2.35, p = .309
Ethnicity (number, % White British)	56 (90.3)	24 (77.4)	67 (85.9)	χ^2 (2) = 2.85, p = .240
Main carer (number, % both parents)	38 (61.3)	25 (80.6)	57 (73.1)	χ^2 (4) = 6.28, p = .179
Fatigue – CFQ [c, d]	22.95 (6.01)[a,b]	12.00 (2.54)[a]	10.46 (3.76)[b]	F[2, 94.17]= 101.36, p <.001, η^2= .624
Physical functioning – SF36PFS [e, c]	53.28 (23.36)[a,b]	88.39 (12.14)[a]	91.30 (15.05)[b]	F[2, 88.47]= 63.35, p <.001, η^2= .499
Depressive symptoms – CDI [c, f]	14.55 (7.40) [a,b]	7.24 (5.30)[a]	5.64 (5.18)[b]	F[2, 88.40]= 32.02, p <.001, η^2= .315
Trait anxiety – STAI-T	47.00 (10.23) [a,b]	40.48 (11.19)[a]	37.49 (11.19)[b]	F[2, 165] = 13.01, p <.001, η^2= .136
State anxiety – STAI-S	44.73 (11.95) [a,b]	35.90 (10.61)[a]	34.62 (11.44)[b]	F[2, 164] = 13.87, p <.001, η^2= .145

CDI = Children's Depression Inventory; CFQ = Chalder Fatigue Scale; SF36PFS = Short Form 36 Physical Functioning Scale; STAI = State-Trait Anxiety Inventory

[a, b] Subscript letters are used to indicate significant difference between groups (p<.05).

[c] Homogeneity of variances assumption was violated. Welch's test and Games-Howell reported.

[d] There were significant outliers according to studentized residuals (-3.32, -3,32, -3.10) which were not removed.

[e] There was a significant outlier according to studentized residuals (-3.76). This was removed analysis was run again. Data was found to be non-normal by Q-Q plot, so a transformed ANOVA was run. There was no difference in significant differences between the so the non-transformed results are presented.

[f] Data was found to be non-normal by Q-Q plot, so a transformed ANOVA was run. There was no difference in significant differences between the so the non-transformed results are presented.

[g] There was a significant outlier according to studentized residuals (-3.01) this was not removed.

Table 2. Expectations, anxiety and performance on exercise task; means, standard deviations and result of group comparison

	Numbers in each group (differences are due to missing data)			CFS	Asthma	Healthy controls	Group comparison[b]	Group differences (post-hoc with Bonferroni correction)	Mean difference and confidence intervals of the difference
	CFS	Asthma	HC	Mean (SD)	Mean (SD)	Mean (SD)			
Child Ratings – Pre-exercise task									
"How well do you think you are going to do on this task" (0-100)	55	28	75	M=52.56, SD= 18.47	M=64.36, SD= 17.37	M=67.64, SD= 19.71	F[2,155] = 10.414, p < .001, η^2= .118	CFS < asthma	-11.79, 95% CI [-22.17, -1.42] p=.022
								CFS < HC	-15.08, 95% CI [-23.01, -7.14] p<.001
								Asthma = HC	p=.713
"How difficult do you think you're going to find this task"[a] (0-100)	55	28	75	M= 43.24, SD= 25.31	M= 17.39, SD= 15.43	M= 18.33, SD= 17.08	F(2, 75.26) = 22.02, p = .001, η^2= .266	CFS < asthma	25.84, 95% CI [15.12, 36.57] p<.001
								CFS < HC	24.90, 95% CI [15.51, 34.30] p<.001
								Asthma = HC	-0.94 95% CI [-9.43, 7.55] p=.961
"How anxious are you feeling at this moment in time?"[a, d] (0-100)	55	27	75	M=28.07, SD= 22.71	M=13.96, SD= 9.59	M=16.88, SD= 16.26	F(2, 87.856) = 7.789, p = .001, η^2= .096	CFS < asthma	14.11, 95% CI [5.57, 22.65] p<.001
								CFS < HC	11.20, 95% CI [2.64, 19.75], p.=007
								Asthma = HC	p= .512
Parent ratings - Pre-exercise task									
"How well do you think your child is going to do on this task?"[a] (0-100)	54	22	57	M=55.91, SD= 26.44	M=90.77, SD= 9.46	M=87.35, SD= 13.37	F(2, 71.59) = 37.32, p<.001, η^2= .409	CFS < asthma	34.87, 95% CI [25.00, 44.73], p<.001
								CFS < HC	31.44, 95% CI [21.86, 40.03] p<.001
								Asthma = HC	P=.762
"How difficult do you think your child is going to find this task?"[a,e] (0-100)	53	22	57	M=46, SD= 29.00	M= 9.64, SD= 13.03	M= 8.82, SD=12.56	F(2, 59.20) = 37.70, p<.001, η^2=.435	CFS > asthma	36.36, 95% CI [24.74, 47.98] p<001
								CFS > HC	37.18 95% CI [26.83, 47.53] p<.001
								Asthma = HC	p=.987
Performance									
Average time taken sit-stand (seconds) [a,c]	53	31	75	M= 10.83, SD= 3.23	M= 7.11, SD= 1.77	M= 7.21, SD= 2.06	F(2,81.607) = 28.420, p < .001, η^2=.331	CFS > asthma	3.71, 95% CI [2.41, 5.01] p <.001
								CFS > HC	3.61, 95% CI [2.41, 4.81], p < .001
								Asthma = HC	p=.965
Child ratings post-exercise task									
"How well do you think you did on this task?" [a](0-100)	55	28	75	M= 54.73, SD= 15.75	M= 63.25, SD= 19.65	M= 68.67, SD= 20.56	F(2, 72.10) = 9.66, p < .001, η^2=.101	CFS = asthma	p=.126
								CFS < HC	-13.94 95% CI [-21.49, -6.39] p<.001
								Asthma = HC	p=.442
"How difficult did you find this task?" [a,f] (0-100)	55	28	75	M= 38.80, SD= 24.72	M=8.39, SD= 9.50	M= 10.12, SD= 12.17	F(2, 79.15) = 34.89, p < .001, η^2=.397	CFS > asthma	30.41 95% CI [21.36, 39.45] p<.001
								CFS > HC	28.68 95% CI [20.03, 37.33] p<.001
								Asthma = HC	p=.730

Borg Rating of Perceived Exertion[a]	52	31	75	M= 11.42, SD= 2.59	M= 8.44, SD= 1.83	M= 8.39, SD= 1.87	F(2,76.288) = 27.628, p < .001, η^2=.311	CFS > asthma	3.04, 95% CI [1.86, 4.21] p < .001
								CFS > HC	2.98, 95% CI [1.99, 3.98], p < .001
								Asthma = HC	p=.990

[a] The assumption of homogeneity of variances was violated, as assessed by Levene's test for equality of variances (p = .001). Welch test and Games-Howell are reported.
[b] Data was considered normal or approximately normal enough for ANOVA according to Q-Q plots given its robustness unless stated otherwise.
[c] There were three outliers in the CFS group when assessing studentized residuals (3.76, 3.35, and 3.14). However, these were not removed because it is not possible to say for certain whether these were errors or extreme scores
[d] One significant outlier in the asthma group according studentized residuals (4.32) removed. Re-running analyses there were two datapoints consider outliers according to studentized residuals in the CFS group (3.20, 3.31).
[e] One significant outlier according to studentized residuals and removed from HC(-3.20). Data was found to be non-normal by Q-Q plot, so a Lg10 transformed ANOVA was run. There was no difference in significant differences between the so the non-transformed results are presented.
[f] Data was found to be non-normal by Q-Q plot, so a transformed ANOVA was run. There was no difference in significant differences between the so the non-transformed results are presented.

References

1. Brigden A, Loades M, Abbott A, Bond-Kendall J, Crawley E. Practical management of chronic fatigue syndrome or myalgic encephalomyelitis in childhood. Archives of disease in childhood. 2017:archdischild-2016-310622.
2. NICE. Chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy): Diagnosis and management of CFS/ME in adults and children. In: Excellence NIfHaC, editor. 2007.
3. Crawley E, Sterne JA. Association between school absence and physical function in paediatric chronic fatigue syndrome/myalgic encephalopathy. Archives of disease in childhood. 2009;94(10):752-6.
4. Smith MS, Martin-Herz SP, Womack WM, Marsigan JL. Comparative study of anxiety, depression, somatization, functional disability, and illness attribution in adolescents with chronic fatigue or migraine. Pediatrics. 2003;111(4 Pt 1):e376-81.
5. Kennedy G, Underwood C, Belch JJF. Physical and functional impact of chronic fatigue syndrome/myalgic encephalomyelitis in childhood. Pediatrics. 2010:peds. 2009-644.
6. Loades ME, Rimes KA, Ali S, Lievesley K, Chalder T. The presence of co-morbid mental health problems in a cohort of adolescents with chronic fatigue syndrome. Clinical child psychology and psychiatry. 2017:1359104517736357.
7. Browne T, Chalder T. Chronic fatigue syndrome. Psychiatry. 2006;5(2):48-51.
8. Hulme K, Hudson JL, Rojczyk P, Little P, Moss-Morris R. Biopsychosocial risk factors of persistent fatigue after acute infection: A systematic review to inform interventions. Journal of psychosomatic research. 2017;99:120-9.
9. Pianosi PT, Emerling E, Mara KC, Weaver AL, Fischer PR. Aerobic fitness in adolescents with chronic pain or chronic fatigue: parallels and mechanisms? J Rehabil Med. 2017;49(5):441-6.
10. Wyller VB, Fagermoen E, Sulheim D, Winger A, Skovlund E, Saul JP. Orthostatic responses in adolescent chronic fatigue syndrome: contributions from expectancies as well as gravity. Biopsychosoc Med. 2014;8:22.

11. Lenaert B, Boddez Y, Vlaeyen JWS, van Heugten CM. Learning to feel tired: A learning trajectory towards chronic fatigue. Behaviour research and therapy. 2018;100:54-66.
12. Lenaert B, Jansen R, van Heugten CM. You make me tired: An experimental test of the role of interpersonal operant conditioning in fatigue. Behaviour research and therapy. 2018;103:12-7.
13. Rimes K, Ashcroft J, Bryan L, Chalder T. Emotional Suppression in Chronic Fatigue Syndrome: Experimental Study. Health Psychol. 2016.
14. Richards J, Turk J, White S. Chidlren and adolescents with Chronic Fatigue Syndrome in non specialist settings: Beliefs, functional impairment and psychiatric disturbance. *European Child and Adolescent Psychiatry*. 2005;14:310-8.
15. Stulemeijer M, de Jong LW, Fiselier TJ, Hoogveld SW, Bleijenberg G. Cognitive behaviour therapy for adolescents with chronic fatigue syndrome: randomised controlled trial. Bmj. 2005;330(7481):14.
16. Loades ME, Rimes K, Lievesley K, Ali S, Chalder T. Cognitive and behavioural responses to symptoms in adolescents with chronic fatigue syndrome: A case-control study nested within a cohort. Clinical child psychology and psychiatry. 2019:1359104519835583.
17. Garralda ME, Rangel L. Childhood chronic fatigue syndrome. The American journal of psychiatry. 2001;158(7):1161.
18. Fry AM, Martin M. Cognitive idiosyncrasies among children with the chronic fatigue syndrome: anomalies in self-reported activity levels. Journal of psychosomatic research. 1996;41(3):213-23.
19. Takken T, Henneken T, Van de Putte E, Helders P, Engelbert R. Exercise testing in children and adolescents with chronic fatigue syndrome. International journal of sports medicine. 2007;28(07):580-4.
20. Katz BZ, Boas S, Shiraishi Y, Mears CJ, Taylor R. Exercise tolerance testing in a prospective cohort of adolescents with chronic fatigue syndrome and recovered controls following infectious mononucleosis. The Journal of pediatrics. 2010;157(3):468-72. e1.
21. Solomon-Moore E, Jago R, Beasant L, Brigden A, Crawley E. Physical activity patterns among children and adolescents with mild-to-moderate chronic fatigue syndrome/myalgic encephalomyelitis. BMJ paediatrics open. 2019;3(1).
22. Sharpe MC, Archard LC, Banatvala JE, Borysiewicz LK, Clare AW, David A, et al. A report--chronic fatigue syndrome: guidelines for research. Journal of the Royal Society of Medicine. 1991;84(2):118-21.
23. Chalder T, Berelowitz G, Pawlikowska T, Watts L, Wessely S, Wright D, et al. Development of a fatigue scale. Journal of psychosomatic research. 1993;37(2):147-53.
24. Cella M, Chalder T. Measuring fatigue in clinical and community settings. Journal of psychosomatic research. 2010;69(1):17-22.
25. Ware JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36): I. Conceptual framework and item selection. Medical care. 1992:473-83.
26. Chalder T, Deary V, Husain K, Walwyn R. Family-focused cognitive behaviour therapy versus psycho-education for chronic fatigue syndrome in 11- to 18-year-olds: a randomized controlled treatment trial. Psychological medicine. 2010;40(08):1269-79.
27. Loades ME, Vitoratou S, Rimes K, Chalder T. Assessing functioning in adolescents with chronic fatigue syndrome: psychometric properties and factor structure of the School and Social Adjustment Scale and the Physical Functioning Subscale of the SF36. Behavioural and cognitive psychotherapy. 2020:1-11.
28. Kovacs M, Beck A. An empirical-clinical approach toward a definition of childhood depression. In: Raskin JSA, editor. Depression in childhood: Diagnosis treatment and conceptual models: Washington, DC: Department of Health, Education and Welfare; 1977. p. 1-26.
29. Kovacs M. Children's Depression Inventory (CDI) manual: New York: Multi-Health Systems; 1992.
30. Spielberger C. STAIC preliminary manual. Palo Alto, CA: Consulting Psychologists Press; 1973.
31. Csuka M, McCarty DJ. Simple method for measurement of lower extremity muscle strength. American Journal of Medicine. 1985;78(1):77-81.

32. Bohannon RW. Test-retest reliability of the five-repetition sit-to-stand test: a systematic review of the literature involving adults. J Strength Cond Res. 2011;25(11):3205-7.
33. Gordon BA, Knapman LM, Lubitz L. Graduated exercise training and progressive resistance training in adolescents with chronic fatigue syndrome: a randomized controlled pilot study. Clinical rehabilitation. 2010;24(12):1072-9.
34. Borg G. Borg's perceived exertion and pain scales: Human kinetics; 1998.
35. Coddington A, Chalder T. Do parents of children with CFS have higher expectations of them? British Association of Behavioural and Cognitive Psychotherapists Annual Conference; York2003.
36. Parslow RM, Patel A, Beasant L, Haywood K, Johnson D, Crawley E. What matters to children with CFS/ME? A conceptual model as the first stage in developing a PROM. Archives of disease in childhood. 2015:archdischild-2015-308831.
37. Parslow RM, Anderson N, Byrne D, Shaw A, Haywood KL, Crawley E. Adolescent's descriptions of fatigue, fluctuation and payback in chronic fatigue syndrome/myalgic encephalopathy (CFS/ME): interviews with adolescents and parents. BMJ Paediatrics Open. 2018;2(1).
38. Fischler B, Dendale P, Michiels V, Cluydts R, Kaufman L, De Meirleir K. Physical fatigability and exercise capacity in chronic fatigue syndrome: association with disability, somatization and psychopathology. Journal of psychosomatic research. 1997;42(4):369-78.
39. Fulcher KY, White PD. Strength and physiological response to exercise in patients with chronic fatigue syndrome. J Neurol Neurosurg Psychiatry. 2000;69(3):302-7.
40. Riley MS, O'Brien CJ, McCluskey DR, Bell NP, Nicholls DP. Aerobic work capacity in patients with chronic fatigue syndrome. British Medical Journal. 1990;301(6758):953-6.
41. Bazelmans E, Bleijenberg G, Van Der Meer J, Folgering H. Is physical deconditioning a perpetuating factor in chronic fatigue syndrome? Psycholog Med. 2001;31:107-14.
42. Wyller VB, Eriksen HR, Malterud K. Can sustained arousal explain the Chronic Fatigue Syndrome? Behav Brain Funct. 2009;5:10.
43. De Peuterl S, Van Diestl I, Vansteenwegenl D, Van den Berghl O, Vlaeyenl JW. Understanding fear of pain in chronic pain: interoceptive fear conditioning as a novel approach. European journal of pain. 2011;15(9):889-94.
44. Vlaeyen JW, Morley S, Crombez G. The experimental analysis of the interruptive, interfering, and identity-distorting effects of chronic pain. Behaviour research and therapy. 2016;86:23-34.
45. Beck JS. Cognitive Therapy: Basics and Beyond: Guilford Press; 1995.
46. Chalabaev A, Sarrazin P, Fontayne P, Boiché J, Clément-Guillotin C. The influence of sex stereotypes and gender roles on participation and performance in sport and exercise: Review and future directions. Psychology of sport and exercise. 2013;14(2):136-44.
47. Gordon BA, Lubitz L. Promising outcomes of an adolescent chronic fatigue syndrome inpatient programme. Journal of Paediatrics & Child Health. 2009;45(5):286-90.
48. Chalder T, Tong J, Deary V. Family cognitive behaviour therapy for chronic fatigue syndrome: an uncontrolled study. Archives of disease in childhood. 2002;86(2):95-7.
49. Lloyd S, Chalder T, Rimes KA. Family-focused cognitive behaviour therapy versus psycho-education for adolescents with chronic fatigue syndrome: long-term follow-up of an RCT. Behaviour research and therapy. 2012;50(11):719-25.