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Can the Improvements Reported by Individuals with Chronic Fatigue Syndrome Following Multi-Convergent Therapy Be Sustained in the Longer-Term: A Three-Year Follow-Up Study

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Abstract

Results from a small study into the efficacy of a Multi-Convergent Therapy intervention for patients with Chronic Fatigue Syndrome (CFS) had proved encouraging at the post-therapy and six-month follow-up time points. It was, however, important to re-evaluate these findings over a longer period. Eleven patients who had completed the original therapy trial responded to a follow-up call (91.7% response rate). Subjective data was returned by between 9 and 11 of the participants and 7 completed the objective measures. Participants in the current study completed a similar set of outcome measures as those used to assess treatment success previously. These data suggested that patients attending the therapy continued to show improvements in functioning, had lower levels of fatigue and disability, improved sleep quality and levels of activity and lower symptom scores at a three-year follow-up. The long-term efficacy for this treatment is suggested by these results. Multi-convergent therapy is indicated as a promising approach to the rehabilitation of CFS patients.

Keywords: Chronic Fatigue Syndrome (CFS), Multi-convergent therapy (MCT), Long-term efficacy, Myalgic Encephalomyelitis (ME).

1. Introduction

1.1 Background

Fatiguing illnesses are difficult to accurately assess and diagnose due to the symptom being largely subjective in nature. Fatigue means different things to different people, and the term itself describes conditions ranging from moderate tiredness to clinical exhaustion (Thomas, 2018).

The fatigue experienced in Chronic Fatigue Syndrome (CFS) is not only of sufficient severity to cause substantial functional impairment but it is also accompanied by four or more co-existing symptoms including those of a cognitive or neuropsychiatric nature (Fukuda et al., 1994). The illness must be of at least six months

duration with the potential for it to become debilitating and persistent (Andersen, Permin & Albrecht, 2004). CFS has no known aetiology or distinctive biological diagnostic markers and appears to be more prevalent in middle-aged women who experience measurable cognitive impairment (Thomas & Smith, 2009) and high levels of somatic symptoms, anxiety, and depression (Thomas & Smith, 2006). Together with decreased personal, occupational and social activities which impact negatively on their quality of life, individuals with CFS are more likely to be unemployed than their peers (Smith, Thomas & Sadlier, 2009). Although the incidence of the syndrome is relatively low (Afari & Buchwald, 2003) this does not detract from the severe effect the illness has on the individual. Decreased personal, occupational and social activities accompany the illness and combine to instil a sense of frustration and hopelessness within the patient. In addition, financial concerns have been raised regarding the increased uptake of unemployment benefits, and the drain on healthcare resources brought about by the illness (Reyes et al., 1999; Reynolds, Vernon, Bouchery & Reeves, 2004). For these reasons, the search to find a suitable treatment for this, often, debilitating illness became paramount.

In a report by the Royal Colleges, practitioners were encouraged to provide a service for patients and take steps to manage patients in their care (Royal Colleges of Physicians, Psychiatrists & General Practitioners, 1996). Cognitive Behaviour Therapy (CBT) and graded exercise were recommended as the most successful methods for managing symptoms of the illness (CFS/ME Working Group, 2002). In their 2007 guidance, the National Institute for Health and Care Excellence (NICE) also regarded GET and activity management programmes and recommended that individualised, patient-centred programmes should also address sleep hygiene together with physical, emotional and cognitive symptoms (NICE, 2018).

It was in response to the call for efficacy studies to manage the symptoms associated with CFS that we conducted a small randomised controlled trial of behaviour and graded exercise-based intervention in a multi-convergent therapy (MCT) approach. MCT was developed by a registered NHS Physiotherapist who had recognised qualifications in all aspects of the therapy. The intervention was set up to provide a service for patients with a range of medically unexplained symptoms – such as irritable bowel syndrome and tinnitus – which did not respond to first-line medical intervention and where no solution was readily available (Sadlier & Stephens, 1995; Shaw et al., 1991).

The commonality between these medically unexplained symptoms and CFS implied that MCT might be of value to patients with the syndrome. Indeed, data collected retrospectively on the twenty-four patients completing a pilot study provided preliminary evidence as to the efficacy of the treatment for CFS (Sadlier, Evans, Phillips & Broad, 2000).

MCT incorporates CBT and GET with other appropriate strategies in a holistic approach. The CBT phase aimed to identify factors that can influence, precipitate or prolong the illness and improve sleep quality. Dysfunctional beliefs and thought patterns were explored and positive beliefs, thoughts, and behaviours re-enforced. During the graded exercise phase, the therapist introduced a programme of planned activity and rest (referred to as 'pacing') and explored the relationship between fatigue and cognition. The rationale for this aspect of the therapy was based upon a model suggested by Noakes and colleagues where gentle walking was introduced every second day at a level appropriate for each individual case to prevent post-exertional malaise (Noakes, St Clair Gibson & Lambert, 2005). The distance and time walked were increased as the patient's confidence in the belief that this would not cause a relapse of their symptoms grew, and increases were controlled by the patient in discussion with the therapist.

Mindfulness (or insight) meditation techniques were also blended with the CBT and graded exercise phases and patients were encouraged to fix their thoughts on the present without being distracted by the associations attached to those thoughts or sensations, such as fatigue or pain (Mason & Hargreaves, 2001; Carlson, Speca, Patel & Goodey, 2004; Grossman, Niemann, Schmidt & Walach, 2004; Kabat-Zinn, Lipworth & Burney, 1985). The therapy adopted a multi-dimensional approach which used aspects of behaviour modification, breathing and relaxation techniques, connective tissue massage and psychodynamic counselling. An in-depth description of our randomised controlled trial (RCT) is presented elsewhere (Thomas, Sadlier & Smith, 2006; Thomas, Sadlier & Smith, 2008). However, a brief overview of the trial is outlined below.

1.2 Previous Research

In the original RCT (Thomas, Sadlier & Smith, 2006; Thomas, Sadlier & Smith, 2008), patients were recruited from a CFS Outpatient clinic by a single consulting physician. Inclusion criteria for the trial were: (a) patients fitting the CDC criteria for CFS (Fukuda et al., 1994), (b) scores below 70% on the Karnofsky performance scale (Karnofsky, Abelmann, Craver & Burchenal, 1948) indicating significant functional impairment and (c) were willing to attend all therapy and assessment sessions. Patients were excluded from the study if their fatigue was of known aetiology.

Twelve patients were randomly allocated to the MCT group, 14 were allocated to a relaxation therapy group, and 9 were allocated to a non-intervention control group. Due to the small numbers in the study, patients recruited into the trial were assigned to a treatment group individually. Referral letters for the MCT clinic, the relaxation therapist together with a letter indicating usual medical care were prepared for each patient who agreed to participate. These were placed into a large blank envelope and one letter selected and posted by a colleague blind to the study's protocol. The remaining letters were shredded. The patient was contacted by the appropriate therapist, and subsequent assessment appointments were made through a third party.

The relaxation therapy used in the trial was based on the Rapid Relaxation Technique of Lars-Goran Ost (Ost, 1987). This technique has been successfully used to alleviate a range of problems – such as tinnitus and pain – as well as CFS. Rapid Relaxation offered the patient a way of coping with their symptoms and managing them. The therapist would guide the patient through the relaxation technique over a period of weeks, concentrating on different major muscle group each week. We used this therapy as a comparison to MCT as relaxation therapy had been one of the approaches favoured by various centres and patient groups (Action for ME, for example) throughout England, Scotland and Wales and had been used as a comparison by other research groups (Deale, Chalder, Marks & Wessely, 1997).

Individuals attended ten, 1-hour MCT or relaxation sessions per week for 10 weeks on a one-to-one basis. The time spent on each component within MCT was decided during discussions between the therapist and the patient.

Outcome measures for the trial included those assessing mood, performance and health-related measures that were developed previously (Thomas & Smith, 2009; Thomas & Smith, 2006). In order to align our findings to other intervention studies, functional performance and global measures of health were also administered (Deale, Chalder, Marks & Wessely, 1997). Data collection points included: (a) baseline (before randomisation), (b) immediately post-therapy and (c) 6-months post-therapy. Control group data were collected to simulate a ten-week therapy programme. To provide context to the current study, a brief overview of the RCT is presented here.

At the post-therapy point, the MCT group reported significant improvements in alertness together with improved sleep quality and levels of activity than the relaxation and control groups. They also reported significantly lower levels of anxiety and improvements in cognitive performance (e.g., motor speed and vigilance) than the control group. A health-related measure of the number of physical and mental symptoms indicated that the MCT group reported significantly lower total symptom scores than the relaxation and control groups. The global assessment of function measures suggested that the MCT group reported significantly greater improvements in their overall condition, lower levels of fatigue and a reduction in disability than the relaxation and control groups.

Our findings also indicated that these improvements were maintained over a six-month period. The MCT group continued to report significantly improved motor speed than the relaxation. This group also continued to report: (a) higher levels of alertness, (b) lower levels of anxiety, (c) greater vigilance and (d) improved episodic memory than the control group. Improvements in global measures of health were also reported at this time point including an overall improvement in their condition, lower fatigue levels and feeling far less impaired by their illness. Regarding the primary outcome measure of the trial, attainment of a Karnofsky performance score of 80% or more, the MCT group were significantly more likely to meet the desired outcome.

Although (as indicated above) the sample size for the study was small, a previous retrospective study suggested a recovery rate of 72% among those receiving MCT (Thomas, Sadlier & Smith, 2006) compared with 6% for untreated controls (Thomas & Smith, 2006). These findings indicated that a sample of 8 MCT recipients and 8 controls would have an 80% chance of detecting a treatment effect at the 5% level of statistical significance. Ethical approval for the therapy trial was granted by the Local Health Authority Ethics Committee and covered all aspects of the study up to the six-month follow-up data collection point.

Findings from this small study suggested that MCT had the potential to effectively address a wide range of problems associated with CFS and improved patient outcomes which were sustained over a six-month period. However, whilst the success of our trial was of note, patients with CFS understand the illness is plagued with bouts of apparent recovery. In these instances, the person can feel as if they have returned to normal health only to be struck down again with the illness weeks or even months later. In terms of the longer-term efficacy of interventions for CFS, most trials report findings at 6-month follow-up (Nijhof, Bleijenberg, Uiterwaal, Kimpen & van de Putte, 2012) with a study by White et al (2013) conducting a follow-up assessment 1-year post-therapy (White, Goldsmith, Johnson, Chalder & Sharpe, 2013). We judged it important to assess the efficacy of MCT over a longer period, that is 3-years after the final trial assessment, to see whether the intervention prevented relapses in the condition.

2. Methods

Ethical approval for the 3-year follow-up study was granted by the host institution's departmental Research Ethics Committee.

2.1 Participants

The 12 CFS patients who completed the MCT arm of the original study were contacted by post and asked if they would attend a follow-up evaluation session. The relaxation and control groups were not contacted as, although they had been offered MCT following the outcome of the original study, they had not agreed to be contacted regarding further follow-up sessions.

2.2 Procedure

The MCT group were sent an information sheet describing the nature of the study along with a letter inviting them to participate in the follow-up study. Data collection took place at the Research Unit, and the group completed the same outcome measures that were administered during the original trial. Those who were not able to travel to the Unit completed the measures at home and returned them in a prepaid envelope.

2.3 Primary Outcome Measure

The main indicator for continued treatment success was the Karnofsky Performance Scale which categorises the patient according to their functional performance on a scale of 0 to 100% (Karnofsky et al., 1948). The scale was modified, however, by removing the more catastrophic lower elements. In this way, we were able to assess the ability of the patient to examine improvements in functioning subjectively.

2.4 Secondary Outcome Measures

2.4.1 Mood and performance (Thomas et al., 2006)

The mood and performance test data were collected using a laptop computer which was connected to a simple 3-button response box. The testing session lasted approximately fifteen minutes and recorded data regarding mood, memory, motor speed and vigilance.

Mood: The task presented 18 visual analogue mood scales. Each scale composed of a pair of adjectives (e.g.) drowsy/alert or happy/sad. Using the keys marked left or right on the response box, individuals asked to move the cursor on the screen towards the word they felt most represented their mood at that time. The 18 scales were presented successively and scores between 1 and 51 recorded. Using a factor analysis, three scores were derived from the 18 scales; alertness, hedonic tone, and anxiety.

Free Recall task objectively assessed episodic memory. Individuals were shown a list of 20 words on the computer screen – each word was presented for two seconds. Once all twenty words had been presented, the individual was asked to write down the words that they remembered – in any order. They were given two minutes to complete this task. The number of words remembered, the number of words correctly recalled, and the number of words incorrectly remembered were recorded.

Variable Fore-Period Simple Reaction Time Task is an objective measure of motor speed. During this task, an empty box was displayed in the centre of the screen. At varying intervals (up to 18 seconds) a target square would appear inside the bigger box. Individuals were asked to press a specified response key, using their dominant as soon as they saw the target square appear on the screen. The task lasted for 3 minutes and data recorded included the reaction time for each presentation, the mean reaction time for each minute of the task and the number of trials completed per minute. These data also provided a measure of overall mean reaction time and the total number of trials completed over the duration of the task.

Repeated Digits Detection Task is a visual cognitive vigilance task which measures an individual's ability to detect targets at irregular intervals. The task successively presents 3-digit numbers in the centre of the screen at the rate of 100 per minute. Usually, each 3-digit number differs from the one immediately preceding it (e.g., 463, 563, 562). Eight times per minute, however, the same 3-digit number is repeated on successive trials (e.g., 463, 563, 563). Individuals were asked to respond to the repeated numbers as quickly as possible by pressing the nominated key on the keyboard using the forefinger of their dominant hand. The task lasted for 3 minutes and data recorded included the reaction time for each repeated digit recorded, the mean reaction time for each minute of the task. The number of targets correctly identified, the number of false alarms and the number of missed targets were recorded per minute. These data also provided a measure of overall mean reaction time and the total number of trials completed over the duration of the task.

2.4.2 Global Measures of health (Deale et al., 1997)

Ratings of overall improvement in illness condition and changes in the level of fatigue and disability were recorded on Likert-type scales. Each scale ran from extreme negative through 'no change' to extreme positive responses. Patients were asked to rate their responses in relation to their six-month follow-up scores.

Quality of sleep and levels of activity were measured on Likert-type scales ranging from 'much worse' through 'unchanged' to 'much better' (in the case of sleep quality) and 'significantly decreased' through 'unchanged' to 'significantly increased' (for levels of activity). A symptoms checklist with 28 physical (e.g., *legs feeling heavy*) and psychological ailments (e.g., *anxiety/panic feelings*) from which they could select the individual symptoms they were currently experiencing was also administered. The number of positive responses was summed to provide total symptom score data (Thomas et al., 2006).

2.5 Data Analysis

Data for the current study included those variables which provided significant improvements previously (Thomas et al., 2006; 2008) continue in the longer-term. Frequency data were used to compare the proportion of patients who continued to report normal function (70% and above and 80% or above) on the Karnofsky scale, activity levels and quality of sleep at 6-months and 3-years. For the secondary outcome measures, negative scores were summed into a single variable as were the positive ones with the third variable being 'no change.' Descriptive data were used to compare the performance data for the group at 6-months and 3-years. Only those who competed for measures at both time points were included in the analysis.

3. Results

Of the twelve patients who have completed the original MCT trial, eleven completed at least part of the three-year follow-up study (range=9-11) and seven completed the mood and performance measures.

3.2 Primary Outcome Measure

Nine of the MCT group provided Karnofsky Performance score data group at the 3-year follow-up point. Seven respondents (77.8%) continued to report function scores of over 70%, indicating normal functioning, with 5 recording scores of more than 80%.

3.3 Secondary Outcome Measures

3.3.1 Mood and performance

Seven of the original MCT group completed the mood and performance tests. Table 1 compares data from the 6-month follow-up data from the original trial and the 3-year data.

Table 1. Subjective ratings of mood and objective performance data for the MCT group at six months and three years. Scores are means and s.d.

Measure	MCT patients (n=7)	
	Six-months post-therapy	Three-years post-therapy
Mood:		
<i>Alertness</i>	205.00 (59.45)	183.85 (33.56)
<i>Anxiety</i>	76.00 (20.02)	71.43 (6.68)
Episodic Memory:		
<i>No. of words recalled</i>	10.00 (1.63)	9.00 (1.82)
Simple Reaction Time:		
<i>Mean reaction time (msecs)</i>	394.25 (91.65)	376.86 (109.70)
Vigilance:		
<i>Mean reaction time (msecs)</i>	777.44 (90.31)	751.80 (106.33)
<i>No. of targets correct</i>	15.57 (7.09)	16.28 (4.11)

We can see in Table 1 that, although the small sample size precludes statistical analysis, the MCT patients appear to be maintaining the improvements in mood and performance recorded 6-months post-therapy 3-years later.

3.3.2 Global measures of health

Nine of the original MCT group completed the sleep measure, 10 completed the activity, fatigue, overall improvement in condition and disability measures and 11 completed the 28-item symptom checklist. Table 2 compares data from the 6-month follow-up data from the original trial and the 3-year data.

Table 2. Three-year follow-up secondary health-related outcome measures for MCT patient group when compared to their six-month post-therapy scores. Percentage scores indicate 'better/much better' or 'unchanged' from post-therapy or 6-month scores. Scores are a percentage or mean and s.d.

Measure	MCT patient group	
	Six-months post-therapy	Three-years post-therapy
Improvement in condition (%)	100	90
Fatigue (%)	67	90
Lower levels of disability (%)	83	90
Improved sleep (%)	83	90
Improved activity (%)	100	91
Total symptoms (mean)	11.58 (3.87)	11.54 (7.06)

Only one person reported feeling worse at 3-year follow-up than they had at 6-month follow-up for each of the secondary outcome measures of their overall condition, fatigue, disability, sleep, and activity. There was no difference between the mean total symptom scores at 6-months post-therapy and three-year follow-up.

4. Discussion

Chronic Fatigue Syndrome (CFS) is a condition which comes under the umbrella group of medically unexplained symptoms (MUS). The severity of the fatigue experienced in the condition causes substantial

functional impairment, and it is also accompanied by four or more co-existing symptoms including cognitive deficits (Fukuda et al., 1994). Individuals with CFS experience significant impairments in daily living and in social and occupational settings and spontaneous recovery rates from the illness are low (Thomas & Smith, 2006).

It was the increasing problem that MUS were presenting to both primary and secondary care that prompted the development of an outpatient clinic to provide a service for patients with these types of illnesses. The subsequent intervention, multi-convergent therapy (MCT), had already shown to be of benefit to patients with irritable bowel syndrome and tinnitus as well as Chronic Fatigue Syndrome (Sadlier & Stephens, 1995; Shaw et al., 1991; Sadlier et al., 2000).

MCT is a holistic, individualised programme which aims to address several symptoms associated with CFS including sleep, activity, and fatigue. Poor sleep and reduced activity levels had been identified as confounding factors in perpetuating the illness. The therapy combines aspects of Cognitive Behaviour Therapy (CBT) and Graded Exercise Therapy (GET) which previous studies had identified as the most consistently successful treatments for CFS (Deale et al., 1997; Sharpe et al., 1996; Fulcher & White, 1997). In addition to these components, MCT included aspects of mindfulness meditation (Kabat-Zinn et al., 1985), relaxation techniques and psychodynamic counselling. Heart rate monitors were also used to supervise the progress of exercise therapy.

A small randomised controlled trial of the intervention was conducted where MCT was compared to relaxation therapy and a control group who received general medical care. Overall the trial data provided evidence for the efficacy of the intervention across a range of impairments associated with CFS. This included improved mood, fatigue, symptomology, sleep and activity levels following the 10-week therapy sessions. We were also the first researchers to report objective evidence that intervention for CFS could improve cognitive performance (Thomas et al., 2006; 2008). Whilst our findings were encouraging, and they only indicated the intervention's efficacy over a relatively short period of time – that is 6-months post-therapy. Further assessment of the therapy over an extended period was warranted to assess the endurance of these positive outcomes as it was well established that periods of remission regularly occur in this condition (Reyes et al., 1999). Previous behaviour therapy trials for CFS had, at most, collected follow-up data 12-months post-therapy (White et al., 2013).

The stand-alone study described here reports data collected 3 years after the final assessment of the original trial. Eleven of the twelve CFS patients who attended MCT sessions in the original trial answered our three-year follow-up call (92% response rate). Of these respondents, 78% reported that they were able to conduct the normal day-to-day activity with only a few signs or symptoms of the illness present on the Karnofsky scale (Karnofsky et al., 1948). This scale was used in the original trial as both an inclusion/exclusion criterion and a primary outcome measure. In terms of the secondary measures, the majority of those who had received MCT sessions reported that their overall condition maintained the improvement reported at the 6-month post-therapy level and that they continued to report lower levels of disability. The significantly lower levels of fatigue and total symptom scores reported at 6-months post-therapy were also maintained at 3-year follow-up. This is judged an important finding as fatigue, and the number of associated mental and physical symptoms are good indicators of recovery (submitted manuscript).

We acknowledge that the sample size precluded any meaningful statistical analysis of the 3-year data. However, our aim was to provide follow-up information on this group over an extended period. In a much larger multi-centre trial of CBT, GET, adaptive pacing therapy (APT) and specialised medical care (SMC). White et al. also used several standardised measures of fatigue and physical functioning (Chalder et al., 1993; Bowling, Bond, Jenkinson & Lamping, 1999) to define recovery (White et al., 2013). In their study, recovery was interpreted as those patients who fell within the normal ranges for both scales. Their study found that at the 52-week follow-up point: (a) 30% of those receiving CBT, (b) 28% of those receiving GET, (c) 16% of those receiving APT and (d) 15% of those receiving SMC met the study criteria for recovery. The authors concluded that although CBT or GET was more likely to facilitate recovery, only a small proportion of the patients did recover. They attributed their findings to the heterogeneous nature of CFS and suggested that current therapies needed to be enhanced (White et al., 2013). It is judged that a holistic multi-convergent approach which addresses the

individual needs of the patient and that is patient centred offers the best way forward for sustainable improvement for patients with CFS.

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