Institution: King's College London

Unit of Assessment: UoA4 – Psychology, Psychiatry & Neuroscience

Title of case study: 22: Improved evaluation and treatment outcome for chronic fatigue syndrome

1. Summary of the impact

Chronic fatigue syndrome (CFS) is characterised by prolonged and profound fatigue. The prevalence of CFS is between 0.2% and 2.6% worldwide. Researchers from King's College London (KCL) have shown that Cognitive Behaviour Therapy and Graded Exercise Therapy can improve the symptoms and disability of CFS. This evidence led to both therapies being recommended by the National Institute for Health and Care Excellence and the British Association for Chronic Fatigue Syndrome/ME and becoming standard practice in the UK. These treatments, backed by the KCL studies, are also recommended worldwide including in the United States, Australia and Norway.

2. Underpinning research

Chronic fatigue syndrome (CFS) is characterised by prolonged and profound fatigue not substantially alleviated by rest and is associated with a poor prognosis and long-term disability. Research at Institute of Psychiatry, KCL led by Prof Trudie Chalder (1994-present, Professor of Cognitive Behavioural Psychotherapy), Prof Sir Simon Wessely (1991-present, Chair of Psychological Medicine), Prof Leone Ridsdale (1985-present, Professor of Neurology & General Practice) and Dr Alicia Deale (1999-2009, Post-doc researcher) have made important contributions to the recognition and prevalence of chronic fatigue symptoms and CFS and have developed and evaluated rehabilitative treatments in both primary and secondary care that are the gold standard.

KCL researchers develop the Chalder Fatigue Scale

Initial work by KCL investigators involved finding the best way for patients to describe and rate their symptoms. In 1993 KCL researchers published their Fatigue Questionnaire (later known as the Chalder Fatigue Scale), an 11-item self-rating scale that measures physical and mental fatigue severity. Development research, which involved 374 GP attendees, found the scale to be both reliable and valid with a high degree of internal consistency. It is now adopted as the key measure of therapy response in subsequent studies (1). For instance, it was used in a 1997 KCL-led investigation of 2,376 GP patients aged 18 to 45 to ascertain how widespread the condition was in the UK. In this study, the point prevalence of chronic fatigue and CFS was 11.3% and 2.6% respectively (2).

Development of cognitive behaviour therapy for CFS

At the same time as assessing the prevalence of CFS, KCL researchers investigated potential therapies which include cognitive restructuring and graded activity. KCL researchers developed and refined these types of therapies and investigated their validity. In a KCL-led study comparing 13 sessions of Cognitive Behaviour Therapy (CBT) (n = 25) or relaxation therapy (n = 28), functional impairment and fatigue improved more in the CBT group. At follow-up, 70% of the CBT completers, compared to 19% of the relaxation group, achieved substantial improvement in physical functioning (3). Five years after therapy, two thirds of the CBT patients and one third who received relaxation therapy rated themselves as "much" or "very much" improved. Additionally, significantly more of those who received CBT met criteria for complete recovery, being free of relapse and having symptoms that were either mild or absent since treatment end. CBT completers also had better social outcomes, for instance working more hours per week on average, and the CBT skills taught were still being used by over 80% of participants (4). KCL researchers also developed a CBT self-help booklet (later, a book), given to 70 people presenting to their GP with CFS symptoms, compared to 80 controls. The self-help group showed significantly greater improvements in fatigue and psychological distress than controls. At 3-month follow-up, 63% of the self-help completers achieved a good outcome compared with only 39% of the controls (5).

KCL researchers extend and further test the use of therapies

While 13 sessions of CBT was useful for CFS in secondary care, it was necessary to assess whether a shorter course would be more suitable to treat chronic fatigue in primary care. In 2004, KCL researchers compared six CBT sessions with another form of CFS treatment – graded exercise therapy (GET) – or with standard care plus their CBT booklet. The study involved 144 patients with chronic fatigue, of whom 27% met criteria for CFS. By treatment end, the overall

mean fatigue score decreased by 10 points with either CBT or GET. However, only a quarter who met CFS criteria recovered, suggesting that treatment was too short for those with CFS (6). A comparison of the cost-effectiveness of these interventions showed no significant outcome or cost differences between therapy groups. While costs were on average £149 higher for CBT or GET than standard care plus self-help (but not significantly different), the therapy groups had significantly better outcomes (7).

Due to their expertise in CFS and therapy development, KCL researchers collaborated with colleagues from Queen Mary University and the University of Edinburgh to carry out the largest trial of CFS ever conducted. The PACE trial evaluated the efficacy of 14 sessions of CBT (n = 161), GET (n = 160) or another type of therapy called adaptive pacing therapy (n = 160), compared with three sessions of specialist medical care (n = 160). At one year, fatigue scores for those receiving CBT or GET were significantly lower and physical function scores significantly higher than those receiving the other therapies (8).

3. References to the research

1. Chalder T, Berelowitz G, Pawlikowska T, Watts L, Wessely S, Wright D, Wallace EP. Development of a fatigue scale. J Psychosom Res 1993;37(2):147-53. Doi: 10.1016/0022-3999(93)90081-P (832 Scopus citations)
2. Wessely S, Chalder T, Hirsch S, Wallace P, Wright D. The prevalence and morbidity of chronic fatigue and chronic fatigue syndrome: a prospective primary care study. Am J Public Health 1997;87:1449-55. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1380968/ (205 Scopus Citations)
3. Deale A, Chalder, T, Marks I, Wessely S. Cognitive Behaviour Therapy for Chronic Fatigue Syndrome: a randomized controlled treatment trial. Am J Psychiatry 1997;154; 3; 408-14. http://ajp.psychiatryonline.org/data/Journals/AJP/3674/408.pdf (306 Scopus citations)
4. Deale A, Husain K, Chalder T, Wessely S. Long-term outcome of cognitive behavior therapy versus relaxation therapy for chronic fatigue syndrome: a 5-year follow-up study. Am J Psychiatry 2001;158(12):2038-42. Doi: 10.1176/appi.ajp.158.12.2038 (71 Scopus citations)
5. Chalder T, Wallace P, Wessely S. Self-help treatment of chronic fatigue in the community: A randomized controlled trial. Br J Health Psychol 1997;2(3):189-97.Doi: 10.1111/j.2044-8287.1997.tb00535.x (32 Scopus citations)
6. Ridsdale L, Darbishire L, Seed PT. Is graded exercise better than cognitive behaviour therapy for fatigue? A UK randomized trial in primary care. Psychol Med 2004;34(1):37-49. Doi: 10.1017/S0033291703001247 (37 Scopus citations)
7. McCrone P, Ridsdale L, Darbishire L, Seed P. Cost-effectiveness of cognitive behavioural therapy, graded exercise and usual care for patients with chronic fatigue in primary care. Psychol Med 2004;34(6):991-99. Doi : 10.1017/S0033291704001928 (22 Scopus citations)
8. White PD, McCrone P, Chalder T, et al. Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial. Lancet 2011;377(9768):823-36. Doi: 10.1016/S0140-6736(11)60096-2 (106 Scopus citations)

Grants

- 1993: £105,574; The Wellcome Trust. A RCT of CBT for fatigue in primary care. PI: L Ridsdale.
- 1998: £18,210; South Thames research and development project grant scheme. 5 year follow up of RCT. PI: A Deale.
- 1998: £155,730; Linbury Trust. RCT of the equivalence of GET versus CBT for patients with CFS in general practice. PI: L Ridsdale.
- 2001: £39,831; King's College Hospital Joint Research Committee. Chronic fatigue in general practice: a qualitative study of patients' views. PI: L Ridsdale
- 2003: £6.6M; Medical Research Council and Department of Health. RCT of CBT, GET for CFS (PACE trial). PI at KCL: T Chalder
- 2003: £250,860; The Wellcome Trust. An RCT to compare the effect of GET and counselling, with usual care plus a booklet, for patients with fatigue in primary care. PI: L Ridsdale.
- 2008: £80,000; BRC at South London and Maudsley NHS Trust. A psycho-physiological model of CFS/ME in adolescents. PI: T Chalder.

4. Details of the impact

King's College London (KCL) research on the prevalence of Chronic Fatigue Syndrome (CFS) and its treatment led to the key conclusion that general fatigue can be managed in primary care and

CFS can be treated in secondary care with either Cognitive Behaviour Therapy (CBT) or Graded Exercise Therapy (GET). Prior to this work chronic fatigue was thought to have a poor prognosis but KCL research led to the more optimistic view that patients can recover and that the effects of treatment can be sustained.

KCL research drove National Institute for Health and Clinical Excellence (NICE) guidelines: Current NICE recommendations, developed in 2007, on the management of CFS state that all patients without severe disability should be offered CBT or GET. The recommendations, including the health economics, are based on several KCL papers including Ridsdale et al. 2004; Deale et al. 2001 and McCrone et al. 2004. The guidelines also include mention of the Chalder Fatigue Scale (Chalder et al. 1993), which is used routinely by clinical services to collect outcomes (1).

KCL research changed UK clinical practice: The work of KCL researchers is directly translated into clinical practice at a specialist CFS unit at the South London and Maudsley (SLaM) NHS Foundation Trust. This unit includes specifically trained psychologists and physiotherapists who offer up to 20 CBT or GET sessions to an average 250 people per year (2c). NICE guidelines have been adopted widely by NHS services, where currently around 8,000 adults are treated each year. One study showed that outcomes for fatigue (using the Chalder Fatigue Scale), anxiety and depression for patients at six UK treatment centres are similar to those in clinical trials (2b).

The PACE trial (White et al. 2011) treatment manuals are available to download for free from the trial website which receives an average 5,000 page views per month. These are used by clinical psychologists, psychiatrists, occupational therapists, physiotherapists and behavioural nurse practitioners (2c). The British Association for Chronic Fatigue Syndrome/ME (BACME), formed to "champion evidence-based approaches to treatment of CFS," represents all UK NHS specialist services and members include healthcare professionals and researchers. BACME welcomed the findings of the PACE trial, saying it "provides convincing evidence that GET and CBT are safe and effective therapies and should be widely available ... as per the NICE guidelines." BACME evidence is supported by the National Outcomes Database that currently holds clinical assessment and outcome data on nearly 7,500 CFS patients. The PACE trial provides the gold standard outcomes for National Outcomes Database thus allowing bench-marking of the effectiveness of clinical services (2d).

Telephone CBT has been adapted by KCL researchers from the original face to face trials and CBT has been adapted for adolescents, approaches that have both been shown to be effective in recent clinical trials (2e,f). Telephone CBT is offered by some services in the UK, for example the SLaM National Chronic Fatigue Service (2g). The self-help booklet developed by KCL researchers was published as a book in 2005, with an update in 2009 (2g). This is one of only two CFS books on the 'Reading Well Books on Prescription' core list, a national scheme for England where a range of CBT self-help books are recommended by GPs or other health professionals and are available in all public libraries (2h).

KCL research highlighted on patient-focused websites: KCL research features on a number of patient-focused websites. For instance, the NHS Choices website specifically recommends GET/CBT for CFS (3a). The website also provides a link to the Map of Medicine care pathway for CFS that provides guidance for best-practice treatments for people with CFS. The Map uses as its evidence base several documents that cite KCL work including the NICE guidance (3b). The highly-commended website Patient.co.uk also discusses CBT and GET and cites a number of these resources as well as the PACE trial (3c).

KCL research affects worldwide clinical practice: The results of the PACE trial and other KCL studies, have been used worldwide by government organisations and healthcare practices when discussing the utility of CBT/GET for CFS. For instance, in the US, White et al. 2011 is cited by the Mayo Clinic, a leading medical care and research organisation, to back their therapy choices (4a). The Norwegian Knowledge Centre for the Health Services, which "supports the development of quality in the health services by promoting the use of research results, contributing to quality improvement [and] measuring the quality of health services," has recently published a CFS

treatment guideline also citing the PACE trial when recommending CBT/GET and including the Chalder Fatigue Scale to assess treatment (4b). The US Government Center for Disease Control (CDC) provides an online educational module on 'Diagnosis and Management of CFS' that cites the PACE trial and Deale et al. 2001 when discussing CBT/CET and Wessely et al. 1997 when discussing CFS prevalence (4c). The Deale et al. study is also utilised by the Chronic Fatigue and Immune Dysfunction Syndrome Association of America when discussing therapy. This is one of the largest and most active charitable organisations dedicated to CFS with a number of resources including a large, healthcare professional-aimed e-learning module on CFS supported by the CDC (4d). In Australia, the University of New South Wales houses a Fatigue Clinic and their information page references Deale et al. 1997 and McCrone et al. 2004 to justify why they use CBT/GET (4e).

5. Sources to corroborate the impact

1) National Institute for Health and Clinical Excellence guidelines

NICE Guidelines: Diagnosis and management of chronic fatigue syndrome/myalgic encephalomyelitis (or encephalopathy) in adults and children. 2007: http://www.nice.org.uk/nicemedia/live/11824/36191/36191.pdf

- Systematic Evidence Review: http://www.nice.org.uk/nicemedia/live/11824/36192/36192.pdf

2) CBT and GET in practice

a. SLaM patient brochure: https://www.national.slam.nhs.uk/wp-content/uploads/2011/05/Chronic-Fatigue-Service.pdf
b. Crawley E et al. Treatment outcome in adults with CFS: a prospective study in England based on the CFS/ME NOD. QJM 2013;106(6):555-65. Doi: 10.1093/qjmed/hct061
c. PACE trial treatment manuals: http://www.pacetrial.org/trialinfo/
d. British Association for CFS/ME: http://www.bacme.info/default.aspx
   - PACE trial findings endorsement: http://www.bacme.info/aboutbacme/pace_trial.html
   - National Outcomes Database: http://www.bacme.info/nod/
e. Burgess M, Manoharan A, Chalder T. CBT for CFS in adults: Face to face versus telephone treatment. Behav Cogn Psychother 2012;40(2):175-91. Doi: 10.1017/S1352465811000543
f. Lloyd S et al. Telephone-based guided self-help for adolescents with CFS: A non-randomised cohort study. Behav Res Ther 2012;50(5):304-12. Doi: 10.1016/j.brat.2012.02.014
g. SLaM National Service – Chronic Fatigue (p10) https://www.national.slam.nhs.uk/wp-content/uploads/2011/06/Chronic-Fatigue-Service-booklet.pdf
h. Burgess M, Chalder T. Overcoming Chronic Fatigue. Constable & Robinson Ltd, London. 2009.
i. Books on Prescription: http://readingagency.org.uk/adults/BoP%20core%20booklist%20April%202013.pdf

3) Patient-focused websites

a. NHS Choices: http://www.nhs.uk/Conditions/Chronic-fatigue-syndrome/Pages/Treatment.aspx
b. Map of Medicine (Updated Jan 2013): http://healthguides.mapofmedicine.com/choices/map/chronic_fatigue_syndrome_and_myalgic_encephalopathy_cfs_me_2.html
c. Patient.co.uk: http://www.patient.co.uk/health/Chronic-Fatigue-Syndrome-/-ME.htm

4) Worldwide use of CBT and GET

a. Mayo Clinic. CFS treatment: http://www.mayoclinic.com/health/chronic-fatigue-syndrome/DS00395/DSECTION=treatments-and-drugs
b. Norwegian Knowledge Centre for the Health Services treatment for CFS: http://www.kunnskapssenteret.no/Publikasjoner/Behandling+av+kronisk+utmattelsessyndrom+CFSME.12742.cms?onepage=1
c. CFIDS Association of America provider education project: http://www.cfids.org/community/pcpep/curriculum.asp
d. CDC. Control e-learning course on Diagnosis and Management of CFS: http://www.cdc.gov/cfs/education/diagnosis/course.html
e. University of New South Wales Fatigue Clinic: http://medicalsciences.med.unsw.edu.au/community/lifestyle-clinic/services/fatigue-clinic