CFS topic guide

Lecture 5 topic guide: Definitions of chronic fatigue syndrome

Acknowledgements

My main debt here is owed to the 2011-2 cohort of students on HPSC3028: Alexandra Bonthrone, Thomas Frankel, Edouard Gottlieb, Laura Gumbley, Josephine Hellberg, Katrine Iversen, Carys Lewis, Shakya Manage, Richard Muswell, Belene Podmore and Kirsten Shastri. We spent the spring term of 2011-2 participating in a joint research project on CFS/ME, and I am extremely grateful for their collective interest in, and enthusiasm for, this difficult subject. I would also like to thank them all for permitting me to draw so heavily on their research. I should also like to thank Professor Simon Wessely (KCL psychiatry) and Professor Greg Tower (UCL Infection and Immunity), for their time and attention during this project. As usual, any errors in what follows are mine, rather than theirs.

Introduction

It's normal to be tired sometimes. But is it normal for someone to be tired all the time? Is someone who is tired all the time ill? Well, it depends: depends on their activity levels, their mood, their general state of health. Someone who works three jobs might well be tired all the time, and (I think) we wouldn't necessarily think that their tiredness was an illness, even if we might worry about their health for other reasons. Similarly, it's common for people suffering mental illness (depression, especially), malnourishment (such as vitamin deficiencies), or serious illness in general to be very tired.

But what about the case where someone was tired all the time without any of these causes? Would that persistent tiredness itself count as an illness? This question is the starting point for this case study, which explores a condition known as CFS/ME.

CFS/ME is a condition of uncertain status. While widely diagnosed, the condition is poorly understood. That is, sadly, not unusual - many diseases are less well understood than we might like. What is very unusual is just how differently CFS/ME is understood in different contexts. Broadly, different concepts of the disease are typically found in general medicine, in psychiatry, and in patient support groups. This has led to a remarkable number of disputes between these stakeholders, with the most striking of these disputes being about the very existence of the condition. Other, perhaps less dramatic discussions include those regarding the most appropriate terminology to use to describe it, the cause(s) of the condition, the kinds of pathological processes involved, the most appropriate management strategies, including means of diagnosis. In what follows, I set out a couple of different ways that stakeholders have tried to understand CFS/ME. My intention is to outline some of the substantive differences found in different understandings of this condition. We can then use these differences in our next lecture, which deals with the question of definitions of disease.

A note on terminology

The terminology in this case is complicated, because the case itself is in part an argument about the most appropriate terminology to use. I'll try to explain the many different names used as they come
up. However, I also need a couple of more generic bits of terminology in order to get going. First of all, I've used the catch-all term CFS/ME as a kind of umbrella term. In general, this should be understood to contain all the more specific terms (Chronic Fatigue Syndrome, Royal Free Disease...) that have been used in particular contexts. Second, because part of this argument about terminology concerns the question of whether CFS/ME is a disease or something else (such as a syndrome), I'll use the term condition to refer to it in general terms.

A bit of introduction to CFS/ME

Let's begin with the features that most stakeholders agree on. CFS/ME is a condition of long-lasting post-exertional fatigue that is unrelieved by rest (Wessely 1995). It is common, with a prevalence of somewhere between 0.2% - 0.4%. That means, I suppose, that there are something like 200,000 sufferers from the condition currently in the UK. Sufferers have a poor prognosis, with little chance of a complete recovery from CFS/ME. No cause is known. The impact of the condition is substantial. As the 2001 DoH report puts it, CFS/ME:

"is a relatively common clinical condition, which can cause profound, often prolonged, illness and disability, and can have a very substantial impact on the individual and family" (Report of the Working Party on CSF/ME to the Chief Medical Officer for England and Wales Department of Health 2001, quoted in Clark et al 2002)

While treatment is not a very important part of the story of CFS/ME that I want to explore here, it is worth noting that some treatments do appear to benefit some CFS/ME patients. Two examples are CBT (cognitive behavioural therapy) and GET (graded exercise therapy). See Clark et al 2002 for more details on these. However, despite the impact of the condition, the few sentences above are about the sum-total of agreement in the field. What, then, do stakeholders disagree about?

The beginnings of CFS/ME

If we look back into historical medical texts, we can find a large number of conditions that are characterised by chronic fatigue of one kind of another. Chronologically (and see the review in Straus 1991 for further details), these conditions of chronic fatigue include febricula (introduced 1750), neurasthenia (early C19), DaCosta's syndrome (1870s), chronic Brucellosis (1930s), chronic hypoglycaemia (1970s), total allergy syndrome (1980s), chronic candidiasis (1980s), chronic Epstein-Barr infection (1980s). Note that most of these conditions are defined by their cause: low blood sugar in the example of chronic hypoglycaemia, or infection with EBV in the case of chronic Epstein-Barr infection. This classification of disease in terms of causes will be an issue that we'll explore later in the term, when we discuss medical ideas about causation. Note too that most of these conditions were disputed or controversial in one way or another, largely because the biological causes identified (EBV infection, or actual low blood sugar) were not reliably detected in all cases.

CFS

CFS was introduced in the late-1980s as a "neutral and inclusive" (Straus 1991: S6) term, de-emphasising organic causes. As far as I can see the first use of the term is Holmes et al 1988, although Straus 1988 does a better job of setting out why the adoption of this new term might be valuable to stakeholders. Note that this term is acausal, in contrast to most of the terms used earlier.
Instead, definitions of CFS typically describe constellations of symptoms, as the Centres for Disease Control and Prevention definition of CFS shows (CDC 2011):

Chronic fatigue syndrome (CFS) is a debilitating and complex disorder characterized by intense fatigue that is not improved by bed rest and that may be worsened by physical activity or mental exertion. People with CFS often function at a substantially lower level of activity than they were capable of before they became ill. The cause or causes of CFS have not been identified, and no specific diagnostic tests are available. Therefore, a CFS diagnosis requires three criteria:

1. The individual has had severe chronic fatigue for 6 or more consecutive months that is not due to ongoing exertion or other medical conditions associated with fatigue (these other conditions need to be ruled out by a doctor after diagnostic tests have been conducted)

2. The fatigue significantly interferes with daily activities and work

3. The individual concurrently has 4 or more of the following 8 symptoms:
   1. post-exertion malaise lasting more than 24 hours
   2. unrefreshing sleep
   3. significant impairment of short-term memory or concentration
   4. muscle pain
   5. pain in the joints without swelling or redness
   6. headaches of a new type, pattern, or severity
   7. tender lymph nodes in the neck or armpit
   8. a sore throat that is frequent or recurring

These symptoms should have persisted or recurred during 6 or more consecutive months of illness and they cannot have first appeared before the fatigue. (CDC 2011)

While this definition is widely used, it too is disputed in parts. For example, the definition used in the UK lacks the list of 8 somatic symptoms (malaise, muscle pain, and so on) found in the CDC definition. An important part of the definitions used for CFS is that they are assumed to pick out part (but not all) of a population of individuals with prolonged fatigue. A nice way of demonstrating this is a figure found in Fukada et al's (1994) framework for defining CFS, which is as follows:
As we'll see, there have been other attempts to pick out a sub-set of those suffering chronic fatigue of one kind or another. Here, we can see that most chronic fatigue has nothing to do with CFS (instead, coming about as a consequence of other serious illness, as we discussed above). Note too that the CDC definition above mentions that CFS is a diagnosis of exclusion, in that a practitioner would have to exclude "medical conditions associated with fatigue" before making a CFS diagnosis. Together with the way that CFS de-emphasises organic cause, this suggests that CFS is understood as some kind of psychological or psychiatric diagnosis. That is not to say that it is spurious, or made up - depression is another example of a serious psychological illness that is almost always not brought about by an organic cause. However, this definition does place CFS in this respect a very long way from the most important alternative way of understanding chronic fatigue. This is a much more biological term: myalgic encephalitis (which, loosely translated, means muscle pain + brain swelling).

ME

As the translation of the name suggests, ME accounts for chronic fatigue in strongly biological terms. The precise ways that this gets done are a bit complicated, so I won't review them here, but you can have a look at the clinical features, and some thoughts about aetiology and pathology in the very good (ME-sceptical) review by David, Wessely and Pelosi (1988). One important conclusion of this work:

"Myalgic encephalomyelitis" continues to provoke strong opinions in the medical press' and intense interest in the lay media, as it has for the past four decades. The condition, variously named epidemic neuromyasthenia, Icelandic disease, benign myalgic encephalomyelitis, Royal Free disease, and epidemic myalgic encephalomyelitis, is more appropriately referred to as the postviral fatigue syndrome. Clinical descriptions include a vast array of symptoms and signs but the two main features that emerge are fatigue and emotional disturbance." (David, Wessely and Pelosi 1988: 696)
It's well worth discussing briefly some of the reasons for this biological view of the disease. There are many published accounts of outbreaks of unusual (apparently infectious) neurological diseases, in the absence of obvious cause. One such is the Lake Tahoe outbreak, which occurred in 1985. Physicians in one medical practice serving Incline Village near Lake Tahoe, Nevada, noted a sharp increase in number of patients presenting with an acute infectious-type illness that was followed, in many, by chronic fatigue, myalgias, headache, feverishness, and cognitive problems (Straus 1988: 407). Another, even more spectacular, was the very large outbreak of 'benign myalgic encephalomyelitis' at the Royal Free Hospital in 1955 (Medical Staff, 1957). This was an example of a very large outbreak - almost 300 cases from the 3500 hospital staff - of an obscure illness between July and November 1955.

![Graph showing dates of admission.](image)

From its symptoms, the disease appeared to be an infection, involving the lymphatic and central nervous systems. While - as usual - there was plenty of variation in symptoms between individual cases, most sufferers had early symptoms that might be found in many infectious diseases: malaise, headache, and sore throats. Other symptoms - vertigo, limb pain, nausea, stiffness and pain in the neck and back, nausea - were also fairly common in the early stages of the disease. Later, though, a variety of neurological manifestations began to appear, and most (74%: Medical Staff 1957: 896)
affected individuals would come to show "objective evidence of affection of the central nervous system, and the neurological manifestations formed a characteristic picture that distinguishes this disease from other infections of the nervous system."

This disease was scary, and confusing. Few interventions appeared successful, with bed-rest being the mainstay of treatment. Interestingly, authorities were so worried about the outbreak that the hospital was shut to new patients between 25th July and 5th October 1955.

This cause of this outbreak was never satisfactorily resolved, and it remained confusing for many years, particularly because many other similar outbreaks are reported in the medical literature (Dawson 1987 claims 70 or so). While these outbreaks tended to be known initially by a geographical label - Icelandic disease, Royal Free disease - by the mid-1980s most of these specific labels had been subsumed by a wider label: myalgic encephalitis. I think, but am not sure, that this is also synonymous with post-viral fatigue syndrome, a term which is still used in places (see WHO 2010 for an example), and chronic EBV syndrome (pre-1988). However, research to try and detect EBV in these epidemics failed (see Holmes et al 1987 for an example). Possibly for this reason, ME is the label that eventually emerges from this complicated network of different terms. Whatever its origin, the disease that it was used to refer to was intended to be a real (likely infectious) one. Unlike CFS, it is also associated with a constellation of other diagnoses - fibromyalgia (Wolfe et al 1990) for example. Yet finding these organic features (as opposed to the psychiatric features that are supposed to characterise CFS) has remained frustratingly elusive. This might be a good point at which to try and compare and contrast our two models (CFS and ME)

Comparing ME and CFS

Let's think about the Royal Free outbreak again. What is the likely cause? Let's bring in Hanson, at this point, and his discussion of retroduction (which we briefly discussed while we were thinking about discovery last week). Hanson's account of retroduction is as follows:

1. Some surprising, astonishing phenomena \(p_1, p_2, p_3\ldots\) are encountered.
2. But \(p_1, p_2, p_3\ldots\) would not be surprising were an hypothesis of H's type to obtain. They would follow as a matter of course from something like H and would be explained by it.
3. Therefore there is good reason for elaborating an hypothesis of type H - for proposing it as a possible hypothesis from whose assumption \(p_1, p_2, p_3\ldots\) might be explained (Hanson 1960: 104)

In the case of the Royal Free outbreak, our "surprising, astonishing phenomena \(p_1, p_2, p_3\ldots\)" are the features of the outbreak - the symptoms, the epidemiology, things like that. Can we come up with some hypothesis (our H) that might produce and explain these phenomena? Well, one plausible H might be that our phenomena are caused by a viral infection of some kind. Viral infections can cause similar kinds of encephalitis, and these infections can occur in outbreaks. The question is whether this H does manage to explain our phenomena?

Well, yes and no. This outbreak had several features that seem compatible with a viral cause, particularly the characteristic neurological symptoms. On the other hand, no virus was found in
affected individuals. Even more convincingly, very few patients were affected by the outbreak. This would seem to be a surprising finding if the outbreak were the result of a viral infection: why would a virus spare those who were already sick in favour of attacking the healthy medical staff?)

So perhaps we should try a different H - an H', if you like. Let’s now imagine that our outbreak is caused by something like an attack of mass hysteria. This H' would, like H itself, explain some (but not all) features of the outbreak. In this case, we’d be able to explain the different incidence rates in medical staff vs patients pretty well (possibly because the patients might not be told that there was an outbreak in progress). However, we might struggle to explain the neurological signs found in affected individuals.

Here’s where things get tricky (and if you’re still with me after all that has gone before, very well done): which of these two (partially successful) hypotheses should we prefer? Should we prefer a) the strongly biological H (and, here, I hope the connection with ME is obvious), or should we prefer b) the non-biological H' (CFS)? Even though each term is relatively poorly defined, and there is a degree of overlap between CFS and ME (Aaron and Buchwald 2001), it seems that different groups strongly prefer one term over another:

While most research literature uses the term CFS, patient organizations prefer the term Myalgic Encephalomyelitis (ME). As a consequence CFS and ME are now often used almost interchangeably or combined as CFS/ME. However, as Wojcik et al. describe in this edition of the Journal these terms indicate different views of the illness as reflected in current diagnostic classifications. ICD-10 places CFS in both mental and neurological conditions and ME under only neurological conditions. (Sharpe 2011)

Very roughly, patients and support groups tend to prefer the label ME; while clinicians (particularly psychiatrists) tend to prefer CFS. This probably has more to do with the kind of disease that each label implies: psychological in the case of CFS, biological in the case of ME, rather than because the clinical features of either model significantly differ from one another. We can find evidence of this preference for biological, rather than psychological, understandings of CFS/ME from patient groups from their stated preference for neurological, rather than psychological, practitioners. However, few neurologists (something like 15%) recognised CFS as neurological at all (Deale and Wessely 2001). Other medical practitioners find these diagnoses similarly difficult: it’s poorly recognised by GPs (maybe because it does not rationally ground a course of action - Graham et al. 2010) and 48% of GPs in the UK were not confident in making a diagnosis of CFS (Bowen 2005: 1).

I honestly don’t know which model we should prefer. I think that, faced with this choice, I would do my best to pick c) - none of the above. Perhaps it is this failure to accept one or other competing models of disease that pushes many researchers towards conceiving CFS/ME in ways that dodge the causal question (i.e. preferring CFS/ME over either CFS or ME). It’s worth noting how little some of the hostility that comes from patient groups towards medical practitioners has to do with success of treatments. While the only treatments that offer much by way of improvement to CFS/ME sufferers are psychological (CBT and GET), most CFS/ME patients are dissatisfied with a psychological diagnosis:

"Patients’ comments suggested that psychiatric diagnoses were rejected, either because they were interpreted as meaning that symptoms were imagined or factitious, or because patients felt that
doctors believed all their symptoms were caused by depression or anxiety. This highlights the stigma associated with psychiatric diagnoses and the value of sensitivity: doctors may intend a psychiatric diagnosis as an etiologically neutral observation, but patients often hear it very differently, and rejection of the diagnosis may lead to treatable symptoms being overlooked or minimised. “(Deale and Wessely 2001: 1862-3)

As a final point, CFS/ME clearly provokes strong feelings, particularly around how the disease is defined and classified. While we’re going to explore these issues over the next few lectures, perhaps we should conclude by noting that diagnosis is nothing like the end of the story for those suffering CFS/ME, and we should remember that the ‘right’ diagnosis is "the beginning, and not the end, of the therapeutic encounter." (Huibers and Wessely 2006)

References


