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MEDICAL RESEARCH

Dangers of research into chronic fatigue syndrome

Nigel Hawkes reports how threats to researchers from activists in the CFS/ME community are stifling research into the condition

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There are jobs that carry a risk, such as volunteering as a human cannon ball at a funfair. There are jobs that attract opprobrium and abuse, such as becoming an estate agent, driving a white van, or selling double glazing over the telephone. And then there is the job of trying to conduct research into chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME).

CFS/ME is a common condition, and very debilitating. The evidence suggests a population prevalence of at least 0.2-0.4% in the UK.[1] Patients are incapacitated for years, unable to move, sometimes bed ridden and fed through a tube. Yet it doesn't prevent some people, who claim to be its victims, from conducting a relentless personalised attack on doctors and academics who are trying to discover its cause and improve its treatment.

Simon Wessely, professor of epidemiological and liaison psychiatry at King's College School of Medicine in London, has been the target of such attacks for years. He's been compared on the internet to Josef Mengele, the Nazi doctor who performed experiments on inmates of concentration camps. He's had threats against his life, been accused of throwing a boy into a swimming pool to check if his paralysis was genuine, been bombarded with offensive emails, and had complaints against him made to his employers and to the General Medical Council.

The campaign has gained new life since the publication in March in the *Lancet* of the PACE trial, a comparison of four treatments for CFS that concluded, to the fury of the campaigners, that cognitive behavioural therapy and graded exercise therapy can be effective. Pacing, a treatment favoured by leading ME charities, was found to be ineffective.[2]

The publication prompted a 442 page response to the Medical Research Council (MRC), which part funded the trial, and a shorter 43 page rebuttal to the *Lancet.* Both were written by Malcolm Hooper, emeritus professor of medicinal chemistry at the University of Sunderland, who branded the trial "unethical and unscientific." He wrote: "Entry criteria were used that have no credibility; definitions and outcome measures were changed repeatedly; data appears to have been manipulated, obfuscated, or not presented at all (so it cannot be checked) and the authors' interpretation of their published data as 'moderate' success is unsustainable."

Both the MRC and the *Lancet* have considered the submission and rejected it, the *Lancet* commenting that the volume of critical letters it received about the PACE trial smacked of an active campaign to discredit the research.[3] Frances Rawle, head of corporate governance and policy at the MRC, who spent several days reading the 442 page rebuttal, says it "made many accusations of bias." She adds: "I responded and two weeks later got another list of questions."

Personal attacks

Asking detailed questions about an important trial is a legitimate and proper activity, though questioning academics' integrity and honesty is not normally part of the process. But far more unpleasant are the activities of a group of activists who have resorted to threats and personal abuse.

"It is a relentless, vicious, vile campaign designed to hurt and intimidate," Professor Wessely says. "For some years now all my mail has been x rayed. I have speed dial phones and panic buttons at police request and receive a regular briefing on my safety and specific threats.

"Since PACE was published this has become more intense, and at present the police are looking into two cases in which specific threats have been made to my physical safety. These people are sulphurous, vicious, horrible."

Professor Wessely is not alone. All of those who approach CFS/ME from a psychiatric perspective are the targets of critics who believe the disease has a physical cause that would have been discovered by now if the debate, and the research money, had not been cornered by what they see as a conspiracy of psychiatrists, characterised by them as "the Wessely school."

This point of view, if not the actions it inspires, is defended by Charles Shepherd, medical adviser to and trustee of the ME Association. "The anger and frustration patients have that funding has been almost totally focused on the psychiatric side

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is very justifiable,” he says. “But the way a very tiny element goes about protesting about it is not acceptable.

“It’s not representative of the patients as a whole. It’s a very very tiny minority—50 to 100 people, maybe. What they do is not pleasant and totally unacceptable.”

Dr Shepherd has good reason to know, as he has been the target of attacks. One website claimed he had a psychotic illness, was physically violent, and “a medical failure.” He consulted the police. More recently his scepticism about the claim that CFS/ME is caused by the retrovirus XMRV has exposed him to further attacks.

The personalised nature of the campaign has much in common with that of animal rights activists, who subjected many scientists to abuse and intimidation in the 1990s. The attitude at the time was that the less said about the threats the better. Giving them publicity would only encourage more. Scientists for the most part kept silent and journalists desisted from writing about the subject, partly because they feared anything they wrote would make the situation worse. Some journalists have also been discouraged from writing about CFS/ME, such is the unpleasant atmosphere it engenders.

While the campaigners have stopped short of the violent activities of the animal rights groups, they have another weapon in their armoury—reporting doctors to the GMC. Willie Hamilton, an academic general practitioner and professor of primary care diagnostics at Peninsula Medical School in Exeter, served on the panel assembled by the National Institute for Health and Clinical Excellence (NICE) to formulate treatment advice for CFS/ME.

“Our report, based on a solid review of the evidence, was that graded exercise and cognitive behavioural therapy were the best, indeed only, treatments. This position was resisted vociferously by the patient representatives on the committee, using a very strange mixture of quasi-scientific arguments—“the trials were biased”—and utterly unscientific claptrap.

“Actually, it was a visceral fight not to allow graded exercise and cognitive behavioural therapy to be approved by NICE. Why? To this day I don’t know.”

The NICE guidance was taken to judicial review, its opponents claiming that the experts were biased or had conflicts of interest. The case was dismissed, the judge, Mr Justice Simon, warning that: “Unfounded as they were, the allegations were damaging to those against whom they were made and were such as may cause health professionals to hesitate before they involve themselves in this area of medicine.”

After this, the argument got even more personal. “I was reported to the GMC,” says Dr Hamilton. “The complaint was risible. I was accused of breaking almost every rule in the GMC rulebook. And of course the GMC fell totally into the trap.

“Instead of accepting that its complaints process can be hijacked by pressure groups, it treats all complaints the same. So I had all the rigmarole of a formal complaint, which naturally dragged on for months. Eventually it was chucked out and I got an utterly ungracious letter from the GMC saying the complaint won’t lead to a case but I’m to make sure to obey the GMC rules anyway. It sounded as if it thought I’d got off on a technicality and needed a good telling off.”

Peter White, professor of psychological medicine at Barts and the London School of Medicine, was the principal investigator of PACE. He says the campaign against the trial has gone on ever since it was first funded. “There was a campaign by the ME Association, lots of letters to organisations involved, not least the MRC, and a petition to No 10 Downing Street.

“It did upset our ability to recruit patients, and it took up a lot of time. Complaints and Freedom of Information requests have to be dealt with properly. The paradox is that the campaigners want more research into CFS, but if they don’t like the science they campaign to stop it. They want more research but only research they agree with.”

Professor White has been accused of coercing patients, paying general practitioners to enlist patients, having conflicts of interest, and accepting improper financial contributions. These accusations, which he insists are all untrue, have also been sent to his employers. In Dr Hamilton’s case, the dismissal of the complaint to the GMC was followed by Freedom of Information requests for the evidence the GMC had gathered from his five employers and in its case handling. “The GMC hadn’t the grace to tell me this—it still hasn’t—but my employers did,” he says. “As far as I know this stage still grumbles on.”

While psychiatrists and those who work with them have been the main targets, others also come into the activists’ sights. Esther Crawley, a paediatrician and consultant senior lecturer at Bristol University, is principal investigator for the SMILE trial, which aims to investigate a treatment called the Lightning Process. Developed by Phil Parker, an osteopath, the process claims to combine the principles of neurolinguistic programming, osteopathy, and clinical hypnotherapy to treat a variety of conditions, including phobias and CFS/ME. There has been no proper medical study of whether it works.

Critics of the method opposed the trial, first, Dr Crawley says, by claiming it was a terrible treatment and then by calling for two ethical reviews. Dr Shepherd backed the ethical challenge, which included the claim that it was unethical to carry out the trial in children, made by the ME Association and the Young ME Sufferers Trust. After re-opening its ethical review and reconsidering the evidence in the light of the challenge, the regional ethical committee of the NHS reiterated its support for the trial.

Dr Crawley says it doesn’t make sense to argue that the trial should not be carried out in children. “The aetiology of CFS in children is different, and so is the prognosis. Ninety four per cent of children get better, while only a third of adults do. So you couldn’t just do the trial in adults. Anyway, we’re recruiting teenagers, not children.”

The attacks soon turned personal. “They said I was having an affair with a lightning practitioner, they doctored a video I appeared in, they reported me to the GMC. It was very harassing. The GMC said I didn’t have a case to answer.”

Research threatened

Dr Crawley runs the biggest CFS/ME service for children in the UK, seeing about 200 a year. “If the Lightning Process is dangerous, as they say, we need to find out. They should want to find it out, not prevent research.

“I expected families and patients to have a twisted view of research, given the amount of stuff [criticisms, personal abuse, etc] there is on the internet about CFS, but they don’t. We have to warn them there is this stuff out there, and they get very angry about it—they say we need answers and you mustn’t be stopped.”

Professor Wessely, whose research interests have moved away from CFS/ME, still sees patients and agrees that their attitudes are completely different from those of the campaigners. “I still do the clinic, and it’s perfectly fine. We’ve seen 2000 patients, with very few complaints. The service is the least complained about in the Maudsley [hospital].”

The underlying belief of the campaigners is that CFS/ME has a "real" cause, which would have been discovered by now if serious efforts had been made. So there was great excitement in 2009 when a US team from Whittemore Peterson Institute in Reno, Nevada, published a paper in *Science* claiming a link between CFS/ME and the XMRV retrovirus. The paper said that they had found the virus in 68 out of 101 CFS/ME patients tested. Annette Whittemore, whose husband made money in property and who has a daughter with CFS, had funded the institute. She was joyful at the discovery. "It ends the debate," she said. "CFS is not and never was a psychological disorder. Those who are ill have always known this."

Alas, at least 10 follow-up studies, including one in the *BMJ*,[4] have now failed to reproduce the original results, prompting *Science* to issue an "expression of concern." But some of those who failed to reproduce the finding have found themselves the object of the same intimidatory behaviour as the psychiatrists. John Coffin from Tufts University in Boston, whose team showed that XMRV is a laboratory hybrid, has said that nobody went in with the intention of disproving the link between CFS/ME and the virus. Criticisms of his motivations from patient advocates had been "painful" to read.

Professor Wessely says that scientists have been appalled at their treatment and that some have sworn never to work in the field again. "Many scientists end up being threatened if they publish any research that gives the 'wrong' results. So most just stop."

Pretty typical is a response posted on the ME Association website to the republication of a *Nature* story reporting the failure to reproduce the XMRV results. It quoted Jonathan Stoye, a retrovirologist at the National Institute for Medical Research, as saying; "It's a bust. People who are interested in this condition will have to move on." The comment, posted by somebody calling himself Soloman, reads: "Will HE move on to some decent research instead of just knocking down others' work? And what do we move on to—more nonsense from the psycho-terrorists?"

Dr Crawley admits she did get "very low" as a result of the pressure and was planning to leave the field. "But there isn't anybody else in my generation who's come in and stayed in. If I stop, they'll have won."

Dr Shepherd is more sanguine. "The problems don't relate to all researchers. There are some who would say they haven't had any trouble. It may discourage some people, those on the psychiatric side, because they know about White and Wessely and they know they're going to get the same flak. But what discourages people on the biomedical side is this atmosphere in laboratories that you shouldn't be involved with this at all if you want to advance your career, that it's all a psychiatric condition and there's no point in searching for a physical cause when we've had so many negative results."

Dr Shepherd is pleased by a new initiative by the MRC, which has set aside £1.5m for CFS/ME research. He credits Stephen Holgate, an immunopharmacologist at Southampton University, who set up an expert group to advise the MRC, with moving the process forward. Professor Holgate believes that a lack of good scientists working in the field has held up progress, and the new MRC funding is designed to rectify that. Proposals, which had to include at least one scientist who does not already work on CFS/ME, had to be submitted to the MRC by 7 June. Whoever wins the grants "will have tremendous support" from patient groups, Dr Shepherd promises.

Time will tell if his optimism is justified, but it does little to help those who have been categorised as enemies by the activists. The law appears relatively powerless, just as it did for many years during the campaigns against scientists working with animals.

"I regularly go to see a lawyer on the Medical Defence Union," says Professor Wessely. "They say, 'Yes, it is a gross libel. But if you took them to court, they'd love it. They'd get what they want.' I did get an injunction against the person who was comparing me with Mengele. That was a particularly nasty example, because my grandparents may actually have been murdered by Mengele—they were transported to the camp where he worked and never seen again."

The motivation of the most persistent campaigners puzzles those who are their target. "My gut feeling is that some don't even have this illness at all," says Dr Shepherd. "They have personality problems." Professor Wessely says: "They're damaged and disturbed, with an obsession about psychiatry. With these people, it isn't that they don't want to get better but if the price is recognising the psychiatric basis of the condition, they'd rather not get better."

Dr Hamilton has also been advised by lawyers not to answer complaints—"the complainant will simply twist anything you say." He says he is at a loss to know how to deal with them. "There's no morality here. The judicial review's wrist slap would have made anyone with any conscience stop playing this game. It hasn't. I get hate emails—that's what the delete button is for. The GMC need to realise they are losing the trust of the medical profession by its procedures. Very few doctors feel they will receive 'natural justice' from it."

As for Professor Wessely, he gave up active research on CFS/ME 10 years ago. He now specialises in the problems of war veterans. "I now go to Iraq and Afghanistan, where I feel a lot safer," he says.

Competing interests The author has completed the ICJME unified disclosure form at www.icmje.org/coi_disclosure.pdf (available on request from him) and declares no support from any organisation for the submitted work; no financial relationships with any organisation that might have an interest in the submitted work in the previous three years; and no other relationships or activities that could appear to have influenced the submitted work.

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3 Patients' power and PACE. *Lancet* 2011;377:1808.
4 Van Kuppeveld FJ, de Jong AS, Lanke KH, Verhaegh GW, Melchers WJ, Swanink CM, et al. Prevalence of xenotropic murine leukaemia virus-related virus in patients with chronic fatigue syndrome in the Netherlands: retrospective analysis of samples from an established cohort. *BMJ* 2010;340:c1018.

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