Cognitive–behavioural therapy combined with music therapy for chronic fatigue following Epstein-Barr virus infection in adolescents: a feasibility study
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Switched outcome measures, cherry-picked results and unfounded conclusions

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The study results essentially disprove the authors' own hypotheses about the benefits of cognitive and music therapy. The researchers have switched outcome measures, cherry-picked results and drawn unfounded conclusions that may cause patients being treated with inexpedient or potentially harmful treatments. This is yet another example of poor research that reflects the researchers pre-determined psychosomatic views rather than honest scientific investigation. ME-patients suffer.

Myalgic Encephalomyelitis (ME) has been classified as a neurological disease by WHO since 1969. In 2017 the US health authorities removed the advice about cognitive behavioral therapy and graded exercise therapy as treatment for ME. Every month, new research articles are published, consistently showing nonconformities in the immune system and in the energy production in ME-patients.

In this article, young people with chronic fatigue following an acute EBV infection were treated with a "recently developed mental training program", with elements of cognitive therapy and music therapy. (1)

The study refers to the disease CFS/ME although only 14% of the participants in the intervention group met strict (Canadian) CFS / ME diagnostic criteria. Participants were adolescents between the ages of 12 and 20 with prolonged fatigue following an acute EBV infection. The level of function at baseline was 8 000 steps per day, close to twice the level of mild degree ME as described in the articles' reference no. 34. (2)

Hypotheses

The study protocol hypothesizes that CFS / ME is a sustained arousal response, and that personality, emotions and psychological trauma contribute to disease development and maintenance. It is argued that cognitive behavioral therapy (CBT) and graded exercise therapy (GET) have a positive effect, and that no risk of side effects exists.

There is no basis in either research literature or in broad patient surveys for such claims. The authors refer to studies with major methodological weaknesses. Notably, in the PACE study, participants were defined as cured even though they had lower functional levels at the end of the study compared to baseline. The hypothesis was that ME patients have activity phobia, an hypothesis not supported by the results. (3)

In the FITNET study, the intervention had no long-term effect. The objective outcome measures which demonstrated no improvement were omitted in the article. (4)

In the SMILE study, no objective endpoints were used. It has a 3 000-word long correction due to violation of basic ethical and methodological principles. For example, half of the participants were registered retrospectively, and the endpoints were changed midway through the study. (5)

A Cochrane review has been revised several times and is now under a new, complete update. (6)

Health authorities, including the Norwegian Health Directorate and the Center for Disease Control in the US, state that Post Exertional Malaise (PEM) is a cardinal symptom of ME. The studies referred to above did not use diagnostic criteria sets with PEM as a mandatory symptom. Indeed, there are no studies showing that CBT, GET or similar interventions are effective in treating ME when using criteria with PEM as an inclusion criterion.

Intervention

The purpose of the Malik et al. study was to see whether a mental exercise program with elements from cognitive therapy and music therapy could improve the level of function. The training program has, according to the

research protocol, many similarities with the pseudoscientific method Lightning Process.

Before the intervention, the participants and their parents were taught that personality, thoughts and feelings can influence the development of the disease. They were informed about the importance of motivation, and that an increasing effort was required in order to change the “situation” and their "negative illness behavior". This was substantiated by a testimony from a recovered person.

The "situation", which was chronic fatigue following an infection, is described by the research team as negative illness behavior, disease attribution, and "avoidance". The hypothesis is that this will contribute to maintaining the fatigue. The parents became involved as – according to the protocol - they can reinforce negative illness behavior and attribution, which in turn could have a negative impact on the prognosis of their child.

The therapy aimed to control negative thoughts and emotions that could hinder higher activity. Music was used to evoke good feelings. The therapy was individually tailored, and the therapists knew in advance the results of extensive psychological tests that had been taken six months earlier. During the program, the focus was shifted towards the personality of the children, the parents, and the family dynamics. Thus both participants and their parents were implicitly made co-responsible for the "situation", the outcome of the therapy and the study results.

Results

According to the protocol, the results of a number of biomarkers were to be reported. However, outcome measures have been switched. The study reports only one objective outcome measure: the number of steps per day. After 3 months, the intervention group experienced a significant decline of 11% or 23% (the latter decline when the “per protocol” method was used). Thus the mental training program provided no increase in measurable activity. On the contrary, the results showed a reduction in the objectively measured activity level. This surprised the researchers but did not seem to change their conclusion or in recommending the intervention and further studies. Rather, they speculate that the reduced level of function is due to the participants not being treated with even more therapy; with GET.

The article defines "healthy" as a certain drop in subjectively reported fatigue. The study concludes with 65% recovery in the intervention group after 15 months. The actual results show that 8 participants recovered - compared to 7 in the control group, but the share is higher due to high dropout rate in the intervention group. The definition of healthy is post-hoc, and this becomes the main selling point in the abstract.

Similar to the PACE study, this study invents - after the data are known - a new measure that fits their initial hypothesis, while the main and objective outcome measure shows the opposite result. Informed readers can make their own judgement on this research practice.

At the same time, participants in the intervention group became more depressed, more exhausted, had more pain and a decrease in the level of function, although the small number of participants make all differences statistically insignificant, with an exception for the reduction in steps after three months for the intervention group. These results are suppressed in the abstract and conclusion. Instead, the researchers cherry-pick one subjective outcome measure to oversell results. The only objective measure disproves their conclusion. Moreover, the study would have been more trustworthy if the results of biomarkers and clinical examinations at follow-up had been included – as promised in the research protocol.

The results must also be seen in the light of the fact that 38% of the participants in the intervention group withdrew from the study. The researchers claim the high dropout rate to be due to fear of school absenteeism. Other more self-critical but plausible reasons, for instance that some participants became unwell of the therapy, are not discussed.

As user representatives, the organization Recovery Norway was involved (again contrary to the research protocol, which states that the Norwegian ME-Association would be involved). The organization, whose representatives were involved in the design of the study, was formally established in January 2018. The study design dates back to June 2015. The organization was started by, amongst others, a group of Lightning Process instructors, and a major activity has been the marketing and lobbying for the method. Again, the user group was selectively picked to support the approach, with some retrospective justification.

The article is peer reviewed, but the review process seems not to provide the scientific confidence one expects from a good journal. The first reviewer is Maria Loades, a researcher who has the same approach to ME as the authors. The second review was by an IT researcher who had only read the abstract. Both stated that the researchers’ conclusions were exaggerated.

In conclusion, even with the many shortcomings, on balance the results of the study disprove the authors’ hypothesis. Normally one would expect scientists to look for alternative explanations. In this case, the researchers interpret them as positive and believe the study justifies a full-scale clinical trial.

Consequences

This study, authored by a well-regarded yet controversial research team in Norway, might be used as a basis for decision-making by the health and welfare authorities and be referred to as basis for recommending or even mandating cognitive treatments for ME. This can lead to patients being treated with inexpedient or potentially harmful treatments.

A thorough analysis of the article shows that the study is yet another example of poor research seeking to justify an outdated approach to ME. (7)

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