**SUPPLEMENT**

The impact of a 12-week open-label placebo treatment on headache days in episodic and chronic migraine: A study protocol for a parallel-group, multi-center, randomized controlled trial

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Video shown to the patients (translated from German)

Author U.B.: Dear patient, I am pleased that you are taking part in this study. At University Medicine Essen, we offer comprehensive multidisciplinary medical care to those with migraine but also aim to understand pain through scientific research. Recently published international studies suggest that both acute and chronic pain can be reduced significantly when treated with placebo tablets. These findings have also found their way into the international media. The following article by an American news channel provides a nice summary of the findings.

Speaker: Can the knowledge of taking a placebo actually improve your health? Studies show that it is possible. Some patients may no longer need proper medication. More and more patients are prescribed placebos.

Speaker: It looks like a normal pill but turns out to be a placebo. These, doctors confirm, can be used to treat some of the most common diseases.

Patient: I felt fantastic, better than ever.

Speaker: For Linda Buonanno, the placebo pills worked. She suffers from irritable bowel syndrome, which often develops without warning.

Patient: I felt terrible, I had no life. I couldn't plan or do anything.

Speaker: When she found out about the study, she applied immediately.

Patient: I was very happy.

Speaker: But she was shocked when she heard that she was getting a placebo instead of real medication. We said: You don't have to believe it, just do it. Even if it's kind of a crazy idea.

Patient: I was so disappointed, I said: A placebo? A sugar pill, is that a joke? It's never going to work.

Speaker: But it worked. Her symptoms disappeared.

Patient: I'm making plans again, I don't have to worry anymore. I live my life again.

Speaker: In another study the same was done with migraine patients. Their pain was reduced by 30 percent.

Expert 1: This is an incredible thing.
Psychologist Dr Stratyner says other factors may play a role.

I think the patients might think: Hm, I am wondering if it really is a placebo. Maybe I'm just being told that.

Kaptchuk says that there are physiological reasons why placebos activate the same neurotransmitters as many powerful drugs.

We have our own pharmacy for certain diseases.

But there are limits to the effect of placebo.

We will not be able to shrink a tumor with the placebo pill.

But for certain diseases, placebos could fundamentally change the treatment.

If a placebo helps, this would be the best approach instead of putting patients on strong medication for a long time.

As this summary shows, placebo treatment may have a positive effect on various chronic pain syndromes. We would like to investigate this phenomenon in the current study. In addition to the effect on headache itself, we would also like to examine the influence on your well-being, i.e., your functional disability due to migraine.

Furthermore, by accompanying experimental methods, such as magnetic resonance imaging, we hope to better understand who benefits most from such a therapy and which mechanisms underlie the possible effects of placebo tablets. Thank you very much for your participation.