Homeopathy Works for Attention Deficit and Hyperactivity Disorder (ADHD)

Description

…and is helpful within limits in healing wounds.

Homeopathy and the results of two meta-analyses

A few years ago, the leader of the German Green Party, Robert Habeck, proclaimed in the heart of conviction, that homeopathy is no more than placebo. Many politicians and medical administrators dutifully agreed. Our health blabbermouth, Health Minister Lauterbach, wants to pour this into a set of rules and remove homeopathy completely from all medical books. Since then, it has become politically incorrect to be pro-homeopathy.

I still think homeopathy is good and have done for a long time, thus I have also been politically incorrect for a long time. Because I am less interested in the opinions of people who have only a very limited idea of the matter and certainly not in the arguments that proceed from unreflected theoretical presuppositions. What I am chiefly interested in, is the data. Because I am politically incorrect, a foundation that supports homeopathy a while ago removed me from my role as a blogger, where I used to comment on new data and studies on the blog Homöopathie.info.

Nevertheless, I like homeopathy and engage with it when the opportunity arises, or I am asked. I take the publication of our new meta-analysis on the efficacy of homeopathy in attention deficit hyperactivity disorder in children [1] and our somewhat older meta-analysis on Arnica in wound healing [2], published last year in Frontiers in Surgery, as an opportunity to draw attention to homeopathy.

I would also like to take this opportunity to pass on some methodological knowledge on the subject of meta-analyses in my newest chapter of my methodology blog.

I will start with a small political preface to help understand the general situation, then for those who do not yet

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know much about it, a few words about homeopathy in general.

Current political framework of homeopathy

I started my scientific career with homeopathy research. In 1986, I published my diploma thesis on the subject, which I submitted to the Psychological Institute of the University of Freiburg in 1984 [3]. I made my PhD with an experimental homeopathic drug trial [4, 5], and my habilitation built on a larger post-doctoral project in which I presented a clinical study and further drug trials [6-9]. So I may claim: I know my way around a bit. I have been following the situation ever since. What I noticed over the years: In the beginning, we, the complementary medicine researchers, and especially me with my homeopathy research, were the sonny boys of the German press. There were friendly interviews, in newspapers, on radio programmes, sometimes for film. The journalists were open and receptive. They reported sympathetically and factually.

The mood changed at the beginning of the new millennium. I first noticed it in England when I went there in 2005. The so-called „sceptics“, a scientistic belief community [10], see also this earlier blog, started agitating against complementary medicine in general and especially against homeopathy. Nothing in particular had happened. There were no new studies at the time, except those showing that homeopathy worked well in practice. There were a few benevolent tones from the research department in Brussels that they wanted to fund a study (but to my knowledge, nothing ever came of it). There were nice hearings in the European Parliament from time to time. But nothing really that could have made the sceptics‘ noise understandable or that would have given them cause to do so.

Except: In England, some universities opened their doors with postgraduate courses. And: homeopathy became more and more popular with the public. This, too, was probably a cultural rather than an economic or politically driven development. A small vignette: At that time, in the early 1990s, I was asked by the Federal Association of Guild Health Insurance Funds to evaluate a trial procedure on homeopathy and acupuncture and suggested a long-term observational study because such data did not yet exist [11]. Such trial procedures are instruments of the health insurance funds to test novel procedures and then, if necessary, to bring them into the care system. However, homeopathy was already in the care system, so why suddenly test it? The chairman of the IKK Federal Association wanted to make a political move. He had a relatively serious back problem, if I remember correctly. The doctors said: operate and stiffen it, otherwise he would soon no longer be able to move without pain. A harsh word for an athlete. He resorted to homeopathy and was treated by a famous homeopathic doctor, who apparently cured him of his pain and thus his suffering with a few globules of a high potency. Surgery unnecessary, expert opinion for the bin.

At the end of the 1990s, in contrast to this spirit of optimism, the sceptic movements began with their campaigns in England, and a little later in Germany as well. These were enthusiastically received by the press, presumably also because some colleagues there in the science departments were close to this movement and were happy to distribute the dossiers. The resistance became really fierce in 2011, when we had the first postgraduate course for doctors at the Viadrina European University, which also included homeopathy. The Brandenburg state government opposed it, the sceptic movements ran riot, and so did the press. In 2016, the faculty closed our course. I described this in more detail in a book chapter [12].

Interestingly, around this time, in 2016, a market research report by a US agency became available that predicted significant growth for homeopathy worldwide, driven by developments in Germany: „If the number holds true, the market, which valued at US$ 3,867.7 mn in 2015, is expected to reach US$ 17,486.2 mn by 2024.“ [13] So that would have been a growth of just under 5 times, which was predicted there. What industry could make such a claim? (To access the whole report costs several thousand dollars; I couldn’t afford that, so I only know the summary. But I assume there are people who look very closely at such reports). Even if the total sums are tiny

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compared to the figures of the big pharmaceutical companies, it is no insignificant competition for the conventional industry. Especially since it could have been accompanied by a cultural change in medicine, which I have described and called for time and again [14]. I deliberately say „could have“, because as we know, this cultural change did not happen.

These associations in terms of time and content suggest to me that these sceptic actions against homoeopathy were and are not only to be understood intrinsically, as a service to scientific truth, but that they served and still serve manifest economic interests, and that they were perhaps ordered and paid for.

Therefore, political statements in this regard are above all foolish or perfidious partisanship in the interests of the pharmaceutical industry. They have nothing whatsoever to do with caring for patients or protecting the general public, as they are often sold as. For homeopathy works quite well, as we shall see in a moment. Before that, for those who don’t know, a few words about homeopathy itself.

Homeopathy – a very brief introduction

Homeopathy uses a therapeutic principle that is as old as our culture. Similar things should be cured with similar things, said the founder of homeopathy, Samuel Hahnemann (1755 – 1843). He did not invent this sentence. It is already mentioned in ancient times, e.g. by Hippocrates, the ancient physicians and by Paracelsus. Its origin is the myth of Telephos (Figure 1):

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Figure 1 – Odysseus scraping rust from Achilles‘ spear into the wound of Telephos – relief in Herculaneum.

This myth is reported by Euripides, but has survived only in fragments [15]. Before the Greeks reached Troy, they landed too far south, in the land of the Mysians, and got into a scuffle with them in which Telephos, the king of the Mysians, was injured. The Greeks moved on, the wound festering. When Telephos was at a loss, he did what all Greeks did when they were desperate: He sent to the Delphic Oracle. The oracle told him: „Ho trosas kai iasetai – the one who struck the wound will heal it.“ The riddle was solved by Odysseus. He took the spear of Achilles, who had struck the wound, scraped its rust into Telephos‘ wound, which then healed. This myth was widespread in ancient times, as attested by the relief found in Herculaneum (Fig. 1; there is a similar image on the Pergamon Altar in the Berlin Museum, if I remember correctly).

Hahnemann certainly knew this therapeutic principle. His merit was to have discovered an operationalization, i.e. a concrete application. Namely, he interpreted the „similar“ not as a similar substance, such as Paracelsus, but as „similar symptoms“. He had also discovered this by chance through experimentation. He had taken China bark, a widespread prophylactic and remedy against fever at the time – it was added to water as quinine in the tropics, from where tonic water got its bitter taste. And he discovered in himself sensations similar to those of fever [16]. This is important: it was not the temperature that changed, but the sensation, i.e. the subjective symptoms. Hahnemann concluded from this: „What can produce such symptoms in a healthy person can be applied to similar symptoms in the case of illness. Cure similar things with similar things.

He then took many known medicinal substances and plants and noted down the symptoms. Some of them were

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already known from toxicological observations. Others he „tested“, as it was called, by taking them himself. In the process, he discovered a second important principle of homeopathy, the principle of potentiation. Hahnemann was also a pharmacist and diluted the poisonous substances properly so as not to harm himself or his test subjects. Intuitively, he did this step by step, in a ratio of 1:100, and shook the substances thoroughly in between. He discovered that the more they were diluted and shaken, the more effective they became. At that time, Avogadro’s number, which indicates how many molecules of a substance are contained in one mole of a substance, was not yet known. If you dilute a substance 12 times in a ratio of 1:100 or 24 times in a ratio of 1:10, then theoretically there are no molecules of the original substance left (of course there are still impurities, abrasion from the glass and perhaps a few carried-over molecules, but we will ignore that now). This was intuitively clear to Hahnemann, although he could not yet calculate it. That is why he also called this process „dynamizing“ and spoke of a „spirit-like effect“ of the remedy, i.e. one that is no longer bound to the substance itself.

From my point of view, it is this theoretical imposition that causes a stir in our present-day materialistic culture. Because the assertion is: something works here that is no longer materially present. Whatever that is supposed to be. I don’t want to deal with this question in this blog, maybe later on. Let us state: The actual offensiveness of homeopathy is the assertion of an effect of something that is not materially present. If one allows this idea, then not only does the materialistic paradigm of clinical pharmacology topple, but then we would also have to give some further thought to whether a materialistic world-view is really as scientifically sound as some think. Therefore, the imposition of homeopathy is above all a theoretical provocation. For whether such substances can work or not is – see below – a purely empirical question and not a theoretical one.

Hahnemann and his disciples found: yes, they work. Hahnemann worked for a long time mainly with the potency C30 and later used all kinds of potencies, C 125, C 98, sometimes also low potencies like C1 to C11. A potency C30 is one that has been diluted and shaken 30 times in increments of a hundred (1:100, „centum“ means „hundred“ in Latin, hence „C“), i.e. a dilution of 100^{-30} or 10^{-60}, i.e. a 0, with 60 digits after the decimal point to indicate the substance content, or: nothing. C30 is a standard potency today, and many homeopaths work with potencies up to C 1,000 or beyond (these potencies are usually prepared differently, so that often traces of the starting material might still be present, but I consider this discussion misleading and therefore do not take it further).

The homeopathic pharmacopoeia, or „materia medica“, contains more than a thousand substances, i.e. substances that have been administered in potentized form to healthy people and have produced symptoms that can be used to indicate the remedy in the case of illness. Such drug trials or homeopathic pathogenetic experiments, in which healthy people take potentized substances and note the symptoms, are still done today, thus expanding the treasure trove of remedies. In practice, however, mainly about 150-200 very well tested substances are used. These are also the ones that, according to the German medical training regulations, should be mastered by those who are allowed to print the additional title „homeopathic doctor“ on the practice sign.

The art now consists in finding the right medicine for a concrete, individual patient. This is done by „individualization“: by looking for the important, characteristic symptoms in the concrete case and a remedy that combines as many of these symptoms as possible with the picture that is known from tests. Homoeopathy is thus essentially an art of pattern recognition, in which the symptom picture of a sick person is brought into agreement with that of a remedy. To do this, the symptom picture of the patient must be well known, which is why homeopathic physicians often spend a lot of time on the anamnesis. And the medicines must be well known. It is true that lists of symptoms, so-called repertories, help in the search. But these are only aids. Without a good knowledge of the medicines, they are of little help. The symptoms have to be ordered and weighted. This is, apart from a good conversation, the real art.

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If you find the right medicine, you can in principle treat all diseases. Success will be achieved if the organism is still capable of regulation, i.e. if it can initiate healing processes on its own. This will be difficult or impossible with all pathological processes in late or final stages, such as cancer, dementia, etc. In younger people, especially children, homeopathy usually works very well.

Meta-analysis of homeopathy for ADHD in children

And this is where our meta-analysis comes in. Because there are now seven randomized trials, five of them double-blind and placebo-controlled, that have investigated individualized homeopathic therapy for ADHD. We included six of these in our meta-analysis; the seventh was an early, small, methodologically poorly described pilot study which, moreover, did not use a useful outcome measure and therefore did not meet our pre-formulated criteria.

The project is integrated into a large framework project in which we examine those disease entities for which there are several studies in meta-analyses. There are many hundreds of randomized, double-blind, placebo-controlled studies of homeopathy in any disease entity. The entire database of homeopathic intervention studies contains over 600 studies. These include, of course, those that are non-randomised and those that have not double-blinded controlled against placebo, but against standard treatment. But there are more than 250 placebo-controlled studies. The opinion that there are no studies, which is often and readily propagated by people who do not know anything about the subject, is incompetent because it is poorly researched and wrong.

In the case of ADHD, as I said, there are 6 useful studies. We have summarized these 6 studies. Meta-analysis is a statistical accumulation method invented by psychologists in the 1970s to summarize the results of psychotherapy studies [17]. The idea behind it is simple. Each individual study is a snapshot in a universe of possible outcomes, and therefore subject to uncertainty. If you combine these different studies – those with strong and those with small effects, those with supportive and those with contrary results – you end up with the „true“ effect of an intervention. Therefore, in Evidence Based Medicine (EBM), a meta-analysis or a systematic review is also a data element with the highest reliability. And this is used, for example, as the basis for decisions in the German Federal Joint Committee on which interventions are reimbursable. Theoretical considerations, such as whether we understand how an effect comes about, explicitly do not enter into such considerations. Instead, it is a purely empirical summary of study results.

So we pooled these 6 studies and found a significant effect size of $g = 0.542$ against all possible forms of control and of $g = 0.6$ against placebo. The average size of the studies was small, 52 participants. The size of the studies enters into a meta-analysis as a weight, which means that large studies receive more weight, small ones less. In addition, the statistics of meta-analysis mean that the statistical range of variation is larger for smaller studies. In other words, when you accumulate small studies, it tends to be harder to demonstrate statistical significance. In our case, the significance was clearly significant ($p < .001$) with a z-value (i.e. an ordinate value of the standard normal distribution) of 4.61 for all studies and still beyond the conventional significance limit for the placebo-controlled studies with $z = 2.16$ and $p = .03$.

It is argued that the homeopathic studies are too small. This is often correct. However, this argument is only partially convincing. For the advantages that large studies have – sufficient statistical power with small effects and thus also smaller fluctuations in statistical testing – are only really relevant when the effects are very small. This is exactly why meta-analyses were developed, to accumulate statistical power across different small studies. The result of this aggregation is the final statistical result. In this case: significantly superior to placebo and controls.

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So again for all the sceptics to take note: Homeopathy is significantly better than placebo in double-blind studies for the treatment of ADHD in children, according to the universally accepted methods of EBM. And it is better than all controls, including active control.

Two studies are pragmatic, unblinded trials conducted in England. There, the control was a typical English outpatient treatment with a general practitioner. This usually includes nutritional counselling, i.e. dietary advice and lifestyle counselling (less cola, lots of vitamins, less television, etc.) and also Ritalin or similar substances. Ritalin is an amphetamine-like drug that acts on the dopamine receptor. It is assumed that ADHD is caused by a disturbance in the dopamine balance, and Ritalin intervenes in this. Unfortunately, like all substances with a central nervous effect, it leads to a habituation effect and has strong side effects [18, 19]. This is the reason why many parents want to get away from it, and also the reason why homeopathy is popular as an alternative. Because: Ritalin has shown no effect in long-term studies compared to so-called community controls, i.e. treatment within the framework of counselling [20]. There is an effect in the short term, but in the long term it is averaged out, presumably because children who originally received Ritalin stop because of the side effects and others who were originally in the control start using it.

So homeopathy, our data show, is a viable alternative. The longest study also had the largest effect of over one standard deviation (I'll get to the metrics in the methodological chapter). It lasted over a year. Most of the studies lasted between 2 and 8 months.

Some of these studies were conducted in Bern. There, the Bern working group at the Chair of Complementary Medicine at the University developed a new study design: The children first received an open treatment in which they searched for the right medicine and only when this was found did the double-blind phase start, in which the children then continued to receive either the right medicine or a placebo. I think that's a clever design. Because, as I said, the trick is to find the right drug. And for that, the doctor needs the feedback from the patients. If the drug is given under blinded conditions, then this is difficult because the doctor and patient do not know whether a lack of efficacy is due to the fact that the drug was wrongly chosen or was not given in the first place [21].

Although it is difficult, there are also long-term studies under strict double-blind conditions, as I said here the longest over a year, with very good results. So if you don't want to give your child Ritalin, you could try homeopathy. The data suggests that this can work.

Now some will ask: which medicine to take? The answer is: the most appropriate, the most similar. Therefore, one should not play around or take the one that helped the neighbour, but go to a good homeopathic doctor. Yes, and that, dear medical associations, is also the reason why the additional training and designation „homeopathy" should not be abolished, but on the contrary, strengthened.

Meta-analysis of Arnica in surgical wounds for wound healing

As I said above, this meta-analysis is part of a larger project planning to analyse all disease entities for which several studies are available. One prerequisite of meta-analyses is that the research question is reasonably homogeneous. Although one can also ask, as previous meta-analyses have done: Is homeopathy better overall than placebo? The answer to this is: yes [22]. But clinically such analyses are not very productive, because all kinds of diseases, study types and homeopathy applications are mixed. Therefore, meta-analyses have recently tended to be based on well-defined questions. And our analyses examine either individualized homeopathy or very clear, proven indications.

One such indication is: Does homeopathic Arnica help in wound healing after surgery? [2] The answer to that is: possibly, but maybe Arnica is not the best option. For this, I need to elaborate a bit and say something about

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Arnica (Figure 2).

Figure 2 – Arnica montana

Arnica is an ancient medicinal plant. It is also called the „fall weed“ or the „mountain weed“. It is often found as an extract in old tinctures for rubbing into aches and pains, although external application is not usually favourable because it can cause skin irritation. Arnica grows in the mountains, at altitudes between 800 and 1400 m approximately, depending on the climate. I have often seen it there on mountain hikes, but not at lower altitudes.

This old tradition is based on the experience that Arnica can be helpful for sprains, bruises and bleeding inwards, like bruises, which is why the homeopathic preparation Arnica also has its „proven indication“. That is the name given to clinical situations where the individualization of homeopathic remedies is less important because the situation itself has a clear indication for a remedy. Internal bleeding, for example, is an indication for Arnica. This occurs in sprains, strains, bruises and contusions, in fact in almost all injuries. This is why the remedy is very popular as a first aid remedy for all injuries.

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This has also led to the fact that Arnica has often been used in studies where, for example, bleeding was to be expected after operations and the healing of wounds was to be accelerated.

Therefore, there are relatively many studies for the indication „Arnica for wound healing after operations“. We found 23 studies on this topic in our search. Calculated over all studies, the effect is rather small and disappointing, namely g = 0.18 (z = 1.9, p = .059). In meta-analyses, if the effect is heterogeneous, i.e. if the effect sizes scatter strongly around a mean value, sensitivity analyses are carried out and an attempt is made to find out where this scatter comes from. In the Arnica studies, we see a variation of effect sizes from g = 2.01 to g = -0.2. If we separate the studies according to different categories, we see that most of the studies were of a preventive nature, i.e. gave Arnica for prevention. These had a small effect of g = 0.2, but it was still heterogeneous and not significant despite the large number of studies. Better quality studies showed higher effects than poor ones, an indication that the effect is not an artefact of methodological weaknesses of studies. What I personally find interesting is that the studies that test against active control, mostly aspirin, ibuprofen, diclofenac or similar analgesic, anti-inflammatory substances, produce a positive effect size. Those studies that simply test against „standard care“ – it is not described what this means, but presumably includes analgesic drugs – even have the largest effect with g = 0.5, which is significant.

The efficacy paradox

This is a somewhat paradoxical result that is often found in homeopathy research: Testing against placebo shows a smaller effect than testing against active control, although one would have to assume that active control was also tested against placebo at some point and found superior. To put it another way: If homeopathy is placebo, as is often claimed, then this placebo is more effective than active standard treatment in wound care. This is a paradox that I once proved times ago with the name „efficacy paradox“ [23]. I illustrate it again graphically below (Figure 3):

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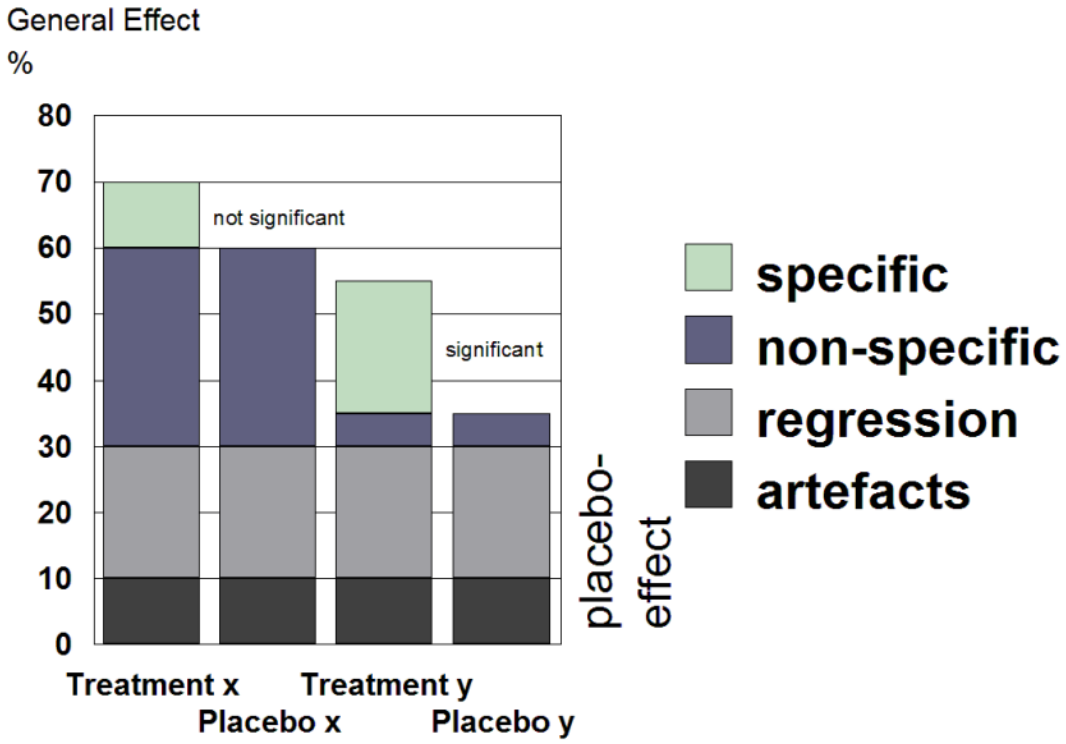

Figure 3 – Schematic representation of the efficacy paradox thought experiment.

A treatment that is „effective“ (treatment y) because it is significantly better than placebo can still be worse than treatment x, which is considered „ineffective“ because it is not superior to placebo. This is because in classical testing of treatments against placebo, only the difference between placebo and treatment is ever examined. If this is significant, we speak of „effective“. If it is not significant, we speak of „ineffective“. The paradox comes from making an assumption that is often wrong: that the placebo component of the treatment, what is called „non-specific“ in Figure 3, would be constant. While other artefacts, e.g. the statistical regression effect or measurement artefacts, are usually comparable in studies with similar patients and diseases and outcome parameters, the non-specific or true placebo effects, which stem from psychological effects of expectation, are anything but. In homeopathy and other complementary medicine methods, they are often much greater. Therefore, the overall treatment success – and that is the only thing patients are interested in – is often very large, while it is very difficult to prove the difference to placebo.

For this reason, it can also happen that meta-analyses, as above, only with difficulty secure an effect compared to placebo, while an effect compared to active control is even greater. Paradox. But that is the way of the world.

Interestingly, the effect size increases over the years in the studies that were controlled against conventional drugs: by 0.03 units every year. This so-called meta-regression can explain the heterogeneity of the studies. Why does the effect size increase? It is difficult to say. Maybe the newer studies measure better. Maybe there are other reasons. Maybe the effect of conventional medicines is decreasing.

Would I recommend homeopathy for wound healing or prevention? Probably not. Because the fluctuations, especially some negative effects, show in my opinion that Arnica can sometimes do harm, namely when it is not

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indicated or is given too early. Apparently it interferes with the flow properties of the blood. This can be deduced from some basic research work [24]. And if this happens too early, then the bleeding increases rather than decreases and the inflammation does not decrease but increases.

This also points to a fundamental problem: such „proven indications“ are only proven within limits. Sometimes one has to consider other medicines for injuries, especially if they are caused by a sharp wound, as in an operation, for example Staphisagria. Or if nerves have been injured, Hypericum. So here, too, one would actually have to individualize. But there are hardly any such studies in surgery.

Would I take Arnica myself if I had an injury? Yes, definitely, if the injury was accompanied by a significant bruise, for example, or produced some other form of internal bleeding. For example, a long time ago I treated a torn ankle ligament that I sustained during sport with a mixture of Arnica and Rhus Toxicodendron myself, without any further measures. I went hiking again after a few days. The swelling and pain were gone.

Something else can be seen in this data-set, which I have often observed: There are always extremely strong effects in homeopathy research that surprise everyone who is familiar with such studies. In conventional research they are not known to this extent, it seems to me. But if you try to repeat them or capture them, they disappear. For example, if you compare only the placebo-controlled trials over the years, there is a slight downward trend overall, but it is not significant in the meta-regression. But more interesting is the pattern (Fig. 4):

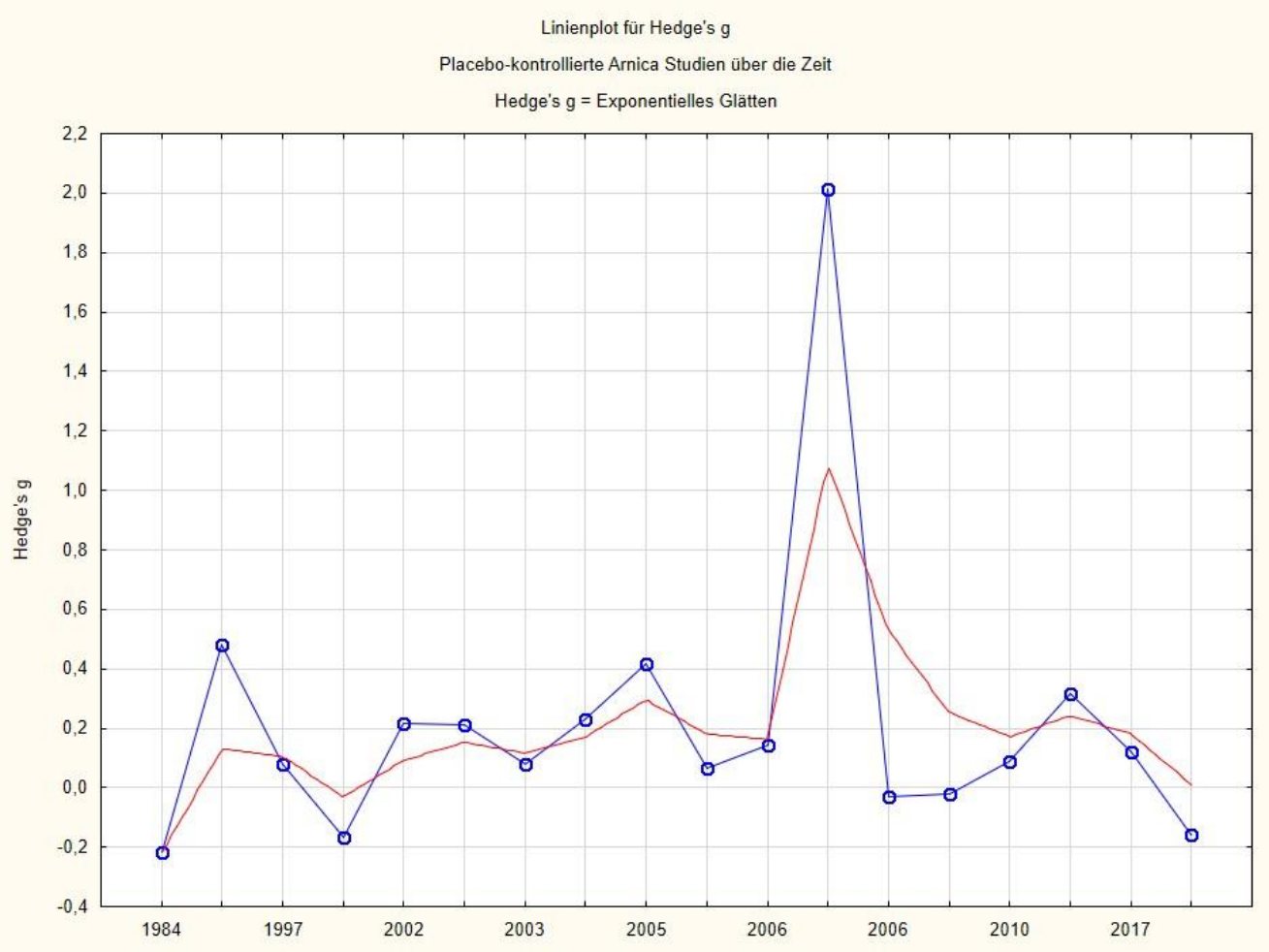

Figure 4 – Effect sizes in homeopathic placebo-controlled Arnica trials over time; blue line: effective data; red line: smoothing.

One can see: There is a slight fluctuation around the zero line, with a large outlier upwards. After that, the effect

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size drops drastically, to recover a little, then to drop again. This pattern is most clear in this sequence. We are dealing here with very similar studies that keep looking at the same thing, in this case Arnica for wound healing, in studies on surgery.

Such data have convinced me that we are not dealing with a causal, i.e. stable effect in homoeopathy, which would always and everywhere be causally available, baked into the globules, as it were, and isolable in studies. [25] Within limits, this can be done, as our meta-analyses show. But in the long run, the study model of the placebo-controlled study can only capture the effect of homeopathy to a borderline degree. Is homeopathy therefore a placebo? I think not. Is it provable that homeopathy is not a placebo? Sometimes, as in our ADHD meta-analysis.

Again, in other words, I think we are definitely dealing with a very specific effect with homeopathy that goes beyond placebo. It is dependent on homeopathy being used correctly and finding the right medicine.

Probably homeopathy is a good example of a whole class of effects that are quite real but are not in our causal availability in the same way as, say, light switches and electricity, cars and motors, or other reliable causal effects that we know. They are more like synchronistic coincidences that most people are familiar with [26]. An example of such a synchronistic coincidence would be the situation where I desperately need a piece of information but don't know where to get it. And by chance, the neighbour brings me a magazine that contains exactly this information. Such effects are most likely systematic, but not causal. This was already seen by C. G. Jung and Pauli, who dealt with these phenomena [27].

Does this make them useless or scientifically uninteresting? No, quite the opposite. Scientifically, I think they are very interesting because they represent anomalies and point us to areas that we have not yet understood well. And practically they are very useful. This is shown above all by the fact that homeopathy studies in direct comparison with conventional treatment very often show, reliably in the case of Arnica, stronger effects than conventional treatment.

So with homeopathy we are dealing with a form of treatment that is at least as good as conventional treatment, but is less easy to grasp causally. You have to think a bit outside the box in order to understand it. It took me a few years to do that, too. Welcome to the new world of thinking.

To complement this post, there is a new chapter in the methods blog that goes deeper into how meta-analyses work: (23) How do meta-analyses actually work?

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