

# The Swedish View on the Placebo

## PLASEBO ÜZERİNDE İSVEÇ GÖRÜŞÜ

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### Abstract

**Objective:** The aim of this project was to investigate if and how the view on the placebo has changed in Sweden during the last 50 years.

**Material and Methods:** To perform this research, we perused the Journal of the Swedish Medical Association (in Swedish: *Läkartidningen*). The material consists mainly of lead articles from this Journal (*Läkartidningen*; abbreviated: LT), but a significant number of other sources have also been consulted.

**Results:** The first article containing the word "placebo", although having nothing to do with the placebo as such, was published in 1959. Within is merely stated that methods have been developed which are suited for statistical processing, and that the placebo may be used as a control. The first time in a LT that the placebo is discussed as an entity is in 1975. The author writes that the "placebo effect" can probably be explained with regard to the intricate interplay between the nervous system and hormone-producing organs. This view has since then been widely held by many scientists. L. Sachs and K. Szybek hold different angles of approach. The former emphasizes the social and cultural dimension for the explanation of the placebo effect, and thereby dramatically widens the realm of the Swedish discussion. The latter attempts to explain the placebo effect from a psychoanalytical point of view. Both of them put great weight in the two other mechanisms frequently referred to over the years (i.e. expectation and conditioning).

**Conclusion:** In recent years, the debate over the placebo has been intensified with one side claiming that the placebo is nothing more than a myth, and the other asserting that the placebo effect is a real and important force to be reckoned with. Judging from the articles, most Swedish investigators of the subject adhere to the latter view.

**Key Words:** Placebo, placebo effect,  
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### Özet

**Amaç:** Bu çalışmanın amacı, son 50 yıl içinde İsveç'te plaseboya bakış açısının değişip değişmediğini ve nasıl olduğunu araştırmaktır.

**Gereç ve Yöntemler:** Bu araştırmayı yaparken Journal of Swedish Medical Association (*Läkartidningen*) üzerinde çalışılmıştır. Çoğunlukla bu dergiden (*Läkartidningen*, LT olarak kısaltıldı) alınan makaleler materyali oluşturur, ancak önemli sayıdaki diğer kaynaklara da başvurulmuştur.

**Bulgular:** Plasebo sözcüğünü içeren ilk makale 1959 da yayınlanmakla birlikte plasebo ile ilgili değildir. Sadece istatistiksel verileri değerlendirmeye uygun olan yöntemlerin geliştirilmesini ifade eder ve araştırma yöntemlerinde kontrol olarak plasebo kullanılır. Aslında plasebonun LT'de ilk kez tartışılması 1975 dedir. Yazar, plasebonun etkisinin büyük olasılıkla sinir sistemi ve hormon üreten organlar arasındaki karmaşık olan karşılıklı etkileşimle açıklanabileceğini yazar. Bu görüş o zamandan beri geniş çapta birçok bilim adamı tarafından desteklenmektedir. L. Sachs ve K. Szybek yaklaşımı farklı açılardan ele alırlar. İlk söylenen plasebo etkisinin açıklanmasında sosyal ve kültürel boyutun vurgulanmasıdır ve tartışma alanını çarpıcı bir biçimde genişletmiştir. Daha sonra plasebo etkisinin psikoanalitik açıdan açıklanmasına çalışılır. Her biri yıllardır sık sık söz edilen beklenti ve koşullanma gibi diğer iki mekanizma üzerinde ağırlık oluşturur.

**Sonuç:** Son yıllarda plasebo üzerindeki tartışma tek bir sonuç üzerinde yoğunlaşmaktadır. Plasebonun mitten daha fazla bir şey olmadığı iddia edilmesi ve diğeri plasebonun etkisinin dikkate alınması gereken gerçek ve önemli bir güç olduğudur. Makalelere göre, konu hakkında birçok İsveç bilim adamının son görüşe bağlı oldukları hükmüne varılmıştır.

**Anahtar Kelimeler :** Plasebo, plasebo etkisi,  
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The word placebo is Latin, meaning "I shall please". It can be traced to a vesper in the Roman Catholic Service in the 14<sup>th</sup> century, "Placebo Domino in regione vivorum", which can be translated to "I shall please the Lord in the land

of the living.” In common speech, it was used as a synonym for flatterer, sycophant or parasite. 500 years later, in Hooper’s Medical Dictionary, it was defined as an “epithet given to any medicine adopted more to please than to benefit the patient”. But the notion that perhaps it is not in fact the medicine that the patient receives that cures, but rather something else, has been expressed by many writers and doctors prior to its first “official” usage in the medical context. After that, according to the Swedish historian K. Johannisson, it disappears, and cannot be found in any larger medical dictionary between 1850-1950.<sup>1</sup> She writes that at the same time, the modern scientific medicine, which gives priority to a biological understanding of the human body, starts its progress.

The placebo is “rediscovered” in the mid 1940s. The most important factor for that seems to be the introduction of the double blind studies. With these new methods of investigation, elaborated by mathematicians, advanced statistical processing of data became available. The double blind studies were mostly used to evaluate new medicines and treatments, which were tested against a control group receiving placebo. What must have been surprising to most was that the placebo group showed significant improvements, sometimes even comparable to the “real” medicine. The reactions were diverse; some said that it was only errors in the measurements, whereas others took the “new force” for something real and important. At first, it was believed that only some people responded to placebo. This is one of the conclusions drawn in the now legendary article by HK Beecher in JAMA 1955.<sup>2</sup> Based on a metaanalysis of 15 studies, Beecher wrote that the placebo had a real therapeutic effect, being produced in 35.2  $\pm$  2.2% of cases. That number, although criticized right from the beginning, has almost been considered as some sort of biological constant.

### Material and Methods

The material was found in three ways. Reviewing the register of *Läkartidningen* from

1946 to 1981 gave 14 results, of which 5 discussed the placebo as a phenomenon. Using the database *Swemed* for keywords “placebo” (confining the search to Swedish articles) yielded 63 hits, the last one from 1982 in LT. Many of these are studies where the placebo is only discussed as a control for the medicine subject to the study. Of these 63, 29 deal specifically with the placebo effect. The third way was by reviewing the reference list of articles already found (by the two ways written above).

### Results

The first time that the placebo is mentioned in *Läkartidningen* (LT) (making it likely to assume that it also was the first time ever in Sweden) was in 1959.<sup>3</sup> The article compares the effect of two anti-depressants. Concerning placebo, it states that new methods of investigation have in recent years developed which allows statistical analysis: in these methods “blind-tablets (dummies or placebo)” are given to a control group. It takes 10 years before the placebo once again appears in LT. In 1969 there is an article about the ethics of double blind studies.<sup>4</sup> The author asks if it really is acceptable to give inefficacious substances to patients. There, thus, no discussion about the placebo effect, since it is already defined as “inefficacious”.

The first time that the placebo is discussed as such is in 1975.<sup>5</sup> The purpose of the article is to clear away some of the mistakes about the placebo, made in a bill proposed by the politician Kerstin Anér earlier that year. The bill suggests that an investigation of the use of the placebo should be carried out in Sweden. Of course, the incitement to the article cannot reasonably have come from any scientist working in Sweden, since – as we have seen - almost no debate about the placebo has occurred. Anér refers to an article written by Sissela Bok from USA. In her article, Bok writes about a double blind study performed in Mexico where contraceptive pills were used against placebo. Perhaps not very surprising, the control group had major secondary effects, in form of unwanted pregnancies. The responsible doctor comforted the women by saying that he would

gladly abort the fetuses, had it not been illegal in Mexico! Bertler states in his article that such a study would never have been allowed in Sweden, and that placebo treatments occur very seldom. This would make an investigation of the use of the placebo in Sweden unnecessary.

Bertler also deals with the placebo itself and writes that it certainly is not imagination, as was thought before. The placebo effect is real and can be objectively measured. Its explanation can probably be sought in the complicated interplay between the nervous system and the hormone-producing organs of the body. This view has since then become increasingly popular, at least among physicians. In 1986 an article states that the mystery of the placebo is perhaps solved.<sup>6</sup> The production of endorphins (which had already been shown to be involved in the placebo effect) also leads to synthesis of ACTH and MSH. This will give a reduction in stress, thereby explaining the effect of placebo in other areas than analgesia. On this matter, N. Uddenberg writes in 1989.<sup>7</sup> that the reference to the endorphins as an explanation of the placebo effect is "somewhat naïve". He means that the endorphins are not an explanation of the placebo effect, nor an effect, but a parallel phenomenon. K. Szybek writes that the endorphin-theory and the two other mechanisms that also have been strong candidates (conditioning and expectation) are theories that explain the placebo effect on different levels.<sup>8</sup> The endorphins would be useful on the molecular level, conditioning on the neuro-physiological and finally the expectations are factors in a psychological model. This clear-minded division is strikingly absent in most other articles.

A different point of view is given in a book published 1979.<sup>9</sup> The authors claim that the placebo effect cannot be separated from the "real" effect since it is not possible to separate the body from the soul. What can only be done is to measure the total effect and the combination method/therapist. Although they claim it to be impossible to define the placebo effect properly without contradictions, they do offer one, which

they admit is in the end fallible, but which they think will probably stand the test of time better than the definitions available for the moment. The placebo effect is said to be induced by influencing our senses, whereas the "real" effect arises via the blood circulation.

So far, the placebo has only been discussed in a medical framework. New perspectives are offered in 1984 in an article by the social anthropologist L. Sachs.<sup>10</sup> She thinks the placebo includes everything that occurs in the therapeutical situation, e.g. the relationship between the doctor and the patient, and both their socio-cultural backgrounds. With that, the realm of the placebo widened dramatically. Another non-medical account for the placebo effect is given by the physiotherapist K. Szybek.<sup>11</sup> She offers a psychoanalytical model, which can be outlined as follows:

The patient becomes aware of his/her illness, and experiences a state of anxiety due the possibility of not existing. S/he will regress to a previous stage of development, and feel helpless. This will result in a crave for an omnipotent protector. If such a protector does not appear, the individual will respond with unconscious feelings of anger, which will be directed towards himself in order to rescue the notion of a benevolent world. The competence to cure oneself will decrease due to the increasing depression. When finding a therapist that can be trusted, the individual will be seen and understood. He will be treated with the placebo, which can be a pharmacologically inactive substance. Together with the therapist the individual's self-confidence and competence for self-healing will be restored.

The increasing awareness of the placebo effect in the 90s results in a conference, arranged by the SBU, in 1999. There, the placebo is considered from many points of view: medical, historical, cultural and ethical. The presentations were then collected in a book, with the title *Placebo* published the following year.<sup>12</sup> E. Hägg writes there that the placebo effect is caused by

psychological, neural, hormonal and immunological factors. Although he does not write it explicitly, nor do most writers, it is reasonable to assume that he, just as K. Szybek, thinks that these factors represent models on different levels. Some of the psychological factors are anxiety suggestion, motivation and expectation.

Another author in Placebo, M. Åsberg thinks that our expectation on the treatment is the most important, and the crucial question is what creates this expectancy and how the processes, which are required for the placebo effect, activate in our body. She is also one of many who think that the term placebo effect is not adequate, since it implies something contrary to real pharmacological effect. Rather, the placebo effect should be seen as “unspecific effect”.

There is also another view on the placebo that gained increasing popularity in the late 90s, one that has existed right from the beginning. In 1995 G. Kiene publishes a book where she reviews all of Beecher's sources and concludes that the placebo really does not amount to anything more than the natural course of the disease, regression to the mean value and irrelevant methods of measurement. Responding to that, J. Ottoson writes in 2001 that the existence of the placebo is not dependant of the accuracy of the article of Beecher, there is enough evidence, which have, beyond any doubt proven that the placeboeffect is something else than what Kiene wants to reduce it to. If Kiene criticism was more or less directed towards Beecher's conclusions, an article published in JAMA was to seriously question the whole notion of the placebo, and drew a lot of attention from both the scientific community and from mass media. The authors had made a metaanalysis on 114 published studies where an untreated group, besides the usual placebo group had been included.<sup>13</sup> The conclusion was that no statistically significant changes could be seen between these two groups. This conclusion has been criticized on many accounts, Boström and Hägg writes for instance that a very narrow definition of the

placebo has been used; placebo as an intervention, and that symbolical stimulus has been excluded.<sup>14</sup> And can it really be said that the untreated control group really was untreated, since the extra attention and control, which they receive, can have placebo effects.

## Discussion

As we have seen, it took a great many years, before there was any discussion about the placebo in Sweden. Not until 1975, 20 years after Beecher's article is the placebo acknowledged as something interesting. This belated introduction must be regarded as surprising, considering the fact that the placebo is such a fundamental ingredient in clinical practise. What seems to have triggered the discussion in Sweden was not a keen interest in the mysterious subject, but rather an assertion that placebo is not used to the alleged extent! However, Bertler's article introduces the debate in Sweden; since it's not used, it certainly have to exist. In the 1980ths, a lot of articles are published on the subject, all of them treating the placebo effect as a real phenomenon worthy of further research. Several articles during the 90s discusses the placebo effect as a neglected force in health care, meaning that more stress has to be put on the relationship between the doctor and the patient, but also on all the other elements in the care of the sick. The opposite view, that placebo does only name an imaginary force have not been widespread in Sweden, and judging from the many articles on the placebo from the past few years, most Swedish scientists consider that there really *exist* something called the placebo, and that more research is needed in order to optimally use it in medical treatments.

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