



Placebo-Effekt in der Psychiatrie. Spreu oder Weizen?

Mittagsseminar
Continuum Psychiatrie & Psychotherapie im Fokus
2. Dezember 2021


Prof. Dr. Jens Gaab
Klinische Psychologie und Psychotherapie
Fakultät für Psychologie
Universität Basel
jens.gaab@unibas.ch



Franz Anton Mesmer (1734-1815)




A. MESMER



Mesmer, 1766

Placebo und Psychotherapie

Mesmer und Mozart




Wolfgang Amadeus Mozart: 1790 Oper Cosi fan tutte

FIORDILIGI, DORABELLA, ALFONSO
Es war Arsenikum,
Was sie getrunken,
Und kraftlos sind sie hier
Tot hangesunken;
.....
DESPINA
Die Kur ist Kleinigkeit
Für meinesgleichen,
Hier soll in Bälle
Das Uebel weichen,
Hier eine Probe
Von meiner Macht.
Zieht einen Magnetstein hervor.
FIORDILIGI, DORABELLA, ALFONSO
Wie, durch ein Eisen
Will er kurieren?
DESPINA
**Hier, ein Magnetstein,
Den ich empfangen
Aus Doktor Mesmers Hand,**
Der rings im deutschen Land
Tote kurieret,
Und dessen Nam' sogar
In England strahlet!
Bestreicht Köpfe und Körper der Kranken mit dem Magnete.
FIORDILIGI, DORABELLA, ALFONSO
O seht, sie regen sich,
Winden sich tanzend,
Wie sie der Schmerz verzehret,
Es ist erbarmenswert!

Placebo und Psychotherapie

Maria Theresa Paradis (1759-1824)



Placebo und Psychotherapie

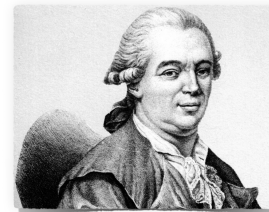
Mesmer und Paradis (Film, 1994)



Placebo und Psychotherapie

5

Die Franklin-Kommission (1784)



Placebo und Psychotherapie

6

Franklin report

REPORT OF THE COMMISSIONERS CHARGED BY THE KING WITH THE EXAMINATION OF ANIMAL MAGNETISM*

BENJAMIN FRANKLIN, MAJALLET LE ROY, SALLIN,
JEAN-FRANÇOIS MALLEU, D'ARCEU, DE BOURG,
JOSEPH-SOINAGE GUILLOTIN & ANTOINE LAVERGIER

On March 12, 1784 the King appointed Physicians chosen from the Paris Faculty, Messieurs Benoit, Salin, d'Arcen, Guillotin, to examine & report on animal magnetism, practiced by Monsieur Mesmer, & as requested by these four Physicians, His Majesty was appointed five of the Members of the Royal Academy of Sciences to conduct this examination with them. Messieurs Franklin, de Roy, Salin, de Bourg, Lavoisier, de St. Ronne died at the beginning of the Commissioners' work. His Majesty chose M. Mairan, a Doctor from the Faculty, to replace him.

The agent that M. Mesmer claims to have discovered, which he has made known under the name Animal Magnetism, is, as he characterizes it himself & according to his own words,

a universally spread fluid, in the manner of a mutual influence between related bodies. The earth, & living bodies, it is continuous as not to event any vacuum, it is immensurable, subtle, it is capable of receiving, emitting, & communicating the vibrations of the matter of which it is composed. In fact, it works. The physical body feels the effects of the agent, & when it receives heat from the substance of nerves, it feels their generation. One recognizes particularly in the human body, properties similar to those of the magnet. One distinguishes it, however, by its nature. The action of the agent is not limited to the attraction of iron, but extends to all the parts of the body, & is not confined to the poles, as in the case of the magnet. This action operates from a distance, without the help of any intermediary body. It is increased when combined by rest, concentration, & spread, & increased by sound; the property may be communicated, conveyed, transferred, although the fluid is not contained in the object, or in the recipient. The influence is not lost, in case the pole property is so strong, that their mere presence destroys all the effects of the fluid in other bodies.

Animal magnetism may itself cure various diseases, & be a medium for curing others; it preserves the action of medications, it induces & gives rise to it, & it is the cause of the generation of the disease. In this way, the Physicians know the state of health of each individual & determine with certainty the nature, nature, & progress of every the most complicated diseases, by perceiving their effects on the face a cure without even exposing the patients to dangerous effects, or an infirmities common

*Reprinted with permission from Haplo's magazine.
The International Journal of Clinical and Experimental Hypnosis, Vol. 16, No. 4, October 2008, 203-204.
© 2008 The International Journal of Clinical and Experimental Hypnosis.
101



Placebo und Psychotherapie

7

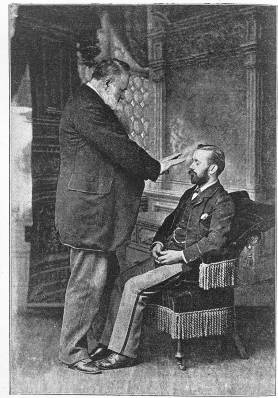
Armand-Marc-Jacques Chastanet, Marquis de Puységur (1751-1825)



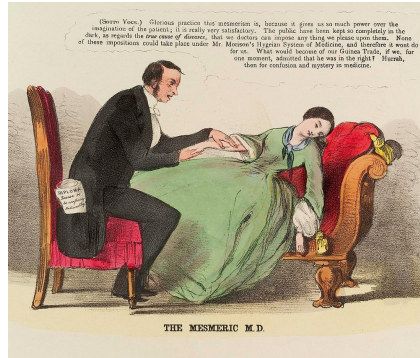
Placebo und Psychotherapie

8

Magnetischer Schlaf



MAKING THE MAGNETIC PASS, FOR PRODUCING OR DEEPENING THE MESMERIC SLEEP.



THE MESMERIC M.D.

Jean-Martin Charcot (1825-1893)

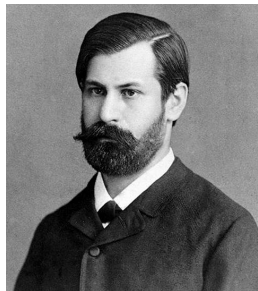


Pinete XIV.

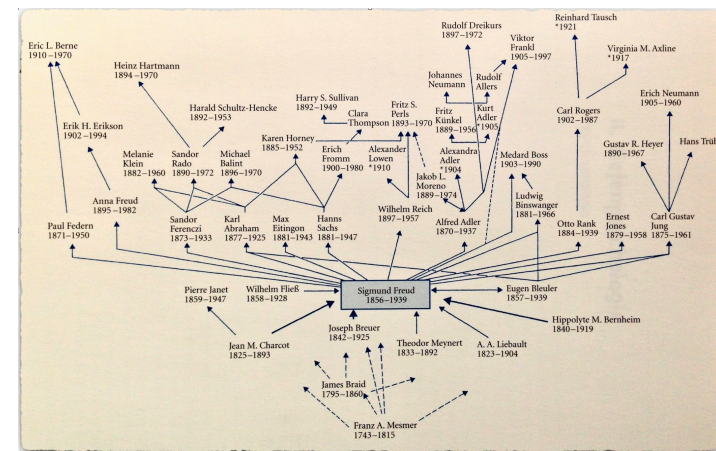


HYSTERO-EPILEPSIE
TEXT NACH: SAUL

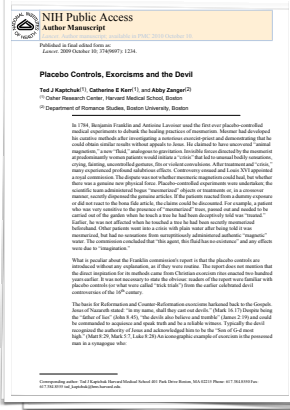
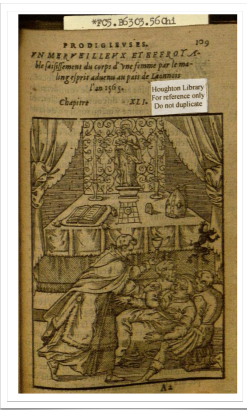
Sigmund Freud



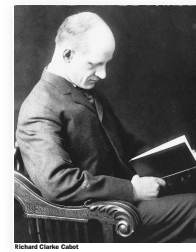
Psychotherapie. Wer hat's erfunden...?



First steps. Animalischer Magnetismus, Luis XVI. und Benjamin Franklin



Einsatz von Placebo in der Medizin

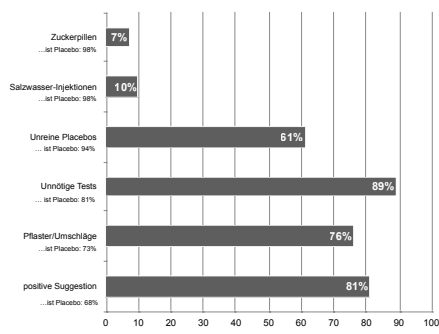


„I was brought up, as I suppose every physician is, to use placebo, bread pills, salt water injections . . . I doubt if there is a physician in this room who has not used them and used them pretty often . . . I used to give them by the bushels.“

Richard Cabot (1868–1939), Harvard Medical School

Einsatz von Placebo in der Medizin

Einsatz in klinischer Praxis



Fässler et al., 2009 BMC Health Serv Res

Placebo controlled trials. Spreu vom Weizen trennen.

A CLINICAL TRIAL OF SANOCRYSLIN IN PULMONARY TUBERCULOSIS

J. BURNS AMBERSON, JR., B. T. McMAHON and MAX PINNER

In 1924 Møllgaard (1) published the results of his study of sanocrysin (sodium-gold-thiosulphate), and made claims that the substance has a specifically curative effect on tuberculosis. He believed that sanocrysin, introduced into the blood-stream, permeates tuberculous lesions and there kills many, if not all, of the offending bacilli. The resulting reaction, manifested most often by fever, albuminuria, erythematous eruptions of the skin and loss of body weight, were interpreted as being due mainly to the liberation of toxins from the disintegrated bacilli and, therefore, as being analogous to tuberculin reactions. The evidence was obtained from the observation of the action of the chemical compound on living cultures of tubercle bacilli, on the treatment of tuberculosis induced experimentally in goats, calves, monkeys and guinea pigs, and on the treatment of tuberculosis in man by various Danish clinicians. Exanthemata, not too acute, pulmonary lesions of early age, being more pervous than the fibrous type, were considered most responsive to treatment, although some urged including chronic cases also. To offset the ill effects, which might be serious or even fatal, an antiserum prepared from horses after injecting them with "defatted" formalin-treated tubercle bacilli was administered at the first sign of reaction, that is, the appearance of albuminuria.

Following Møllgaard's work, the drug was tried in human cases in many parts of the world, and various other gold compounds, some new and some old, received similar attention. These include alloxycin, aurojokol, auroxol, auronon, chlminsol, citaloin, gold chloride, kryojoloin, lipaurol, lopoin, neosancrysin, neoocrysol, phosphocrysol, solganol, sulphocrysol, thiocrysin and triphal. The amount of gold in these compounds varies greatly; sanocrysin, being among the stronger in this respect, contains 57.4 per cent gold.

Burns Amberson J., McMahon B. T. & Pinner M. (1931). A Clinical Trial of Sanocrysin in Pulmonary Tuberculosis. Amer. Rev. Tuberc., 1931, 24, 401–35

The Testing of Sanocrysin: Science, Profit, and Innovation in Clinical Trial Design, 1926–31

JOSEPH M. GABRIEL
Medical Humanities and Social Sciences, College of Medicine, Florida State University
Tallahassee, Florida 32306-2200. Email: joseph.gabriel@fsu.edu

Abstract: This article provides a detailed analysis of the origins and significance of the 1926 clinical trial of Sanocrysin, a gold compound thought at the time to be useful in the treatment of tuberculosis. This experiment is generally considered to be the first clinical trial in the United States that used a formal system of randomization to divide research subjects into treatment and non-treatment groups. It was probably also the first clinical trial in the United States to use placebo-shams in a non-treatment control group to overcome the problems of what researchers at the time called "psychic influence." As such, it was an extremely important moment in the history of clinical trial design. Yet, as I argue, the Sanocrysin experiment also needs to be understood in terms of both the regulatory environment at the time and the commercial interests of Parke, Davis & Company, the pharmaceutical manufacturer that was interested in introducing the drug. Although some historians argue that therapeutic reformers in the twentieth century used experimental science to erode the commercial forces of the market, this article suggests that, at least in this case, the promotion of rigorous clinical science and the pursuit of corporate profit were deeply intertwined. Keywords: pharmaceutical, clinical trial, tuberculosis, therapeutic reform, Parke, Davis & Co., Sanocrysin.

In April 1926, James Burns Amberson, Jr., B. T. McMahon, and Max Pinner tested a new tuberculosis remedy made from gold called Sanocrysin in a sanatorium near Detroit. The researchers divided patients into two groups: a placebo and a treatment group.

The powerful placebo.



168 JAMA, Dec 14, 1953

THE POWERFUL PLACEBO

Henry K. Beecher, M.D., Davis

Placebo have doubtless been used for centuries to bring relief to the sick. In fact, it is only recently that the clinical significance of placebo has been fully appreciated. It is a clinical phenomenon that has been the subject of a number of recent studies. It has been shown that placebo has a powerful effect on the patient's response to treatment. It has been shown that placebo has a powerful effect on the patient's response to treatment. It has been shown that placebo has a powerful effect on the patient's response to treatment.

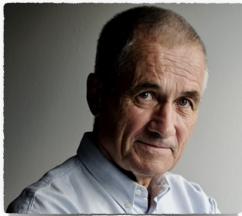
Reasons for the use of placebo are indicated in the accompanying text. In certain instances, it is a purely psychological phenomenon. In other instances, it is a purely physiological phenomenon. In still other instances, it is a purely psychological phenomenon. In still other instances, it is a purely physiological phenomenon.

Die Suche nach der spezifischen Wirkung...



Galenos von Pergamon 128-199

The powerless placebo?



The New England Journal of Medicine

Special Article

IS THE PLACEBO POWERLESS?

An Analysis of Clinical Trials Comparing Placebos with No Treatment

Arnold H. Steinmann, M.D., and P. M. D. C. Gifford, M.D.

ABSTRACT
Placebo treatments have been reported to be effective in many clinical trials, but the quality of the evidence supporting this finding has not been systematically evaluated. We conducted a systematic review of clinical trials in which patients were randomly assigned to either placebo or no treatment. A placebo could be defined as a tablet, pill, or injection that is pharmacologically inactive. In this review, we included only randomized, controlled trials. We identified 120 trials that met our inclusion criteria. Of these trials, 40 trials without random data on outcomes, there were 25 with binary outcomes involving 2729 patients, with a median of 51 patients per trial and 62 with continuous outcomes involving 2729 patients, with a median of 51 patients per trial. All randomized trials in which placebo had no significant effect on binary outcomes, regardless of whether those outcomes were subjective or objective. For the trials with continuous outcomes, placebo had no significant effect on subjective outcomes, but it had a significant effect on objective outcomes. In 27 trials involving the treatment of pain, placebo had a beneficial effect as indicated by reduction in the number of days of pain or the number of days of moderate to severe pain.

CONCLUSIONS
We found little evidence in general that placebo had powerful effects on subjective outcomes. However, we did find evidence that placebo had a beneficial effect on objective outcomes in general. In studies with continuous subjective outcomes and in studies with continuous objective outcomes, placebo had no significant effect on subjective outcomes, but it had a significant effect on objective outcomes. In studies with continuous subjective outcomes and in studies with continuous objective outcomes, placebo had no significant effect on subjective outcomes, but it had a significant effect on objective outcomes.

Was sind die Effekte einer Behandlung und vom Placebo?

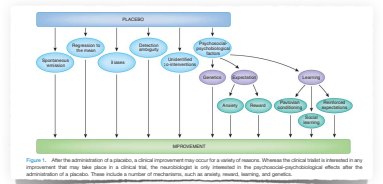
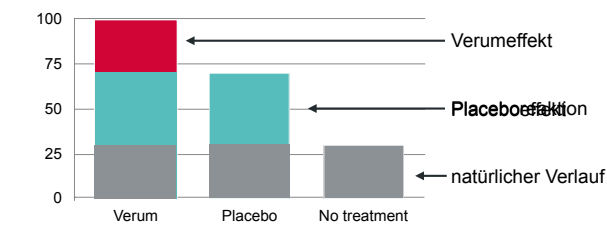
REVIEW

How Placebos Change the Patient's Brain

Richard Bennett¹, Lisa Colloff² and Andrew P. Gold¹

¹Department of Neuroscience, University of East Anglia School and National Institute of Neuroscience, York, UK

Although placebo has long been considered a mysterious clinical phenomenon, little is known about the underlying mechanisms. We used functional magnetic resonance imaging (fMRI) to investigate the neural mechanisms underlying placebo-induced analgesia. We found that placebo-induced analgesia is associated with activation of the endogenous opioid system, specifically the nucleus accumbens and the amygdala. These findings suggest that placebo-induced analgesia is mediated by the same neural mechanisms as those underlying natural pain relief.



Fair play? „fake and ineffective medication“ vs. „real and effective medication“

Open Access **Research**

BMJ 2017;355:g2018. doi: 10.1136/bmj.g2018

ANALYSIS

Informed consent and clinical trials: where is the placebo effect?

Lack of knowledge about placebo affects participants' understanding of risks and increases the ethical obligations of researchers, argues C R Blease, P L Bishop, and T J Kaptchuk

C R Blease, philosopher of medicine¹, P L Bishop, health psychologist², T J Kaptchuk, director³

¹School of Philosophy, University College London, London, UK; ²Department of Psychology, University of Pennsylvania, Philadelphia, PA, USA; ³Department of Psychiatry, Harvard Medical School, Boston, MA, USA

Abstract Informed consent requires participants to understand the risks and benefits of the research. However, participants often do not understand the risks and benefits of placebo. This lack of understanding affects participants' understanding of risks and increases the ethical obligations of researchers. We argue that researchers should be more forthcoming about the risks and benefits of placebo. We also argue that researchers should be more forthcoming about the risks and benefits of placebo. We also argue that researchers should be more forthcoming about the risks and benefits of placebo.

Placebo responses Placebo responses are a well-documented phenomenon in clinical research. They are a result of a complex interplay of psychological, social, and biological factors. Placebo responses can be a powerful tool for researchers, but they can also be a source of bias. Understanding placebo responses is essential for conducting high-quality clinical research.

Placebo and verum effects of surgery

EDITORIALS

Arthroscopic surgery for degenerative knee

Andi Cui, professor and director

Background: Arthroscopic surgery for degenerative knee is a common procedure. However, recent evidence suggests that the benefits of this procedure may be limited. This editorial discusses the current state of research on this topic and offers recommendations for clinicians and patients.

Abstract Arthroscopic surgery for degenerative knee is a common procedure. However, recent evidence suggests that the benefits of this procedure may be limited. This editorial discusses the current state of research on this topic and offers recommendations for clinicians and patients.



Placebo and verum effects of surgery

Open Access **Research**

BMJ Open 2016;10:e20150201. doi: 10.1136/bmjopen-2015-020101

To what extent are surgery and placebo procedures effective beyond a placebo response? A systematic review with meta-analysis of randomised, sham controlled trials

Wayne B Jonas, Qing Chen, Laura Colburn, Tael J Kaptchuk, Bruce Moskowitz, Francisco G Miller, Lawrence Kravitz, Melissa Lurie, Gabe Moskowitz

Abstract The placebo response is a well-documented phenomenon in clinical research. It is a result of a complex interplay of psychological, social, and biological factors. Understanding placebo responses is essential for conducting high-quality clinical research.

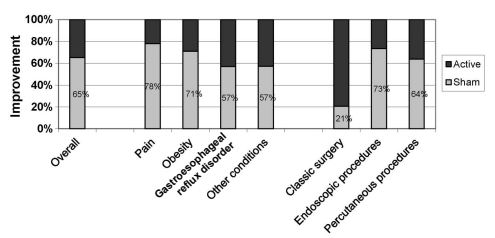
Objectives To assess the quality and quantity of evidence for the effectiveness of surgery and placebo procedures beyond a placebo response. We conducted a systematic review and meta-analysis of randomised, sham controlled trials.

Design Systematic review and meta-analysis.

Setting PubMed, Cochrane Database of Systematic Reviews, Embase, Scopus, and ClinicalTrials.gov.

Participants Randomised, sham controlled trials comparing surgery and placebo procedures.

Primary results We included 10 randomised controlled trials comparing surgery and placebo procedures. The overall improvement in the active group was 65%, compared to 21% in the sham group. The improvement in the active group was significantly greater than in the sham group for all conditions except for classic surgery.



Placebo and pain medication. Strong and getting stronger...

Research Paper

PAIN

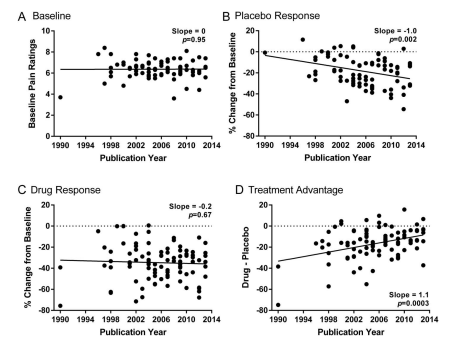
Increasing placebo responses over time in U.S. clinical trials of neurotropic pain

Gary J Bennett, Jeffrey S Mogil

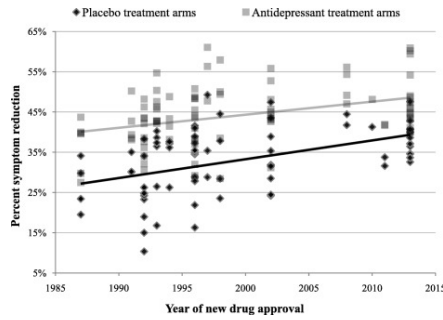
Abstract The placebo response is a well-documented phenomenon in clinical research. It is a result of a complex interplay of psychological, social, and biological factors. Understanding placebo responses is essential for conducting high-quality clinical research.

Introduction The placebo response is a well-documented phenomenon in clinical research. It is a result of a complex interplay of psychological, social, and biological factors. Understanding placebo responses is essential for conducting high-quality clinical research.

Methods and results We conducted a meta-analysis of U.S. clinical trials of neurotropic pain. We found that the placebo response has increased over time, from 1990 to 2014. The slope of the increase was 0.2, with a p-value of 0.0003.

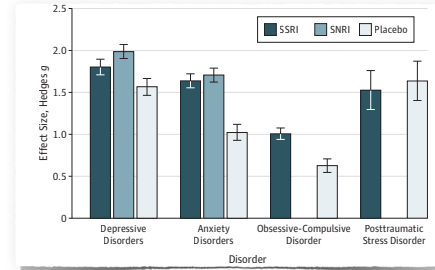


Placebo effect and antidepressants. Strong and getting stronger...



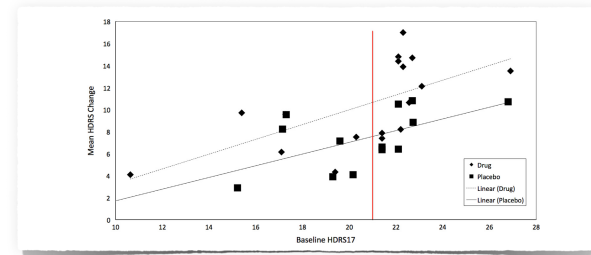
Khan et al., 2017
World Psychiatry

Placebo effect and antidepressants. Kinder und Jugendliche.

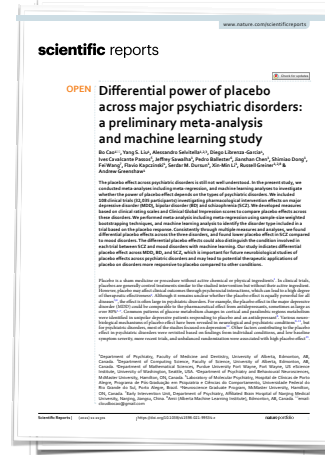


Author Affiliation: ...
Correspondence: ...

Placebo effect and antidepressants. 60+.

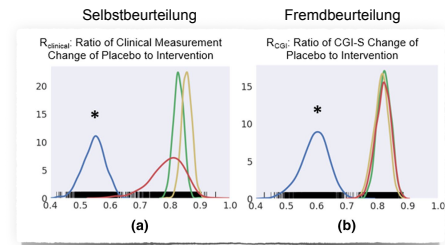


Placebo effect across disorders. MDD, BD, SCZ.

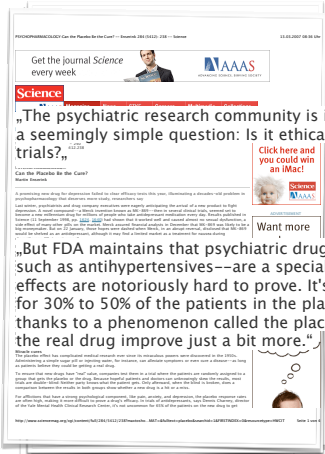


(a) $R_{clinical} = \frac{\Delta Clinical Scales_{Active Drug}}{\Delta Clinical Scales_{Placebo}}$, the ratio of the average clinical measurement change from baseline for placebo to the active drug; the $\Delta Clinical Scales$ was calculated as the baseline measurement minus the endpoint measurement to indicate a decrease of the symptoms.

(b) $R_{CGI} = \frac{\Delta CGI_{Active Drug}}{\Delta CGI_{Placebo}}$, the ratio of the average CGI-S change from baseline for placebo to the active drug; the ΔCGI was calculated as the baseline CGI-S minus the endpoint CGI-S to indicate a decrease of the clinical severity.



Struck by "the curse of the placebo effect"

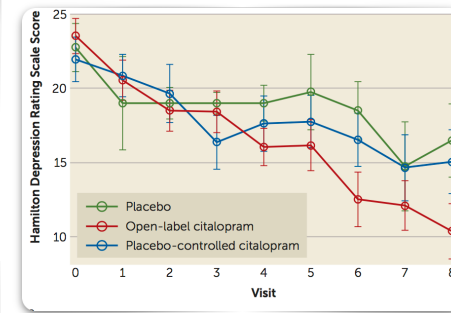


„A promising new drug (MK 869) tests this year, illuminating a trend that deserves more study“

„But FDA maintains that psychiatric drugs--and some others, such as antihypertensives--are a special case because their effects are notoriously hard to prove. It's common in these trials for 30% to 50% of the patients in the placebo group to improve, thanks to a phenomenon called the placebo effect, while those on the real drug improve just a bit more.“



The powerful placebo: Erwartung



„Entweder Placebo oder Medikament“

50% Erwartung

„Medikament“

100% Erwartung

Rutherford et al., 2016
Am J Psychiatry

Play the man, not the ball...

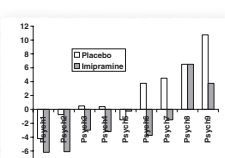


Fig. 1. HDRS residual gain score as a function of type of treatment (PLA, IM, or IM+IM) for each psychiatrist (1-9). Note that lower scores indicate better outcomes; negative residualized gain scores indicate better than average outcomes.

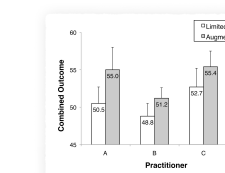
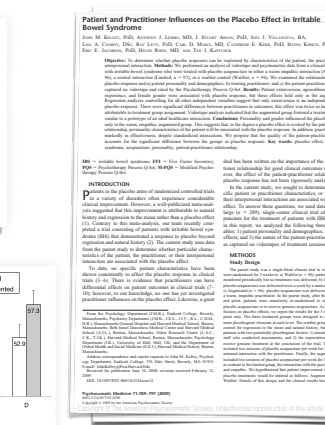
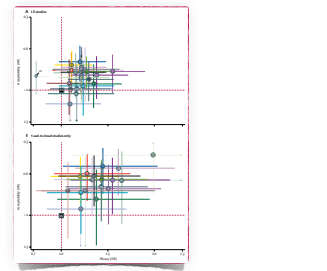


Fig. 2. Practitioner effects by treatment group. Error bars represent standard error of the mean.



Antidepressiva vs. Placebo.



The relative efficacy of antidepressants compared with placebo is also shown for remission (appendix pp 152, 153). The random-effects summary SMD for all antidepressants was 0.30 (95% CrI 0.26–0.34; p<0.0001; appendix pp 150, 151). In terms of dropouts due to

Antidepressiva vs. Placebo.

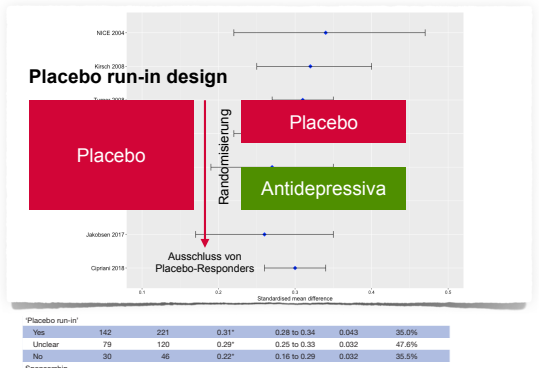
BMJ Open Considering the methodological limitations in the evidence base of antidepressants for depression: a reanalysis of a network meta-analysis

Klaus Munkholm, Ansgar Sauer, Patrick-Martin Kim Dassen

Abstract
 Objectives To evaluate whether the evidence base of antidepressants for depression is methodologically sound. We conducted a network meta-analysis of randomised controlled trials (RCTs) comparing antidepressants with placebo. We assessed the quality of the evidence base using the GRADE approach. We also investigated the impact of methodological quality on the results of the network meta-analysis.

Strengths and limitations of this study
 This study is the first network meta-analysis of antidepressants for depression. It included 10 RCTs and 10 000 patients. The results show that the evidence base is of low to moderate quality. The impact of methodological quality on the results of the network meta-analysis is unclear.

Conclusion
 The evidence base of antidepressants for depression is of low to moderate quality. The impact of methodological quality on the results of the network meta-analysis is unclear.



Antidepressiva vs. Placebo.

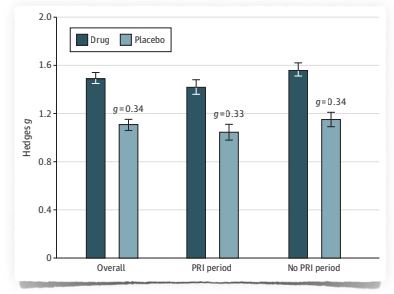
JAMA Psychiatry Association of Single-Blind Placebo Run-in Periods With the Placebo Response in Randomized Clinical Trials of Antidepressants: A Systematic Review and Meta-analysis

Anna-Lena Pöhl, Lorenz Bauer, PhD, Johannes Bauer, PhD, Benjamin G. Müller, PhD, Benjamin Müller, PhD

Abstract
 Objective Single-blind placebo run-in (SBR) periods are increasingly used in clinical trials of antidepressants. We investigated the association of SBR periods with the placebo response in randomized clinical trials (RCTs) of antidepressants. We conducted a systematic review and meta-analysis of RCTs comparing antidepressants with placebo. We assessed the impact of SBR periods on the placebo response.

Results
 We included 10 RCTs and 10 000 patients. The results show that SBR periods are associated with a higher placebo response. The effect size is moderate to large.

Conclusion
 SBR periods are associated with a higher placebo response. The effect size is moderate to large.



Fair play? Breaking the blind.

Psychiatry Research A systematic review and meta-analysis of the success of blinding in antidepressant RCTs

Andrés A. Soto, Leslie Shapiro, Ben Goldberg

Abstract
 Objectives To evaluate the success of blinding in antidepressant RCTs. We conducted a systematic review and meta-analysis of RCTs comparing antidepressants with placebo. We assessed the success of blinding using the CONSORT checklist.

Results
 We included 10 RCTs and 10 000 patients. The results show that the success of blinding is low to moderate. The impact of blinding on the results of the RCTs is unclear.

Conclusion
 The success of blinding in antidepressant RCTs is low to moderate. The impact of blinding on the results of the RCTs is unclear.

Table 3 Blinding data for participants.

Study	Assigned to Active		Assigned to Placebo		Blinding Index		Hedges' g (95% CI)
	Sworn correct (%)	Guess placebo (%)	Sworn correct (%)	Guess placebo (%)	Active Bl	Placebo Bl	
Richard et al., 2002	76 (15/72)	52 (28)	19 (36/77)	13 (33)	45 (30/33)	38 (30/33)	1.06 (0.47, 1.65)
Devesse et al., 2005	44 (28/44)	38 (38)	22 (44)	24 (32)	27 (33)	34 (33)	2.05 (1.54, 2.56)
Köhler et al., 1983	20 (13/30)	7 (30)	4 (9)	15 (43)	30 (31)	25 (20)	2.44 (1.84, 3.04)
Depression Depression Trial Study Group, 2002	75 (37/49)	17 (23)	100 (24/24)	39 (39)	10 (31)	6 (42)	3.88 (3.26, 4.50)
Edwards and Liddle, 1993	19 (12/43)	7 (31)	10 (24)	8 (40)	36 (32)	14 (14)	2.08 (1.26, 2.90)
Robins et al., 1986	63 (16/99)	7 (11)	17 (15)	22 (36)	78 (67)	6 (19)	8.82 (7.35, 10.29)
Murchison et al., 2013	23 (7/30)	4 (17)	15 (42)	7 (28)	27 (29)	6 (67)	1.40 (0.87, 1.93)

Table 4 Blinding data for investigators.

Study	Assigned to Active		Assigned to Placebo		Blinding Index		Hedges' g (95% CI)
	Sworn correct (%)	Guess placebo (%)	Sworn correct (%)	Guess placebo (%)	Active Bl	Placebo Bl	
Richard et al., 2002	76 (57/75)	59 (25)	19 (24/32)	13 (38)	59 (51)	42 (31)	0.71 (0.14, 1.27)
Devesse et al., 2005	44 (29/48)	38 (36)	16 (29/32)	17 (37)	27 (33)	28 (34)	0.61 (-0.35, 1.47)
Köhler et al., 1983	23 (12/30)	8 (40)	2 (4)	19 (76)	18 (18)	18 (18)	0.52 (-0.77, 1.73)
Robins et al., 1986	66 (77/96)	9 (19)	11 (9)	42 (82)	79 (67)	6 (6)	0.65 (0.11, 1.15)

available evidence from RCTs suggests that patient outcomes among unblinded trials are exaggerated by $d = 0.56$ on average, and between 0.41 and 0.71 (Hrobjartsson et al., 2014). This substantial difference is likely due to the well-documented effect of treatment expectancies (i.e. participants' beliefs about the efficacy of treatment, along with their perceived treatment assignment) on symptom improvement (Cogatur, 2010). In addition to other non-specific factors like spontaneous improvement and regression to the mean, the use of blinded placebo

3. Psychotherapie und Placebo sind beides psychologische Interventionen

Psychological Medicine Comparison of psychotherapies for adult depression to pill placebo control groups: a meta-analysis

F. Colquhoun, S. E. Tunney, D. C. Maki, S. G. Hofmann, G. Andersson, M. Wessely, and J. C. Cole

Abstract
 Objectives To compare psychotherapies for adult depression to pill placebo control groups. We conducted a meta-analysis of RCTs comparing psychotherapies with placebo. We assessed the effect size of psychotherapies compared to placebo.

Results
 We included 10 RCTs and 10 000 patients. The results show that psychotherapies are associated with a higher effect size compared to placebo. The effect size is moderate to large.

Conclusion
 Psychotherapies are associated with a higher effect size compared to placebo. The effect size is moderate to large.

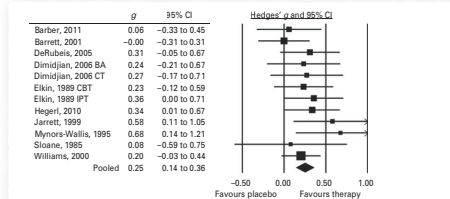


Fig. 2. Standardized effect sizes of psychotherapy for adult depression compared with control conditions: Hedges' g.

3. Psychotherapie und Placebo sind beides psychologische Interventionen

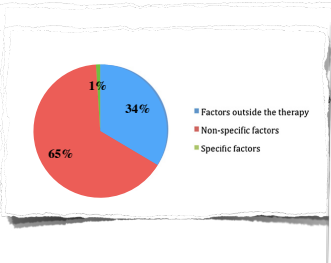
Clinical Psychology Review

The efficacy of non-directive supportive therapy for adult depression: A meta-analysis

Elisa Di Giuseppe, Ellen Driessens, Steven D. Hollies, Patricia van Opdenbosch, Sjoera Bant, Gerhard Andersson

Abstract

Objective: To evaluate the efficacy of non-directive supportive therapy (NDST) for adult depression. **Design:** Systematic review of randomised controlled trials (RCTs) comparing NDST to control conditions. **Setting:** Outpatient and inpatient settings. **Participants:** Adults with major depressive disorder. **Interventions:** NDST and control conditions. **Measurements and Main Results:** The meta-analysis included 146 RCTs with 11,938 participants. NDST was significantly more effective than control conditions in the short term (OR 1.18, 95% CI 1.02 to 1.37). The effect size was moderate to large. **Conclusions:** NDST is an effective treatment for adult depression. **Registration:** PROSPERO 201502005547.



Results: We identified 146 eligible meta-analyses that synthesised data from a total of 1198 unique RCTs. Only 25 of the meta-analyses (17.2%) reported allegiance and only 6 (4.1%) used a proper method to control its effect. Of the 1198 eligible primary RCTs, 793 (66.3%) were allegiance. Authors in 25 of these 793 RCTs (3.2%) reported their allegiance while only one study (0.2%) controlled for its effect.

BMJ Open

Disclosure of researcher allegiance in meta-analyses and randomised controlled trials of psychotherapy: a systematic appraisal

Elina Dagnas, Ismaela Dimulicu, Evangelos Evangelou

Abstract

Objective: To appraise the disclosure of researcher allegiance in meta-analyses and randomised controlled trials (RCTs) of psychotherapy. **Design:** Systematic review. **Setting:** Peer-reviewed journals. **Participants:** Meta-analyses and RCTs. **Interventions:** Disclosure of researcher allegiance. **Measurements and Main Results:** The meta-analysis included 146 RCTs with 11,938 participants. Disclosure of researcher allegiance was reported in 25 (17.2%) of the meta-analyses and in 6 (4.1%) of the RCTs. **Conclusions:** Disclosure of researcher allegiance is rare in meta-analyses and RCTs of psychotherapy. **Registration:** PROSPERO 201502005547.

Cuijpers et al., 2012 Clin Psych Rev

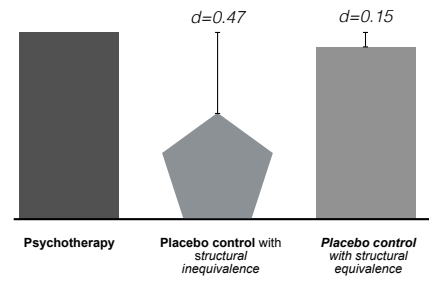
3. Psychotherapie und Placebo sind beides psychologische Interventionen

Establishing Specificity in Psychotherapy: A Meta-Analysis of Structural Equivalence of Placebo Controls

Thomas W. Bakin, Sandy Cullen-Turney, Tatyana Mrazek, and Bruce E. Wampold

Abstract

Objective: To evaluate the specificity of placebo controls in psychotherapy research. **Design:** Meta-analysis. **Setting:** Peer-reviewed journals. **Participants:** Meta-analyses of placebo-controlled trials. **Interventions:** Placebo controls. **Measurements and Main Results:** The meta-analysis included 146 RCTs with 11,938 participants. The effect size for placebo controls was moderate to large (d = 0.47). **Conclusions:** Placebo controls are effective in psychotherapy research. **Registration:** PROSPERO 201502005547.



- Criteria for structural equivalence
- Number, format and duration of sessions
 - Training of therapists
 - Topic restriction

Bakin et al. (2003). Establishing Specificity in Psychotherapy: A Meta-Analysis of Structural Equivalence of Placebo Controls. Journal of Consulting and Clinical Psychology, 71(6), 973-979

Cheat sheet. How (not) to do it...

How to prove that your therapy is effective, even when it is not a guideline

F. Cuijpers and J. A. Cuijpers

Abstract

Objective: To provide a cheat sheet for researchers on how to prove that their therapy is effective, even when it is not a guideline. **Design:** Systematic review. **Setting:** Peer-reviewed journals. **Participants:** Researchers. **Interventions:** Cheat sheet. **Measurements and Main Results:** The cheat sheet includes 10 methods to help researchers prove that their therapy is effective. **Conclusions:** The cheat sheet is a useful tool for researchers. **Registration:** PROSPERO 201502005547.

- Table 1. Ten methods that can help prove that your intervention is effective (even when it is not)**
- Express in all communications about the intervention that you as developer or expert believe it to be best intervention ever (helps to increase expectations in participants).
 - Do everything else that can increase expectations, such as writing books about the intervention, going to conferences to convince other professionals that this is the best intervention ever, giving interviews in the media showing your enthusiasm, preferably seasoned with some personal stories of participants who declare they have benefited very much from the intervention.
 - Use the "weak spots" of randomised trials: let the assignment to conditions be done by research staff involved in the trial or do yourself (not by an independent person not involved in the trial).
 - Do not conceal conditions to which participants were assigned to for the assessors of outcome.
 - Analyse only participants who completed the intervention and ignore those who dropped out from the intervention or the study (and do not examine all participants who were randomised).
 - Use multiple outcome instruments and report only the ones resulting in significantly positive outcomes for the intervention.
 - Use a small sample size in your trial (and just call it a "pilot randomised trial").
 - Use a waiting list control group.
 - Do not compare the intervention to already existing ones (but to tell your colleagues that based on your clinical experiences you expect that this intervention is better than other existing ones (good for the expectations)).
 - If the results are not positive, consider not publishing them and wait until one of the clinicians you have persuaded about the benefits of this intervention conducts a trial that does find positive outcomes

~~Control conditions in psychotherapy research~~

OK, got it...

Therefore, in evaluating the efficacy of psychotherapy, the placebo effect cannot and should not be controlled...

Controlling for the Placebo Effect in Psychotherapy: Noble Quest or Tiling at Windmills?

Irving Kirsch, Bruce Wampold, John M. Kelley, Richard Cullen, and Richard M. Schulz

Abstract

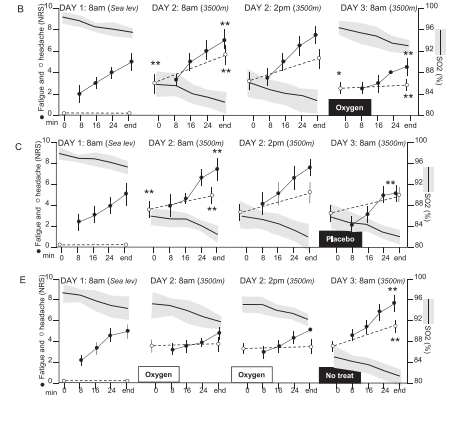
Objective: To evaluate the necessity of controlling for the placebo effect in psychotherapy research. **Design:** Meta-analysis. **Setting:** Peer-reviewed journals. **Participants:** Meta-analyses of placebo-controlled trials. **Interventions:** Placebo controls. **Measurements and Main Results:** The meta-analysis included 146 RCTs with 11,938 participants. The effect size for placebo controls was moderate to large (d = 0.47). **Conclusions:** Placebo controls are effective in psychotherapy research. **Registration:** PROSPERO 201502005547.

Tief einatmen: Fake air!



Placebo

41

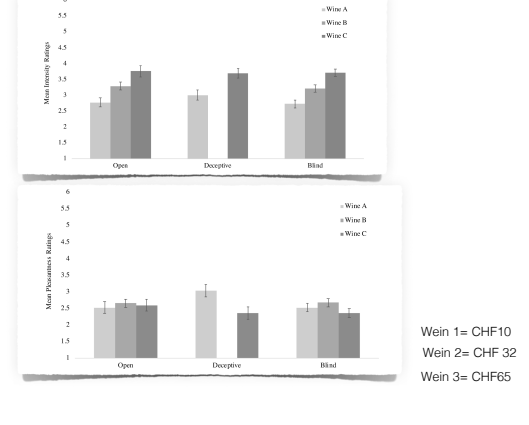


In vino veritas...



Placebo

42



Werner et al., 2021, Food Quality and Preference

Anima sana in corpore sano?

Aerobic Exercise and the Placebo Effect: A Controlled Study
 Ravenna Dharmaiah, PhD, Ivan Iparraguirre, PhD, Gustavo Colell, MS, Leon Stricker, MS, and Corinne Dumas, PhD

An experimental paradigm was used to test whether exercise acts as a placebo for the psychological benefits of aerobic exercise. Participants were randomized to either a real exercise group or a placebo exercise group. The results showed that exercise significantly improved psychological outcomes compared to placebo. These findings suggest that exercise may have a placebo effect on psychological well-being.

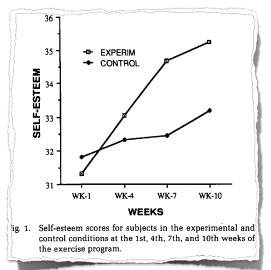


Fig 1. Self-esteem scores for subjects in the experimental and control conditions at the 1st, 4th, 7th, and 10th weeks of the exercise program.

Deshmarnais et al., 1993 Psysom Med

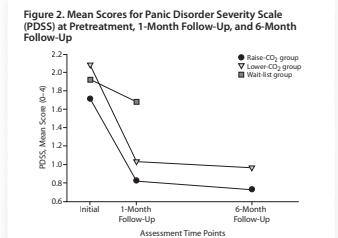
Placebo

43

Placebo ist Psychotherapie ist Placebo

Opposing Breathing Therapy for Panic Disorder: A Randomized Controlled Trial of Lowering vs Raising End-Tidal P_{CO2}
 Spreund Kn, PhD, Ellen Wolfberg, PhD and Willem J. R. B. M.

Abstract
 Breathing therapy has been widely used as a component of panic disorder treatment. However, the underlying mechanisms are not fully understood. We investigated the effects of opposing breathing therapy (lowering vs raising end-tidal P_{CO2}) on panic disorder symptoms. Participants were randomized to either a lowering or raising group. The results showed that both groups experienced significant improvements in symptoms. These findings suggest that breathing therapy may have a placebo effect on panic disorder symptoms.



Effektstärken (Cohens d)

- Therapy A vs Waitlist: 1.53
- Therapy B vs Waitlist: 1.34

Prädiktoren

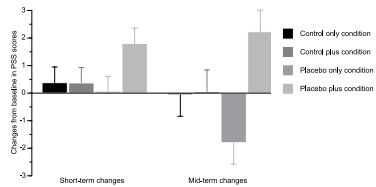
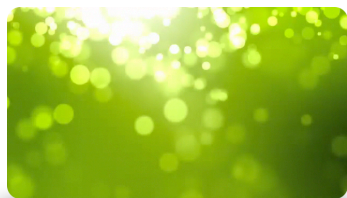
- 1 month follow-up: Beziehung
- 6-month follow-up: Plausibilität

Kim et al., 2012 J Clin Psychiat
 Kim et al., 2015 Bull Menn Clinic

Spreu und Weizen

44

Psychologische Placebos. Man und es muss glaubhaft sein...

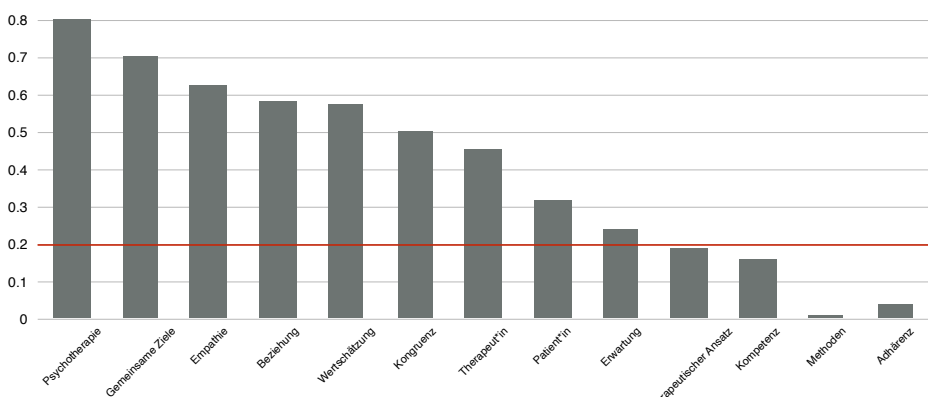


Gaab et al. 2019 Scientific Reports

Placebo

45

Psychotherapie ist eine psychologische Intervention



Wampold & Imel, 2015

Spreu und Weizen

47

Psychotherapie und Placebo sind beides psychologische Interventionen

The old debate about whether or not psychotherapy and placebos have similar mechanisms consists of ascertaining whether psychotherapy is nothing but a placebo effect, and thus whether a placebo procedure is a very simple form of psychotherapy.

Benedetti (2009). *Placebo Effects: Understanding the Mechanisms in Health and Disease*. Oxford University Press, p.141-143

There is a problem with identifying psychotherapy with the placebo effect. A placebo is something that is sham, fake, false, inert, and empty. Psychotherapy is none of these.

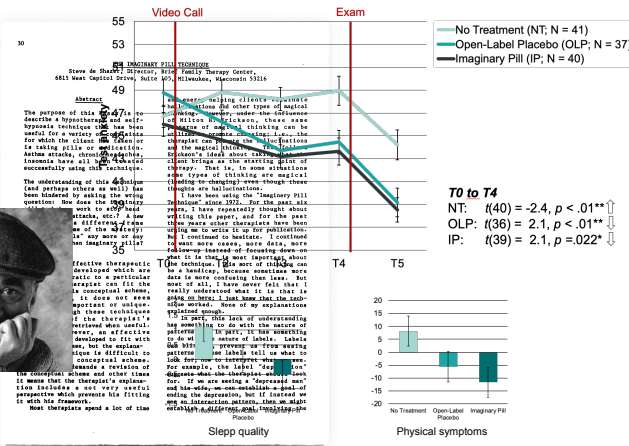
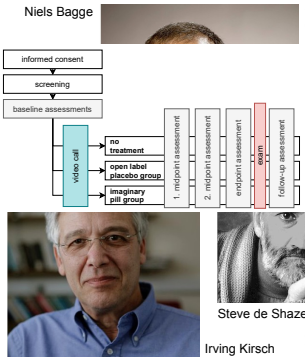
Kirsch (2005). *Placebo Psychotherapy: Synonym or Oxymoron?* J Clin Psychology Vol. 61(7), 791-803

Spreu und Weizen

48

Open-label placebo ist Psychotherapy

Imagine, it works...



Abstract
 The purpose of this study was to evaluate the effectiveness of an open-label placebo (OLP) and an imaginary pill (IP) in the treatment of depression. The study was a randomized, controlled trial. The OLP and IP groups received a video call and an imaginary pill. The results showed that both the OLP and IP groups showed significant improvement in depression symptoms compared to the no treatment group. The OLP group showed a mean improvement of 2.1 points (p < .01**), and the IP group showed a mean improvement of 2.1 points (p = .022*). The no treatment group showed a mean improvement of -2.4 points (p < .01**). The study was conducted at the University of Wisconsin-Madison, Department of Psychology, 6081 West Capitol Drive, Suite 5516, Madison, Wisconsin 53706.

Nothing new under the sun

Nonblind Placebo Trial
 An Evaluation of Nonblind Patients' Perceptions of Placebo
 When the Placebo Effect is Discovered

TABLE 1.—Patient and Doctor Mean Improvement Ratings*

Patient Ratings	Initial Score	Final Score	Change	No. Pt
Symptom Checklist (per item)	1.04	0.61	0.43	13
Target Symptoms (per item)	1.76	1.01	0.77	14
Overall change			2.07	13
Doctor Ratings				
Overall change	3.79	2.43	1.79	14
Pathology			1.30	12

* N equals 14 completed patients.

Patient C was a 28-year-old married female, mother of five children, who complained of extreme tension, shortness of breath, trembling, crying spells, insomnia, suicidal thoughts, and poor appetite with weight loss. She indicated her symptoms centered around inter-personal relations with her husband, who somewhat sadistically provoked her with acting-out behavior. She had previously received medication for her symptoms (mostly anticonvulsants and a sedatives) with no improvement.

(...) the patient said that she needed something really strong; on the other hand, she was quite hesitant about taking medicine because of her (...) mother (...) had (attempted) suicide (...) with drugs.

As soon as it was clear to her that these pills were inactive, she dropped her objections and eagerly agreed to take the pills. She reported at that point, "I do feel better today, I'll be honest with you. Before I came in here I was very upset and when I was talking with you before I was very upset." At the subsequent visit the patient reported she had been doing "fine." "I've had more control and I've felt better." Her somatic symptoms had almost completely disappeared.

She made it clear that she never considered the pills to be anything but placebo and reported no side-reactions.

Commenting on the factors accounting for her marked improvement, the patient remarked that if a person takes a pill "in the right frame of mind," she may feel improved because the pill gives her "moral support." She also felt that the doctor was quite reassuring. Finally, the patient stated, "I think that I had a lot to do with it myself, to be honest. By knowing myself that I had to control myself to keep myself in the right frame of mind."

She then indicated that the most important factor in her improvement was that she helped herself. Our feeling was that the patient did help herself but that she was able to do this only after the placebo gave her an alternative solution to that chosen by her mother in such situations. The patient wanted to continue seeing the doctor, but unfortunately, was not asked whether she wanted to continue with the pills.

Fin

