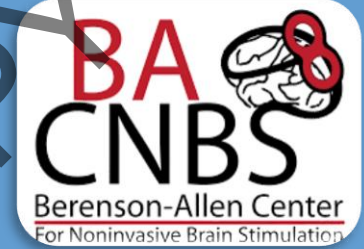


*Intensive Course in Transcranial Magnetic Stimulation, 10/26/18*

# PLACEBO EFFECTS & TRANSCRANIAL MAGNETIC STIMULATION

**MATTHEW BURKE, MD FRCPC**

SIDNEY R. BAER, JR. FOUNDATION FELLOW  
BERENSON-ALLEN CENTER FOR NONINVASIVE BRAIN STIMULATION  
DIVISION OF COGNITIVE NEUROLOGY  
BETH ISRAEL DEACONESS MEDICAL CENTER  
HARVARD MEDICAL SCHOOL, BOSTON MA



# DISCLOSURES

None

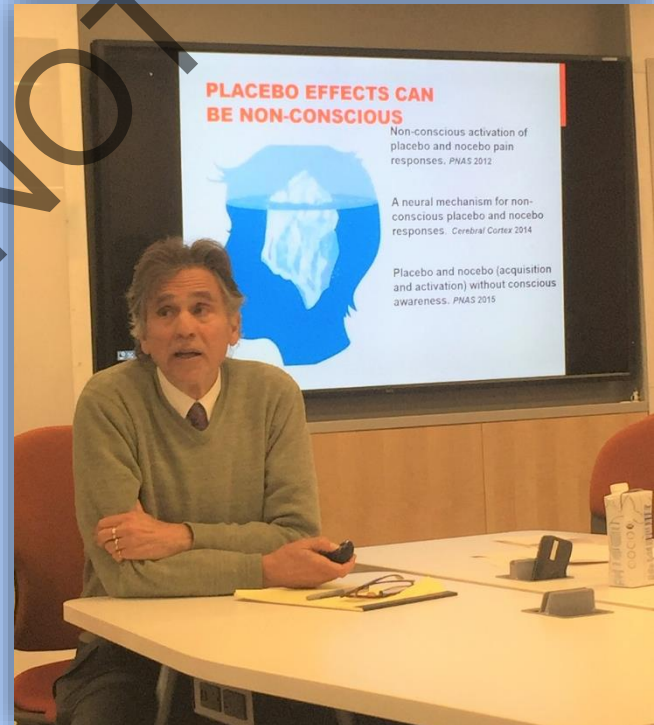


# CONTEXT



**Dr. Alvaro Pascual-Leone**

Director of the Berenson-Allen Center for  
Noninvasive Brain Stimulation



**Dr. Ted Kaptchuk**

Director of the Harvard University Program in  
Placebo Studies

THE TIME IS NOW...



# OUTLINE

## 1. Neurobiology of Placebo Effects

- Definitions
- Mechanisms of action
- Evidence and theories

## 2. “Differential” Placebo Effects

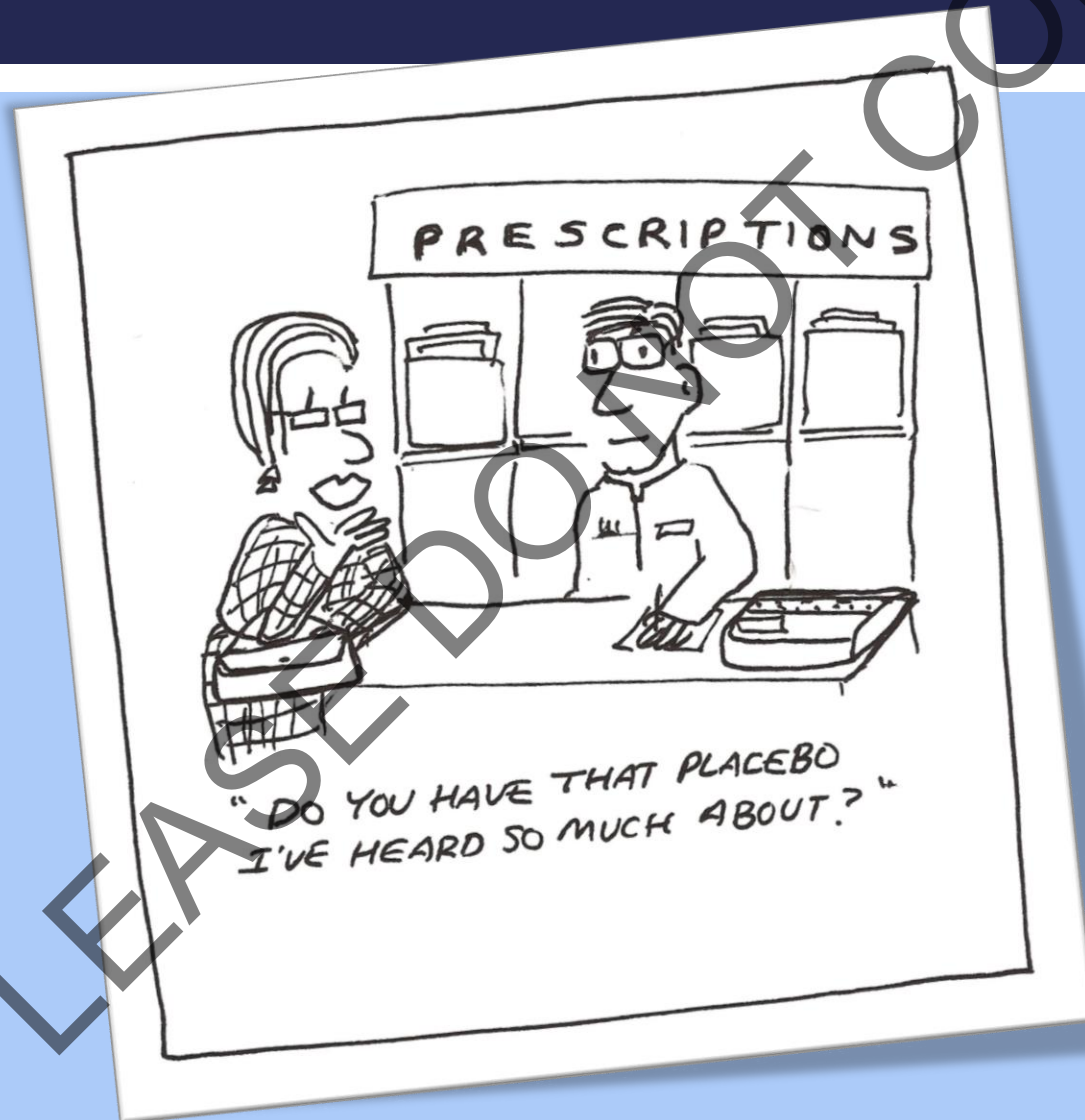
- Historical context
- Meta-analytic approaches
- Prospective approaches

## 3. TMS and Placebo Effects

- Sham devices
- Quantifying magnitude
- Implications on clinical trial results

# 1

# NEUROBIOLOGY OF PLACEBO EFFECTS



# PLACEBO EFFECTS

## The neuroscience of placebo effects: connecting context, learning and health

Tor D. Wager<sup>1</sup> and Lauren Y. Atlas<sup>2</sup>

NATURE REVIEWS | NEUROSCIENCE

### External context

**Verbal suggestions:**  
“This is going to make you feel better”

**Place cues:**  
Doctor’s office

**Social cues:**

- Eye gaze
- Body language
- Voice cues
- White coat



**Treatment cues:**

- Syringe
- Needle puncture

### Internal context

- **Outcome expectancies:**  
“My pain will go away”
- **Emotions:**  
“I am less anxious”
- **Meaning schema:**  
“I am being cared for”
- **Explicit memories**
- **Pre-cognitive associations**

# NEUROIMAGING STUDIES

Science

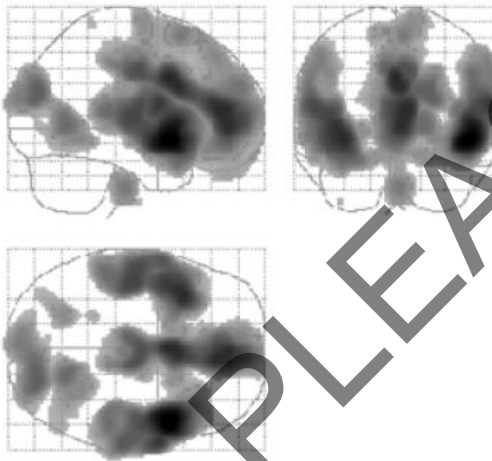
## Placebo and Opioid Analgesia-- Imaging a Shared Neuronal Network

Predrag Petrovic, Eija Kalso, Karl Magnus Petersson and Martin Ingvar

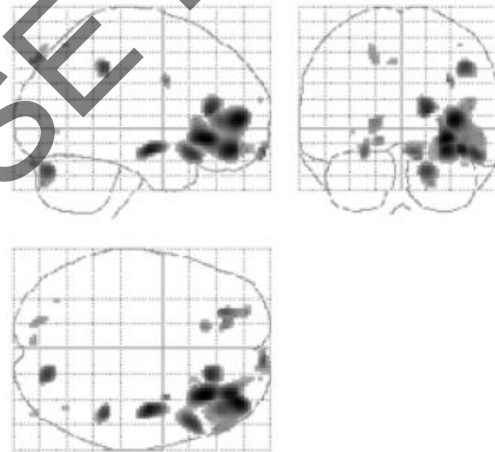
*Science* **295** (5560), 1737-1740.

DOI: 10.1126/science.1067176 originally published online February 7, 2002

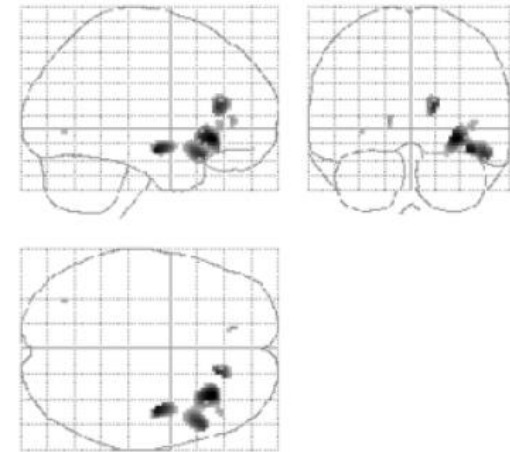
**A** Opioid network



**B** Placebo analgesia network

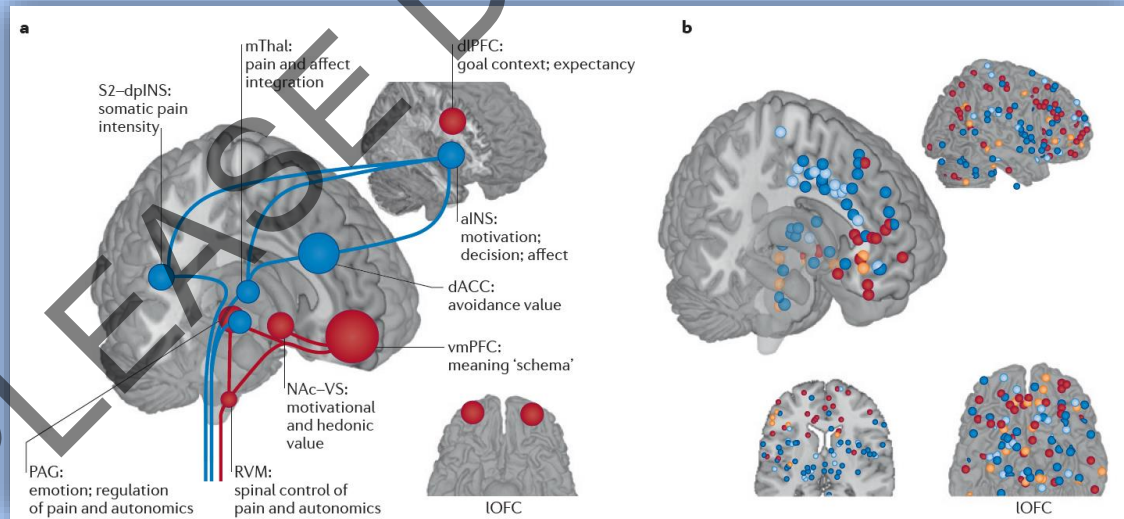
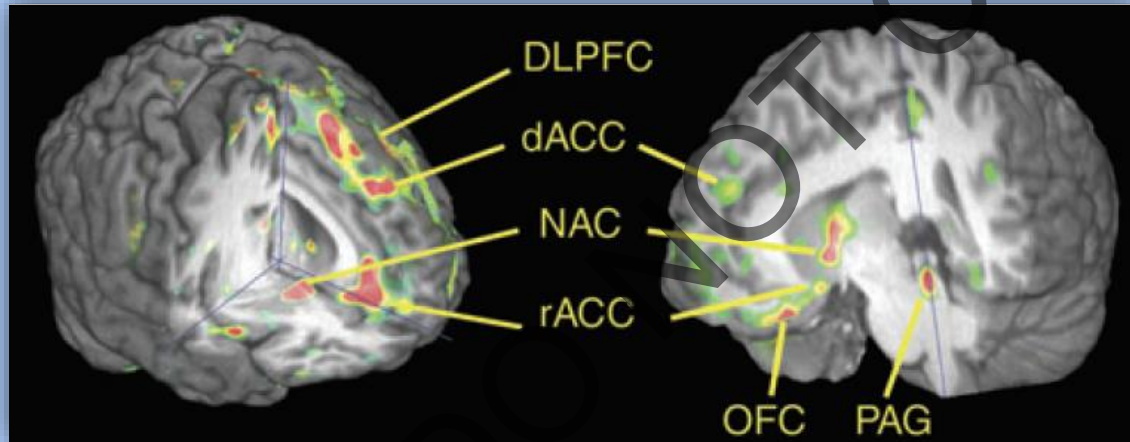


**C** Placebo analgesia network masked with the opioid network





# META-ANALYSES AND MODELS



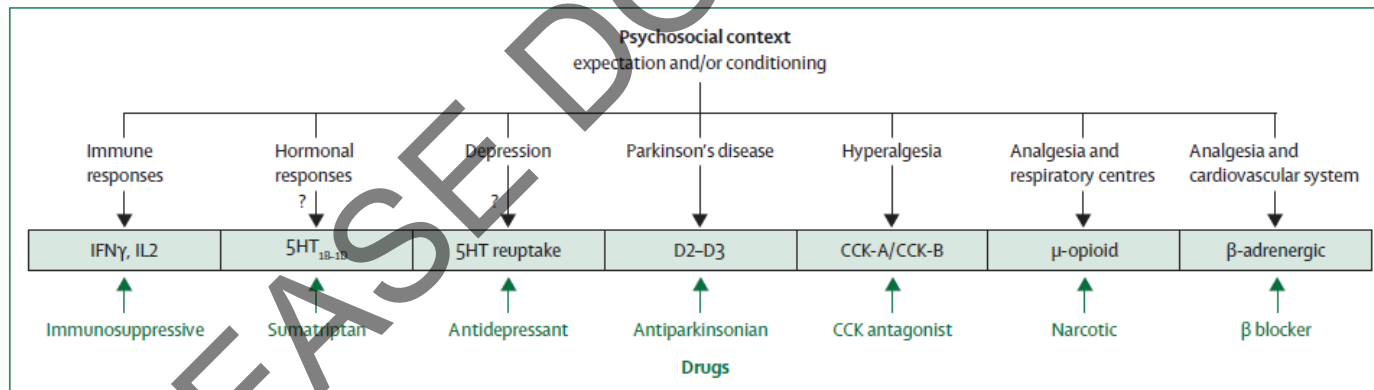
# BIOLOGICAL MECHANISMS

- Opioid, dopamine, cannabinoid, serotonergic, neuroendocrine, and neuro-immunological pathways (+ others) have all been implicated in placebo effects

## Biological, clinical, and ethical advances of placebo effects

Damien G Finniss, Ted J Kaptchuk, Franklin Miller, Fabrizio Benedetti

*Lancet* 2010; 375: 686–95



**Figure 2: Receptor pathways activated by both psychosocial context and drugs**

Social stimuli around the treatment might activate, through expectation or conditioning mechanisms, several receptor pathways in different diseases and therapeutic interventions (the involvement of serotonin [5-hydroxytryptamine; 5HT] receptors in hormonal responses and depression is not definitive). These receptors are the same to which different drugs bind, suggesting that psychosocial factors are capable of modulating the action of drugs. This interference has implications for our understanding of drug action: when a drug is prescribed, the very act of giving it to a patient (ie, the psychosocial context) might affect the system and change the response to the drug. Reproduced with permission from reference 39. IFN $\gamma$ =interferon  $\gamma$ . IL2=interleukin 2. CCK=cholecystokinin.

# NEUROPHARMACOLOGICAL STUDIES

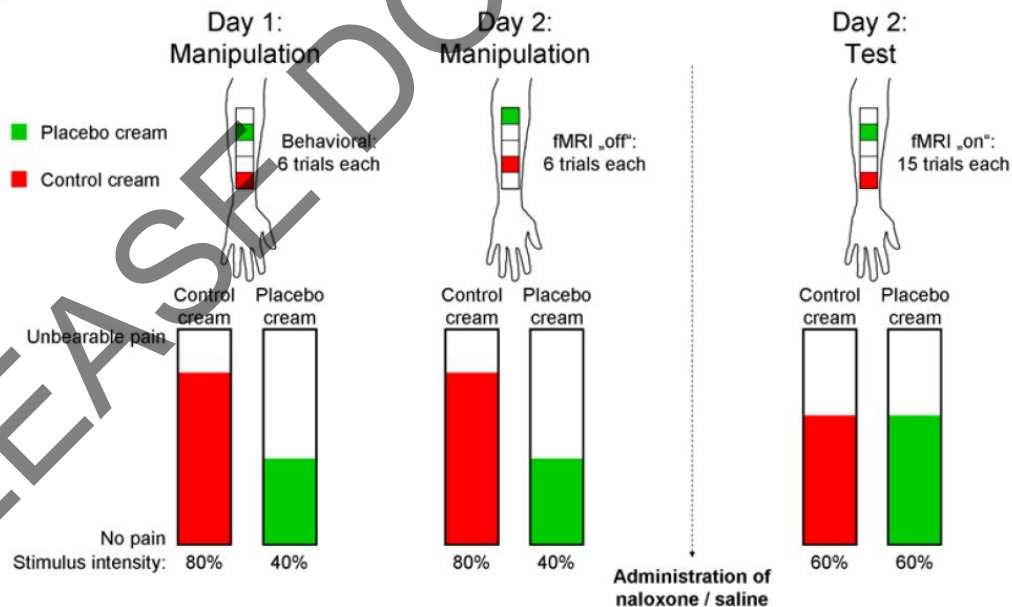
Neuron  
Article

Cell  
PRESS

## Activation of the Opioidergic Descending Pain Control System Underlies Placebo Analgesia

Falk Eippert,<sup>1,\*</sup> Ulrike Bingel,<sup>2</sup> Eszter D. Schoell,<sup>1</sup> Juliana Yacubian,<sup>1</sup> Regine Klinger,<sup>3</sup> Jürgen Lorenz,<sup>4</sup> and Christian Büchel<sup>1</sup>

A



# THEORIES OF PLACEBO EFFECTS

- Two major theories to explain placebo effects:



EXPECTATION

The diagram consists of two large circles on a light blue background. The left circle is red and contains the word 'EXPECTATION' in white. The right circle is blue and contains the words 'LEARNING/CONDITIONING' in white. A large, diagonal watermark reading 'PLEASE DO NOT COPY' is overlaid across the entire slide.

LEARNING/  
CONDITIONING

# EXPECTATION

---

## Response Expectancy as a Determinant of Experience and Behavior

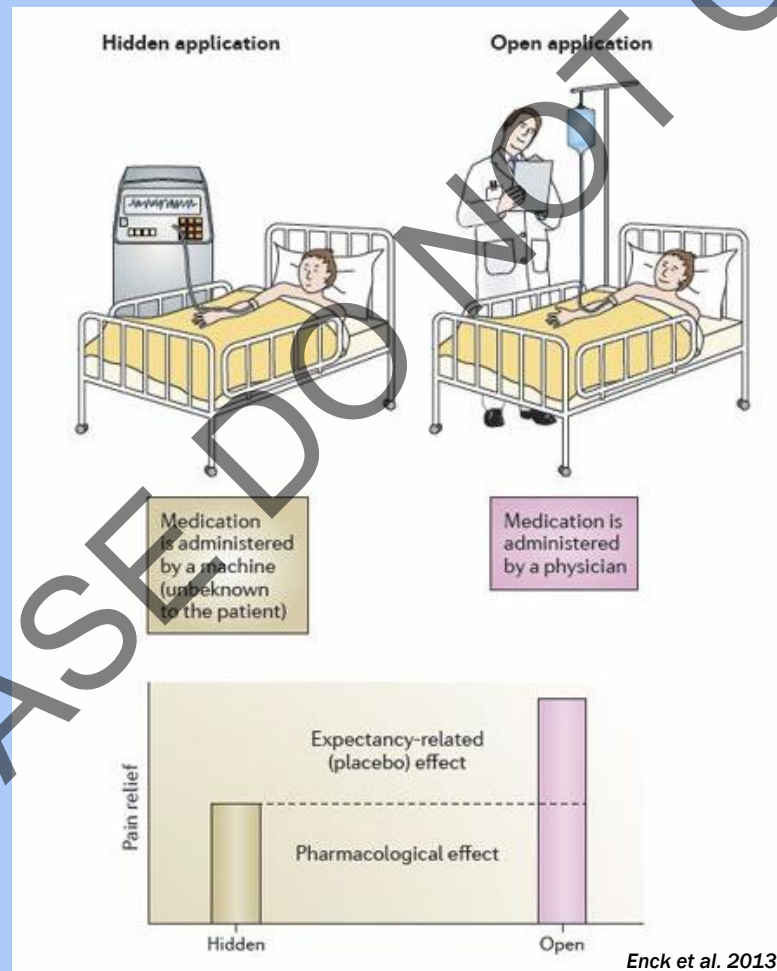
---

Irving Kirsch *University of Connecticut*

---

*“Placebo effects generally correspond to people’s knowledge or beliefs about the kind of drug they believe they are receiving, and for that reason, a causal relation between expectancy and placebo reaction has generally been assumed...”*

# OPEN-HIDDEN PARADIGMS



# THEORIES OF PLACEBO EFFECTS

- Two major theories to explain placebo effects:

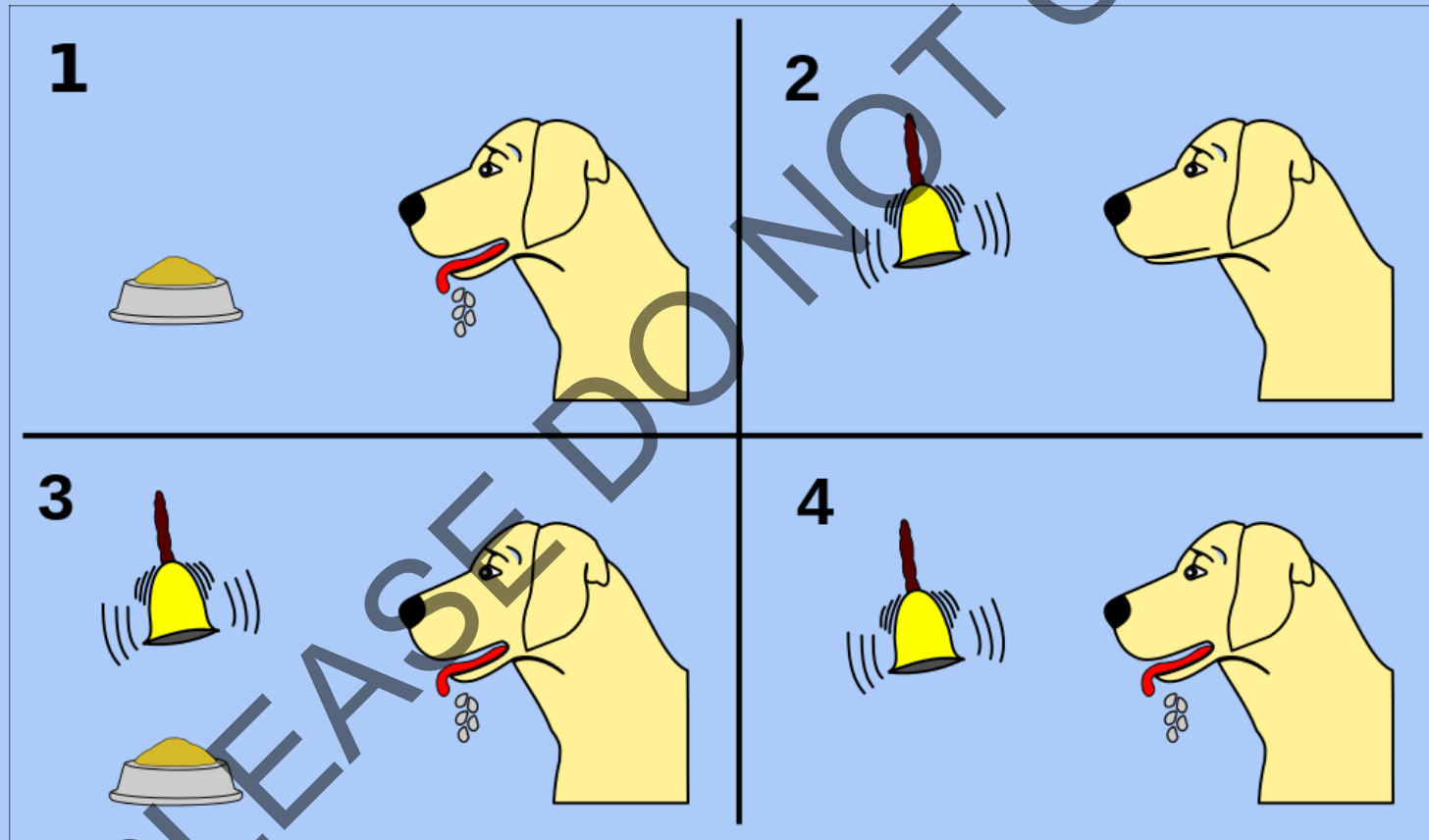


EXPECTATION

The diagram consists of two large circles on a light blue background. The left circle is dark blue and contains the word 'EXPECTATION' in white. The right circle is bright pink and contains the words 'LEARNING/CONDITIONING' in white. A large, diagonal watermark reading 'PLEASE DO NOT COPY' is overlaid across the entire slide.

LEARNING/  
CONDITIONING

# CONDITIONING





# CONDITIONING PARADIGMS

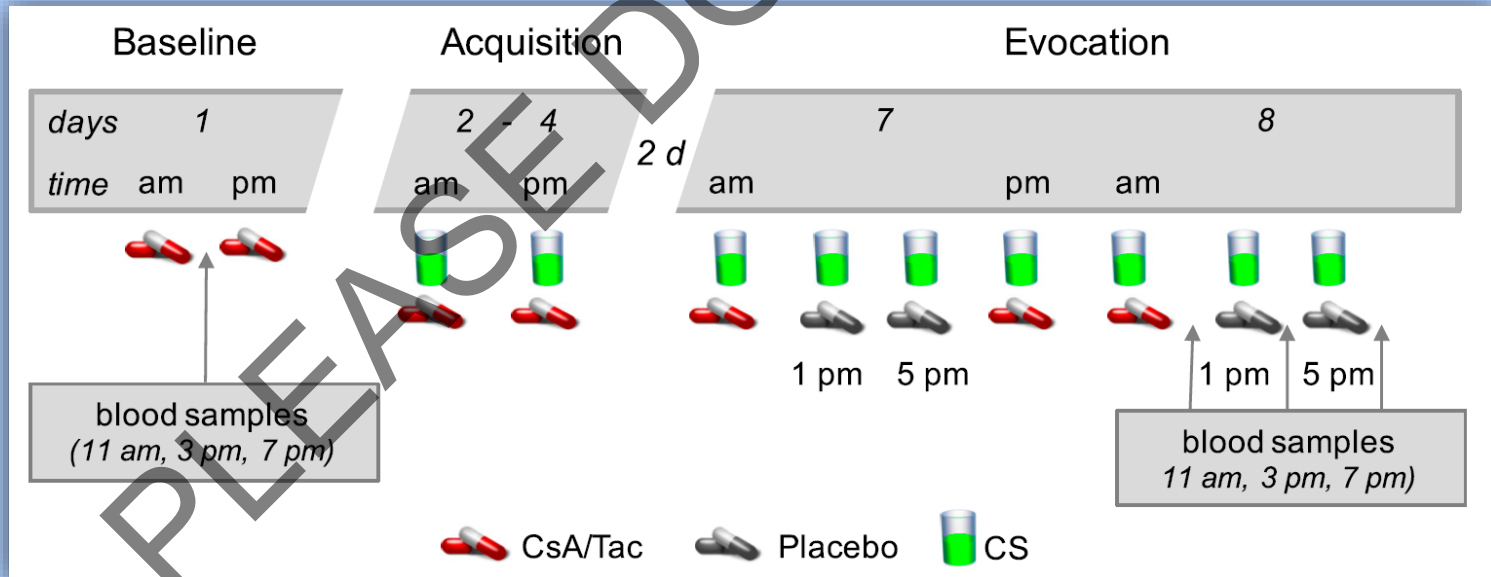
## Learned immunosuppressive placebo responses in renal transplant patients

Julia Kirchhof<sup>a</sup>, Liubov Petrakova<sup>a</sup>, Alexandra Brinkhoff<sup>b</sup>, Sven Benson<sup>a</sup>, Justine Schmidt<sup>a</sup>, Maike Unteroberdörster<sup>c</sup>, Benjamin Wilde<sup>b</sup>, Ted J. Kaptchuk<sup>d</sup>, Oliver Witzke<sup>e</sup>, and Manfred Schedlowski<sup>a,f,1</sup>

<sup>a</sup>Institute of Medical Psychology and Behavioral Immunobiology, University Hospital Essen, University of Duisburg-Essen, 45122 Essen, Germany;

<sup>b</sup>Department of Nephrology, University Hospital Essen, University of Duisburg-Essen, 45122 Essen, Germany; <sup>c</sup>Clinic of Neurosurgery, University Hospital Essen, University of Duisburg-Essen, 45122 Essen, Germany; <sup>d</sup>Program in Placebo Studies, Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, MA 02215; <sup>e</sup>Department of Infectious Diseases, University Hospital Essen, University of Duisburg-Essen, 45122 Essen, Germany; and <sup>f</sup>Department of Clinical Neuroscience, Karolinska Institutet, 171 77 Stockholm, Sweden

March 7, 2018



# THEORIES OF PLACEBO EFFECTS

- Two major theories to explain placebo effects:



The diagram consists of two circles on a light blue background. The left circle is dark blue and contains the word 'EXPECTATION' in white. The right circle is a lighter blue and contains the words 'LEARNING/CONDITIONING' in white. A large, diagonal watermark reading 'PLEASE DO NOT COPY' is overlaid across the entire slide.

**EXPECTATION**

**LEARNING/  
CONDITIONING**

“Rather than being viewed as an alternative to expectancy, classical conditioning can be understood as one method by which expectancies are formed”

# FROM NUISANCE TO TREATMENT

Neuron  
**Perspective**

CellPress

## Placebo Effects: From the Neurobiological Paradigm to Translational Implications

Fabrizio Benedetti<sup>1,\*</sup>

<sup>1</sup>Department of Neuroscience, University of Turin Medical School and National Institute of Neuroscience, 10125 Turin, Italy

\*Correspondence: [fabrizio.benedetti@unito.it](mailto:fabrizio.benedetti@unito.it)

<http://dx.doi.org/10.1016/j.neuron.2014.12.008>

## Placebo Effects in Medicine

Ted J. Kaptchuk and Franklin G. Miller, Ph.D.



N ENGL J MED 373;1 NEJM.ORG JULY 2, 2015

OPINION

NATURE REVIEWS | DRUG DISCOVERY

## The placebo response in medicine: minimize, maximize or personalize?

Paul Enck, Ulrike Bingel, Manfred Schedlowski and Winfried Rief

# HETEROGENEITY IN RESPONSES?



# RESPONDERS AND NON-RESPONDERS

Review

CellPress

## Genetics and the placebo effect: the placebome

Kathryn T. Hall<sup>1,2</sup>, Joseph Loscalzo<sup>3</sup>, and Ted J. Kaptchuk<sup>1,2</sup>

Table 1. Polymorphisms in candidate genes that may be part of the placebome

Placebo pathway	Gene name	Gene symbol	Chromosomal location	Placebo SNPs	Refs
Dopamine	Catechol-O-methyltransferase	COMT	22q11.2	rs4680	[38]
	Monoamine oxidase	MAO-A	Xp11.3	rs6323, rs6609257	[43,55]
	Dopamine B hydroxylase	DBH	9q34	rs2873804	[43]
	Dopamine receptor 3	DRD3	3q13.31	rs6280	[59]
	Brain-derived neurotropic factor	BDNF	11p14.1	rs6265	[66]
Serotonin	Tryptophan hydroxylase-2	TPH2	12q21.1	rs4570625	[75]
	5-Hydroxytryptamine transporter	SLC6A4	17q11.2	rs4251417	[43]
	5-Hydroxytryptamine receptor 2A	HTR2A	13q14.2	rs2296972, rs622337	[43]
	Serotonin transporter gene-linked polymorphic region	5-HTTLPR	17q11.2	Variable tandem nucleotide repeat	[75]
Opioid	Opioid receptor	OPRM1	6q25.2	rs510769	[69]
Endocannabinoid	Fatty acid amide hydrolase	FAAH	1p33	rs324420	[73]

# ALL DISEASES?

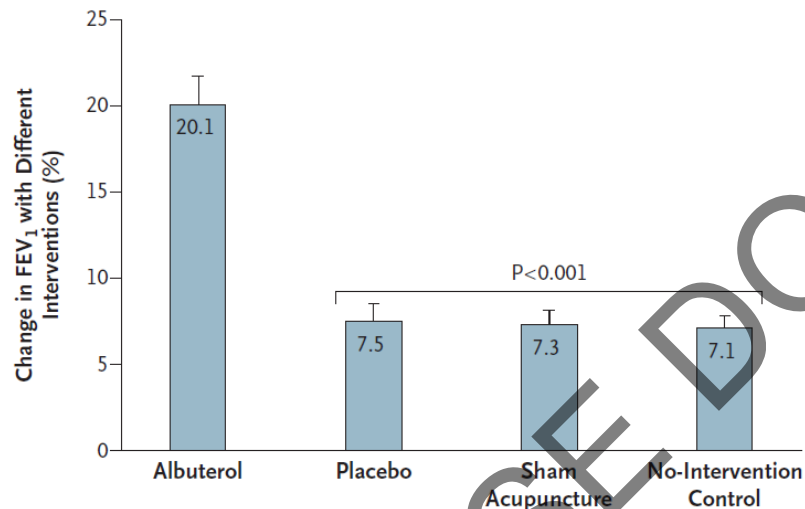
*The* NEW ENGLAND JOURNAL *of* MEDICINE

ORIGINAL ARTICLE

## Active Albuterol or Placebo, Sham Acupuncture, or No Intervention in Asthma

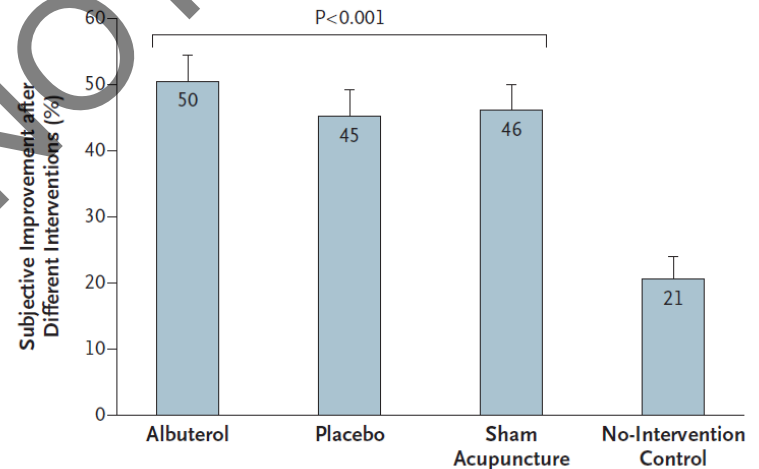
Michael E. Wechsler, M.D., John M. Kelley, Ph.D., Ingrid O.E. Boyd, M.P.H.,  
Stefanie Dutilleul, B.S., Gautham Marigowda, M.B., Irving Kirsch, Ph.D.,  
Elliot Israel, M.D., and Ted J. Kaptchuk

# PLACEBO EFFECTS?



**Figure 3.** Percent Change in Maximum Forced Expiratory Volume in 1 Second (FEV<sub>1</sub>) with Each of the Four Interventions.

The relative improvement in FEV<sub>1</sub> achieved with albuterol was significantly greater than that achieved with each of the other three interventions ( $P<0.001$ ). No other differences among the four experimental conditions were significant. T bars indicate standard errors.



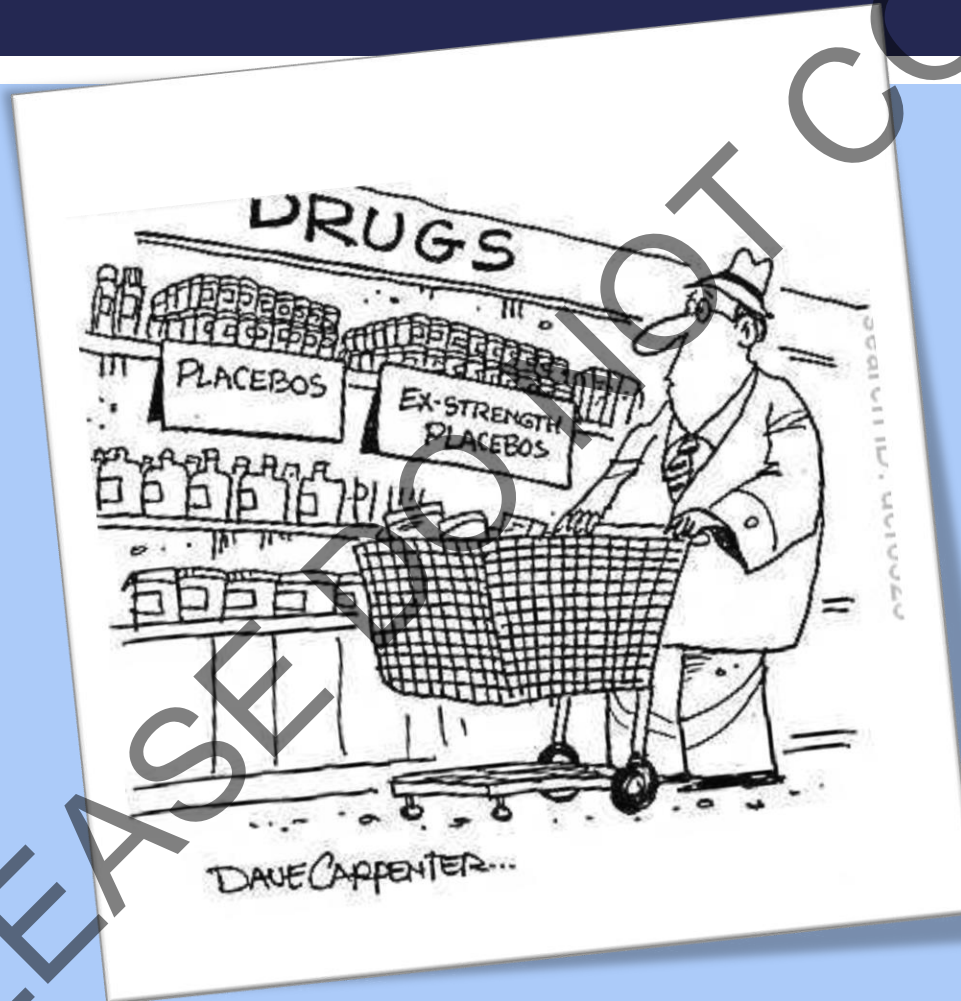
**Figure 4.** Percent Change in Subjective Improvement with Each of the Four Interventions.

The relative improvement in subjective outcomes, assessed with the use of a visual-analogue scale (with 0 indicating no improvement and 10 indicating complete improvement), was significantly greater with the albuterol inhaler, placebo inhaler, and sham acupuncture interventions than with the no-intervention control ( $P<0.001$ ). No other differences among the four experimental conditions were significant. T bars indicate standard errors.



## 2

# “DIFFERENTIAL” PLACEBO EFFECTS



- The concept that different types of placebos may yield different magnitudes of placebo effects



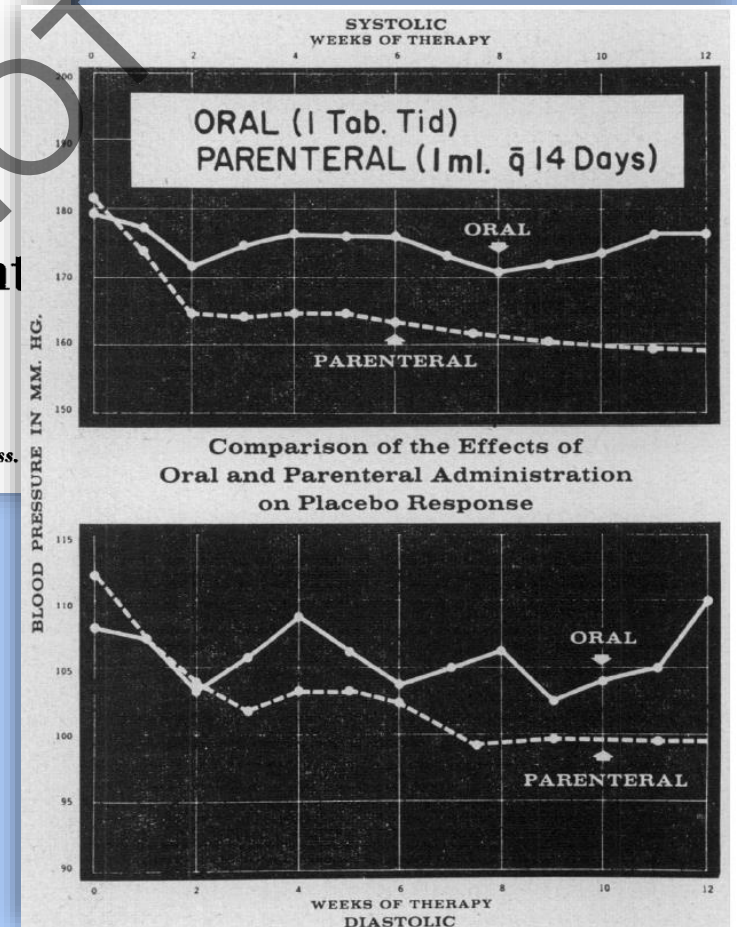
# EARLY CONCEPTIONS...

124

J.A.M.A., April 15, 1961

## A Double-Blind Study of the Treatment of Hypertension

*Raymond F. Grenfell, M.D., Arthur H. Briggs, M.D., and William C. Holland, M.D., Jackson, Miss.*



# SHAM-CONTROLLED SURGICAL TRIALS

ANNALS OF SURGERY  
Vol. 235, No. 2, 303-307  
© 2002 Lippincott Williams & Wilkins, Inc.

## Surgical “Placebo” Controls

Robert Tenery, MD, Dallas, TX—Chair; Herbert Rakatansky, MD, Providence, RI—Vice-Chair; Frank A. Riddick, Jr., MD, New Orleans, LA; Michael S. Goldrich, MD, Highland Park, NJ; Leonard J. Morse, MD, Worcester, MA; John M. O'Bannon, III, MD, Richmond, VA; Priscilla Ray, MD, Houston, TX; Sherie Smalley, MD, Salt Lake City, UT—Resident Member; Matthew Weiss, Chicago, IL—Student Member. Staff to the Council on Ethical and Judicial Affairs: Audiey Kao, MD, PhD, Acting Vice President, Ethics Standards Group, American Medical Association; Karine Morin, LL.M., Council Secretary and Staff Author; Andrew Maixner, Council Staff Associate; Sam Seiden, Council Staff Associate.



# SHAM-CONTROLLED SURGICAL TRIALS

THE NEW ENGLAND JOURNAL OF MEDICINE  
Vol. 260 No. 22 INTERNAL-MAMMARY-ARTERY LIGATION — COBB ET AL. 1115

## AN EVALUATION OF INTERNAL-MAMMARY-ARTERY LIGATION BY A DOUBLE-BLIND TECHNIC\*

LEON

The New England Journal of Medicine

VOLUME 347

JULY 11, 2002

NUMBER 2 FOR SEVERE



## A CONTROLLED TRIAL OF ARTHROSCOPY FOR OSTEOARTHRITIS OF THE KNEE\*

J. BRUCE MOSELEY, M.D., KIMBERLY O'MALLEY, PH.D., NANCY J. BARUCH, A. BRODY, PH.D., DAVID H. KUYKENDALL, PH.D., CAROL M. ASHTON, M.D., M.P.H., AND NELDA

*The NEW ENGLAND JOURNAL of MEDICINE*

ORIGINAL ARTICLE

## A Controlled Trial of Renal Denervation for Resistant Hypertension

Deepak L. Bhatt, M.D., M.P.H., David E. Kandzari, M.D., William W. O'Neill, M.D., Ralph D'Agostino, Ph.D., John M. Flack, M.D., M.P.H., Barry T. Katzen, M.D., Martin B. Leon, M.D., Minglei Liu, Ph.D., Laura Mauri, M.D., Manuela Negoita, M.D., Sidney A. Cohen, M.D., Ph.D., Suzanne Oparil, M.D., Krishna Rocha-Singh, M.D., Raymond R. Townsend, M.D., and George L. Bakris, M.D.,  
for the SYMPPLICITY HTN-3 Investigators\*

# RECENT ATTENTION...

Articles

## Percutaneous coronary intervention in stable angina (ORBITA): a double-blind, randomised controlled trial



*Rasha Al-Lamee, David Thompson, Hakim-Moulay Dehbi, Sayan Sen, Kare Tang, John Davies, Thomas Keeble, Michael Mielewczik, Raffi Kaprielian, Iqbal S Malik, Sukhjinder S Nijjer, Ricardo Petraco, Christopher Cook, Yousif Ahmad, James Howard, Christopher Baker, Andrew Sharp, Robert Gerber, Suneel Talwar, Ravi Assomull, Jamil Mayet, Roland Wensel, David Collier, Matthew Shun-Shin, Simon A Thom, Justin E Davies, Darrel P Francis, on behalf of the ORBITA investigators\**

Articles

## Arthroscopic subacromial decompression for subacromial shoulder pain (CSAW): a multicentre, pragmatic, parallel group, placebo-controlled, three-group, randomised surgical trial



*David J Beard, Jonathan L Rees, Jonathan A Cook, Ines Rombach, Cushla Cooper, Naomi Merritt, Beverly A Shirkey, Jenny L Donovan, Stephen Gwilym, Julian Savulescu, Jane Moser, Alastair Gray, Marcus Jepson, Irene Tracey, Andrew Judge, Karolina Wartolowska, Andrew J Carr, on behalf of the CSAW Study Group\**



# META-ANALYTIC APPROACHES

## Placebo interventions for all clinical conditions (Review)

Hróbjartsson A, Gøtzsche PC

“Meta-regression analyses showed that larger effects of placebo interventions were associated with physical placebo interventions” (e.g. sham devices)

**THE COCHRANE  
COLLABORATION®**



Not head-to-head comparisons

# DIRECT APPROACHES



ELSEVIER

Journal of Clinical Epidemiology 53 (2000) 786–792

**Journal of  
Clinical  
Epidemiology**

## Do medical devices have enhanced placebo effects?

Ted J. Kaptchuk<sup>a,\*</sup>, Peter Goldman<sup>a,b</sup>, David A. Stone<sup>a,b</sup>, William B. Stason<sup>b</sup>

<sup>a</sup>*Center for Alternative Medicine Research, Beth Israel Deaconess Medical Center, Harvard Medical School, 330 Brookline Avenue, Boston, MA 02215, USA*

<sup>b</sup>*Harvard School of Public Health, Boston, MA, USA*

Received 10 November 1999; received in revised form 5 January 2000; accepted 21 January 2000

Research

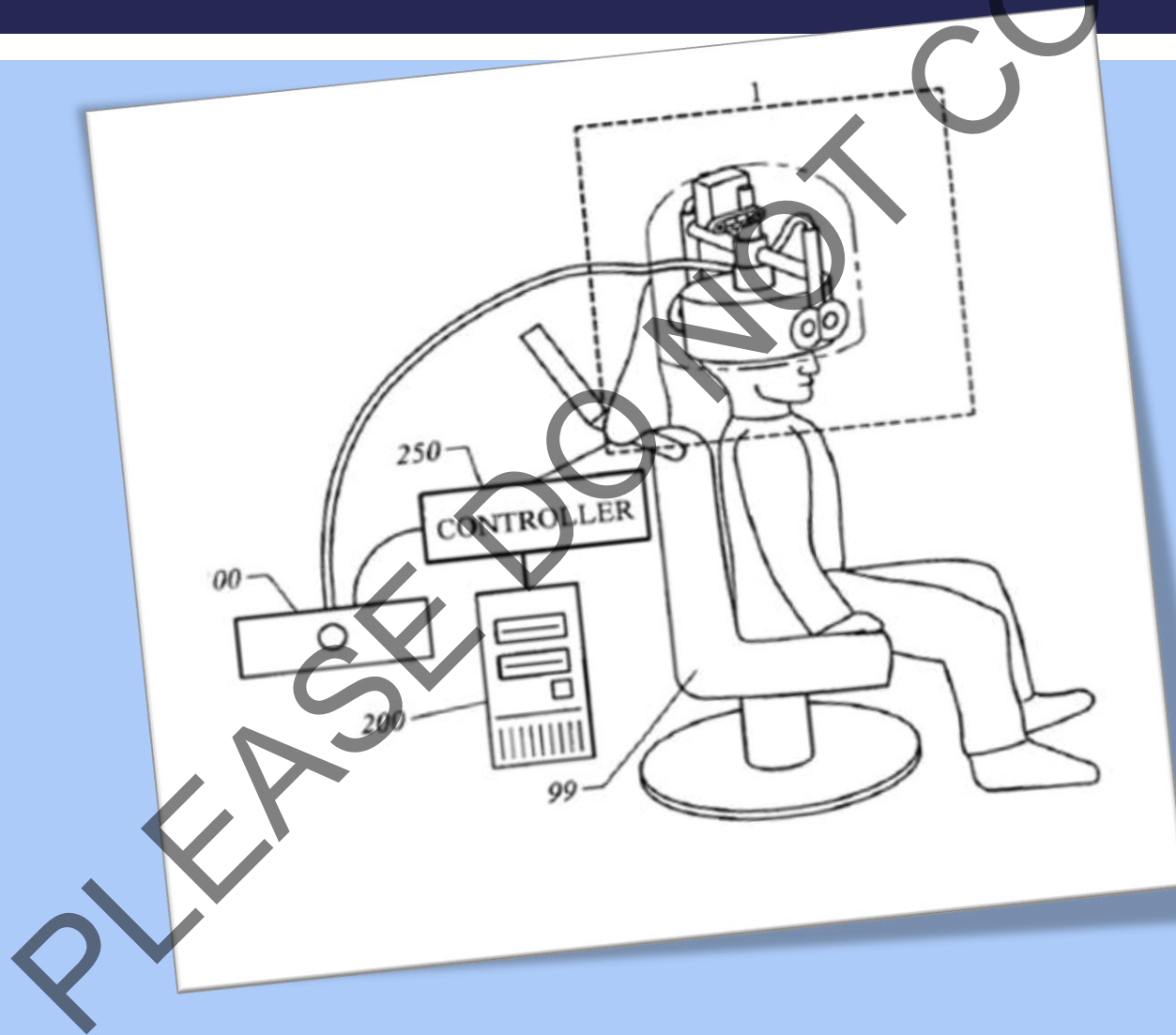
BMJ

## Sham device *v* inert pill: randomised controlled trial of two placebo treatments

Ted J Kaptchuk, William B Stason, Roger B Davis, Anna T R Legedza, Rosa N Schnyer, Catherine E Kerr, David A Stone, Bong Hyun Nam, Irving Kirsch, Rose H Goldman

# 3

## TMS AND PLACEBO EFFECTS





# EXEMPLIFICATION OF AN ELABORATE THERAPEUTIC TECHNOLOGY





# SHAM TMS

- Achieve blinding but avoid meaningful stimulation to the brain
- Goal: Mimic TMS's visual and auditory (+/- tactile) experience but shield the brain from the magnetic fields
- Many different sham device techniques



*European Journal of Neuroscience*, Vol. 38, pp. 2973–2977, 2013

doi:10.1111/ejn.12307

## TECHNICAL SPOTLIGHT

### TECHNICAL SPOTLIGHT

Challenges of proper placebo control for non-invasive brain stimulation in clinical and experimental applications

Nick J. Davis,<sup>1</sup> Edward Gold,<sup>2</sup> Alvaro Pascual-Leone<sup>2</sup> and R. Martyn Bracewell<sup>1,3,4</sup>

**\*Include a measure assessing success of blinding!**

# QUANTIFYING PLACEBO EFFECTS

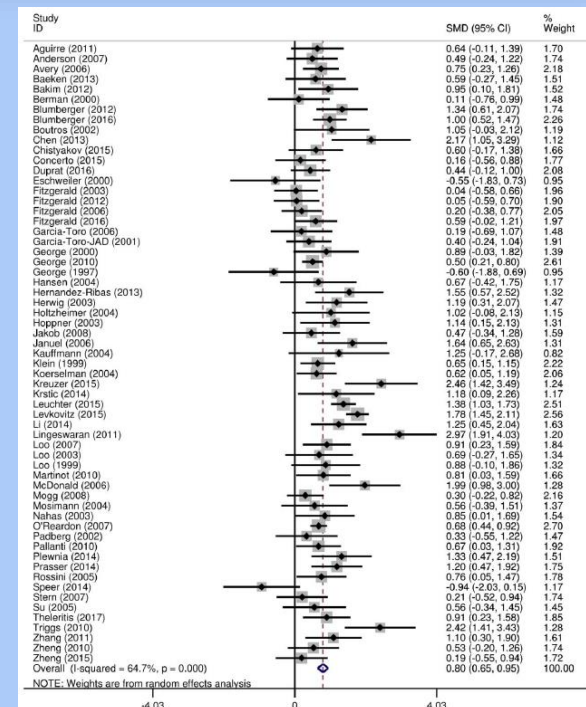
A systematic review and meta-analysis on placebo response to repetitive transcranial magnetic stimulation for depression trials



Laís B. Razza<sup>a</sup>, Adriano H. Moffa<sup>a</sup>, Marina L. Moreno<sup>a</sup>, Andre F. Carvalho<sup>b</sup>, Frank Padberg<sup>c</sup>, Felipe Fregni<sup>d</sup>, André R. Brunoni<sup>a,c,\*</sup>

(2018) 105–113

- 61 studies, large effect size of 0.8 (Hedge's g)
- Meta-regression
  - Placebo response magnitude was positively associated with the year of publication (increasing sham TMS responses over time).
  - Studies that included patients with treatment-resistant depression had lower placebo responses



# VARIABILITY IN PLACEBO RESPONSES

JAMA Psychiatry | Original Investigation

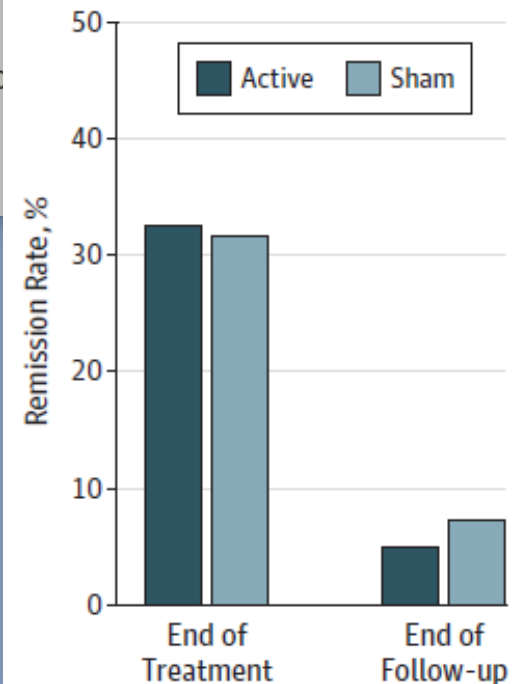
## Effect of Repetitive Transcranial Magnetic Stimulation on Treatment-Resistant Major Depression in U.S. Veterans: A Randomized Clinical Trial

Jerome A. Yesavage, MD; J. Kaci Fairchild, PhD; Zhibao Mi, PhD; Kousick Biswas, PhD; Anne Davis-Karim, PharmD; Ciaran S. Phibbs, PhD; Steven D. Forman, MD, PhD; Michael Thase, MD; Leanne M. Williams, PhD; Amit Etkin, MD, PhD; Ruth O'Hara, PhD; Gerald Georgette, RN; Tamara Beale, MA; Grant D. Huang, MPH, PhD; Art Noda, MS; Mark S. George, MD; for the VA Cooperative Studies Program Study Team

**“41.0% of the veterans in the active treatment group achieved remission of depressive symptoms”\***

*\*No difference from sham group (37%)*

**B** MDD with PTSD



# PLACEBO MODULATION OF AMYGDALA

*Psychophysiology*, 48 (2011), 1119–1128. Wiley Periodicals, Inc. Printed in the USA.  
Copyright © 2011 Society for Psychophysiological Research  
DOI: 10.1111/j.1469-8986.2011.01178.x

## A follow-up fMRI study of the anxiolytic effect

WENCAI ZHANG,<sup>a</sup> SHAOZHENG QI<sup>b</sup>

<sup>a</sup>Key Laboratory of Mental Health, Institute of Psychology, Chinese Academy of Sciences

<sup>b</sup>Learning and Cognition Laboratory, Capital Normal University

<sup>c</sup>Center for Cognitive Neuroimaging, Donders Institute for Brain, Cognition and Behavior



Neuropsychopharmacology (2012) 37, 2222–2232

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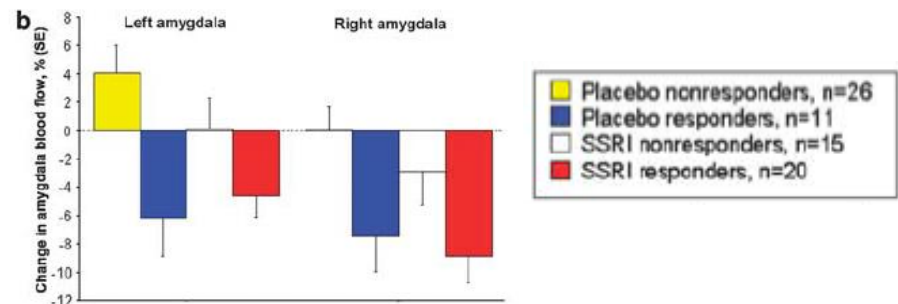
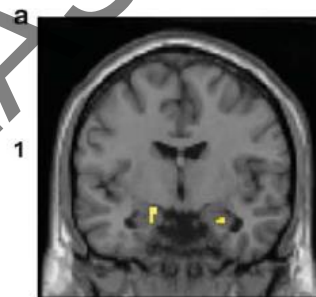
www.neuropsychopharmacology.org

## Amygdala Subregions Tied to SSRI and Placebo Response in Patients with Social Anxiety Disorder

Vanda Faria<sup>\*,1</sup>, Lieuwe Appel<sup>2</sup>, Fredrik Åhs<sup>3</sup>, Clas Linnman<sup>4</sup>, Anna Pissiota<sup>1</sup>, Örjan Frans<sup>1</sup>, Massimo Bani<sup>5</sup>, Paolo Bettica<sup>5</sup>, Emilio M Pich<sup>5,6</sup>, Eva Jacobsson<sup>7</sup>, Kurt Wahlstedt<sup>7</sup>, Mats Fredrikson<sup>1</sup> and Tomas Furmark<sup>1</sup>

### Amygdala subregions in anxiolysis

V Faria et al



# AN EXTREME EXAMPLE...

Original Article

**Cephalalgia**  
An International Journal of Headache



International  
Headache Society

## Randomized, proof-of-principle clinical trial of active transcranial magnetic stimulation in chronic migraine

Adriana B Conforto<sup>1,2</sup>, Edson Amaro Jr<sup>1,3</sup>, André L Gonçalves<sup>1</sup>,  
Juliane PP Mercante<sup>1</sup>, Vera Z Guendler<sup>1</sup>, Josione R Ferreira<sup>1</sup>,  
Clara CFB Kirschner<sup>1</sup> and Mario FP Peres<sup>1,4</sup>

Cephalalgia  
2014, Vol. 34(6) 464-472  
© International Headache Society 2013  
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sagepub.co.uk/journalsPermissions.nav  
DOI: 10.1177/0333102413515346  
cep.sagepub.com  
SAGE

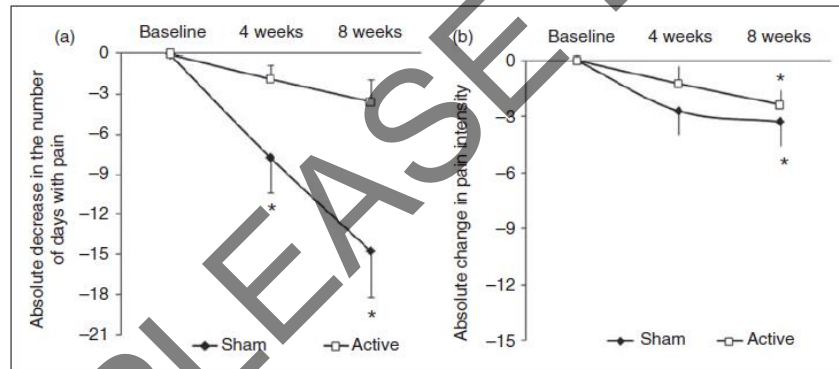
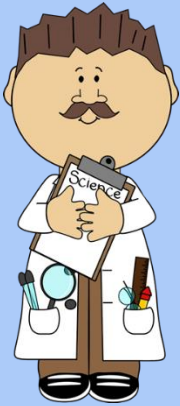


Figure 2. Absolute differences (mean, standard errors) compared to baseline, in the number of days with pain (a) and pain intensity (b), after four and eight weeks of treatment. \* $p$  value  $\leq 0.05$ .



*“Contrary to our primary hypothesis, the number of headache days decreased significantly more in the sham group than in the group treated with active rTMS-DLPFC at eight weeks. Average decrease in headache days was >50% in the sham group, indicating a powerful placebo response.”*

# EVIDENCE FOR “DIFFERENTIAL EFFECT”?



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## Placebo Response of Non-Pharmacological and Pharmacological Trials in Major Depression: A Systematic Review and Meta-Analysis

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- Compared inert pill group from escitalopram medication trials to the sham TMS group of TMS trials
- Reported no significant difference...BUT
- Methodological limitations
  - Heterogenous patient populations – “refractory”
  - Blinding – double vs single
  - Dated (only included trials 2002-2008)



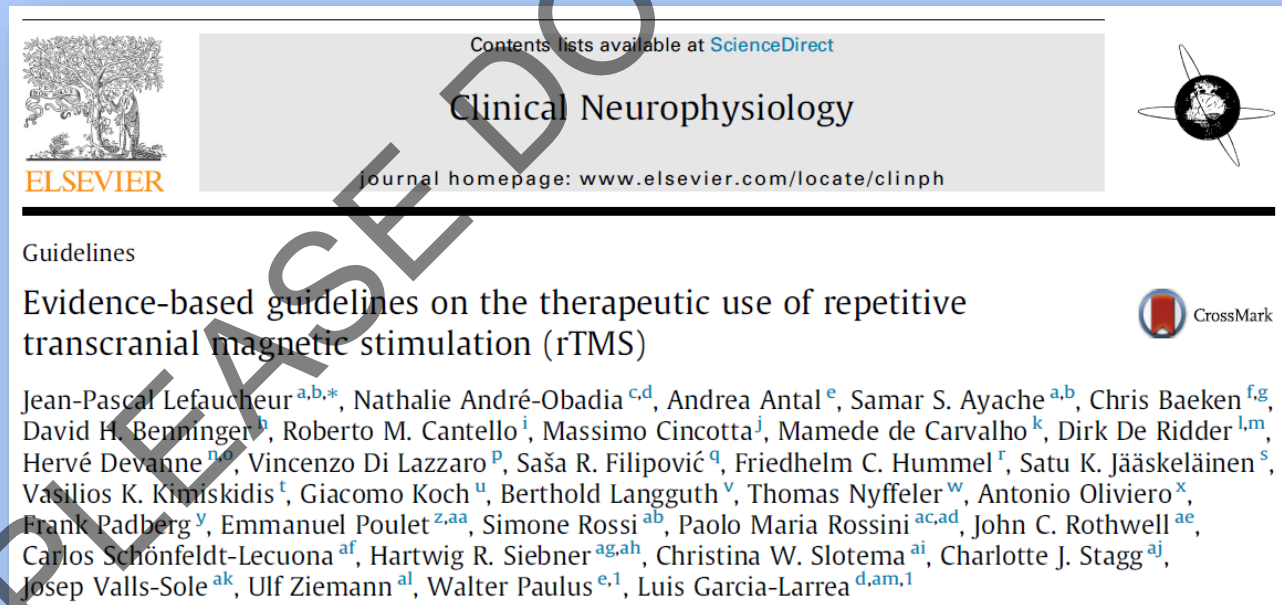
# FURTHER RESEARCH?

- No studies comparing sham TMS to “no treatment” control
  - Needed to delineate placebo effects from “other” effects (including activation of coming to hospital for treatment)



# IMPLICATIONS

- Unfavorable impact on statistical power for sham controlled treatment trials
  - *RCT investigating a treatment with a large embedded placebo effect will generally need more subjects to prove efficacy than a treatment with a smaller placebo effect (Kaptchuk et al. 2000)*





# ONGOING ISSUES...

The screenshot displays the Nexstim website's 'News and Events' page. At the top, the Nexstim logo is accompanied by the tagline 'Targeting a Paradigm Shift in Stroke Rehabilitation'. A navigation bar includes links for HOME, ABOUT US, HEALTHCARE PROVIDERS, PATIENTS, NEWS AND EVENTS, and INVESTORS. A search bar and Nasdaq listing information (NXTMH and NXTMS) are also visible. The main content area features a large blue banner with the text 'News and Events' and 'Press Releases', alongside a photograph of a diverse group of healthcare professionals. Below this, a 'Press Releases' sidebar lists years from 2017 down to 2012, with a link to the 'Press Releases Archive'. The central focus is a press release titled 'Final Results from NICHE Phase III trial presented at the International Stroke Conference', dated 23 February 2017. The release text indicates that the final results from the NICHE Phase III trial were presented at the International Stroke Conference.

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## News and Events

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/ Final Results from NICHE Phase III trial presented at the International Stroke Conference

### Final Results from NICHE Phase III trial presented at the International Stroke Conference

23 February 2017


# ISSUES REQUIRING CRITICAL REFLECTION...

How should we  
measure efficacy?  
New approaches?



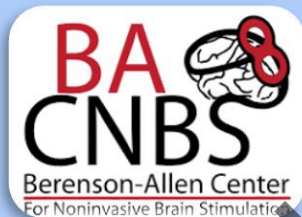
How do we leverage  
enhanced placebo  
effects?

# QUESTIONS



Could studying the placebo effect  
change the way we think  
about medicine?

- *The New Yorker* on PiPS Research



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