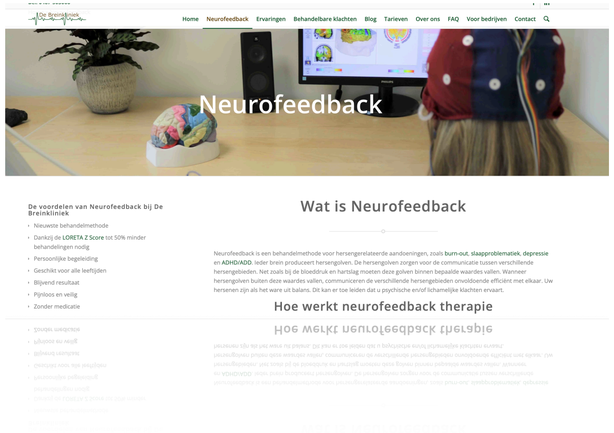
# Nieuwe behandelingen: Grensverleggend of ongeloofwaardig?

Tom Beckers

VGCt Najaarscongres 2025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Neurofeedback
De voordelen van Neurofeedback bij De Breinkliniek
Nieuwste behandelmethode
Dankzij de LORETA Z Score tot 50% minder behandelingen nodig
Persoonlijke begeleiding
Geschikt voor alle leeftijden
Blijvend resultaat
Pijnloos en veilig
Zonder medicatie
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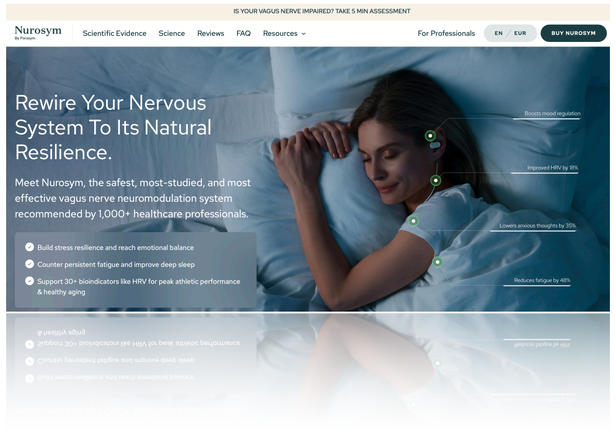
Hoe werkt neurofeedback therapie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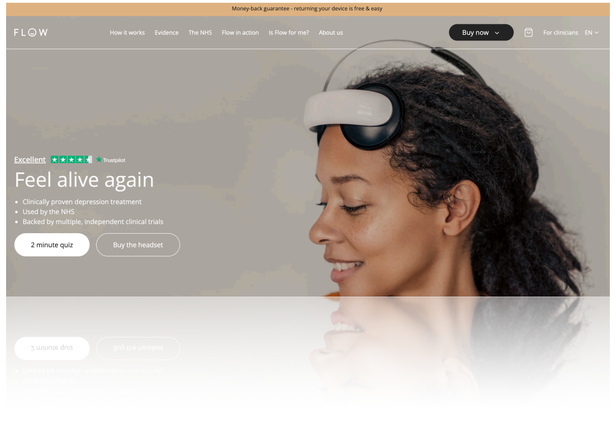
Reduces fatigue by 48%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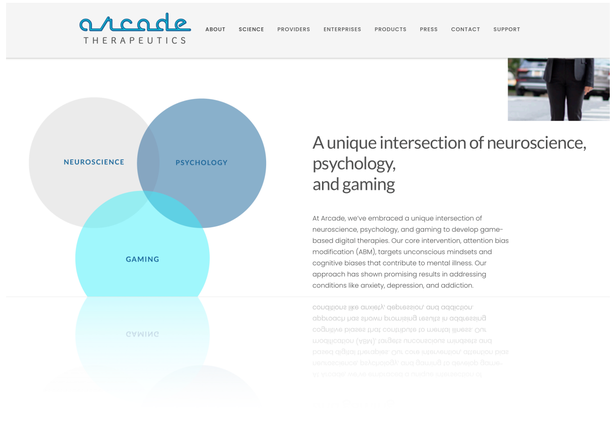
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Memrec voor de behandeling van angst
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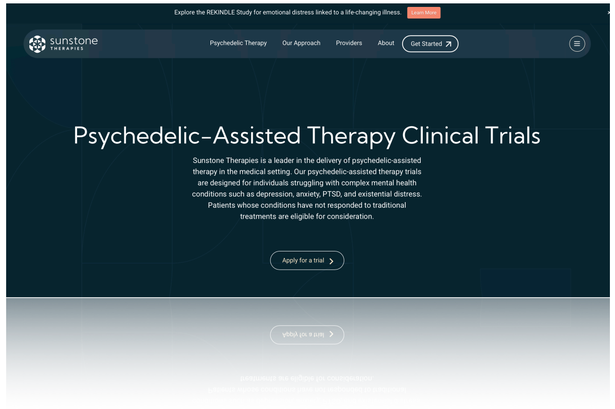
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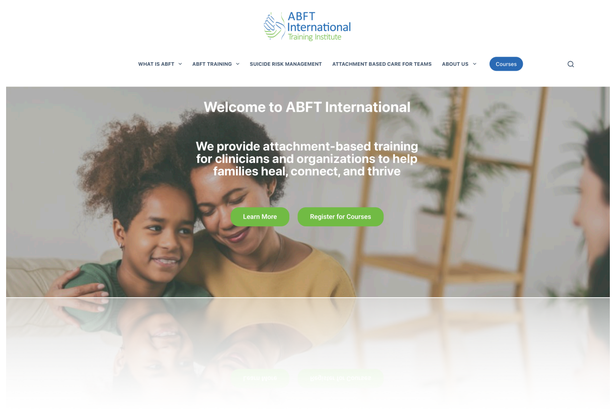
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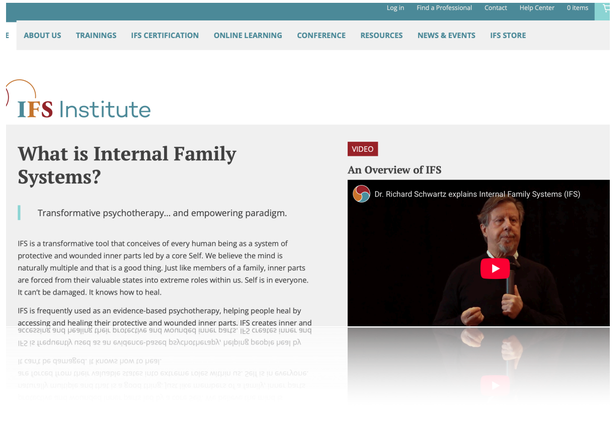
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What is Internal Family Systems?
Transformative psychotherapy... and empowering paradigm.
IFS is a transformative tool that conceives of every human being as a system of protective and wounded inner parts led by a core Self. We believe the mind is naturally multiple and that is a good thing. Just like members of a family, inner parts are forced from their valuable states into extreme roles within us. Self is in everyone. It can't be damaged. It knows how to heal.
IFS is frequently used as an evidence-based psychotherapy, helping people heal by accessing and healing their protective and wounded inner parts. IFS creates inner and
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Dr. Richard Schwartz explains Internal Family Systems (IFS)


# Neurofeedback

### De voordelen van Neurofeedback bij De Breinkliniek

- Nieuwste behandelmethode
- Dankzij de LORETA Z Score tot 50% minder behandelingen nodig
- Persoonlijke begeleiding
- Geschikt voor alle leeftijden
- Blijvend resultaat
- Pijnloos en veilig
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## Hoe werkt neurofeedback therapie

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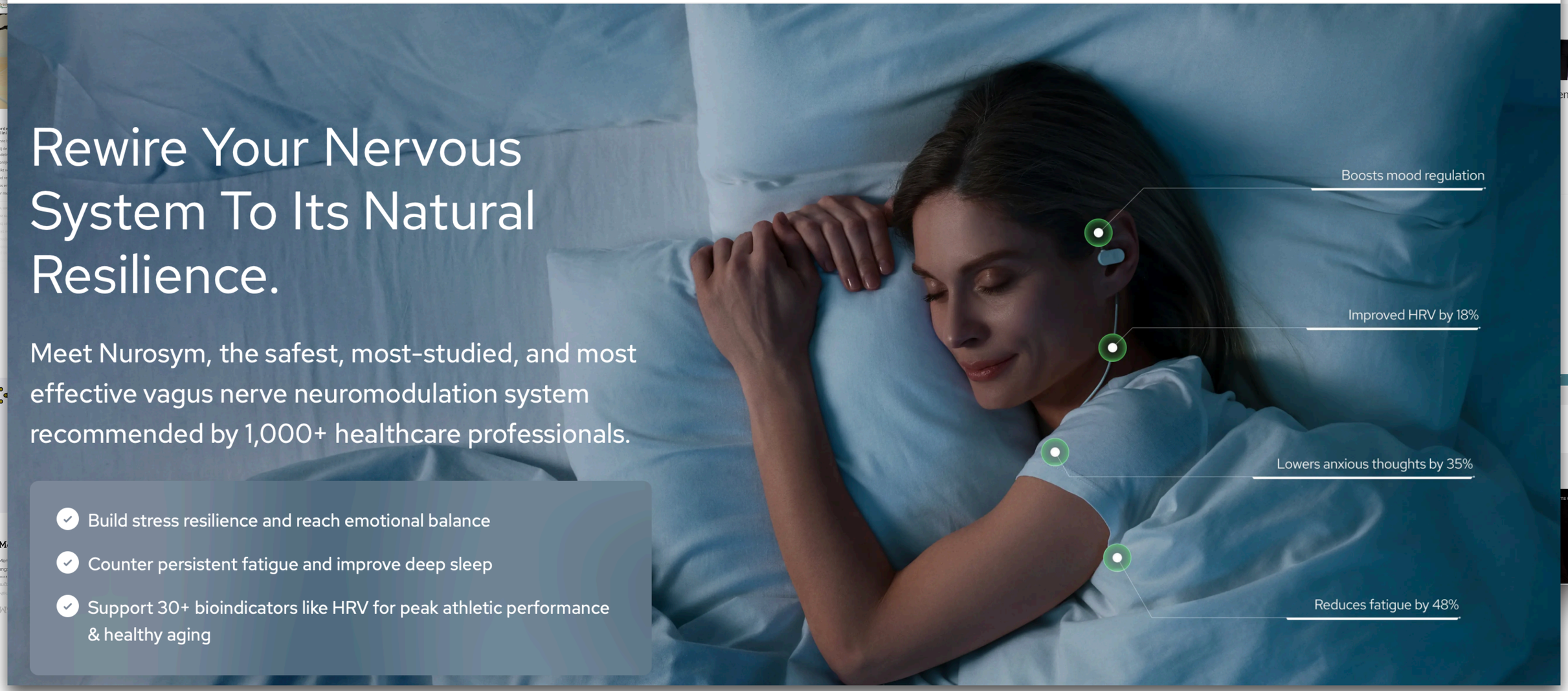

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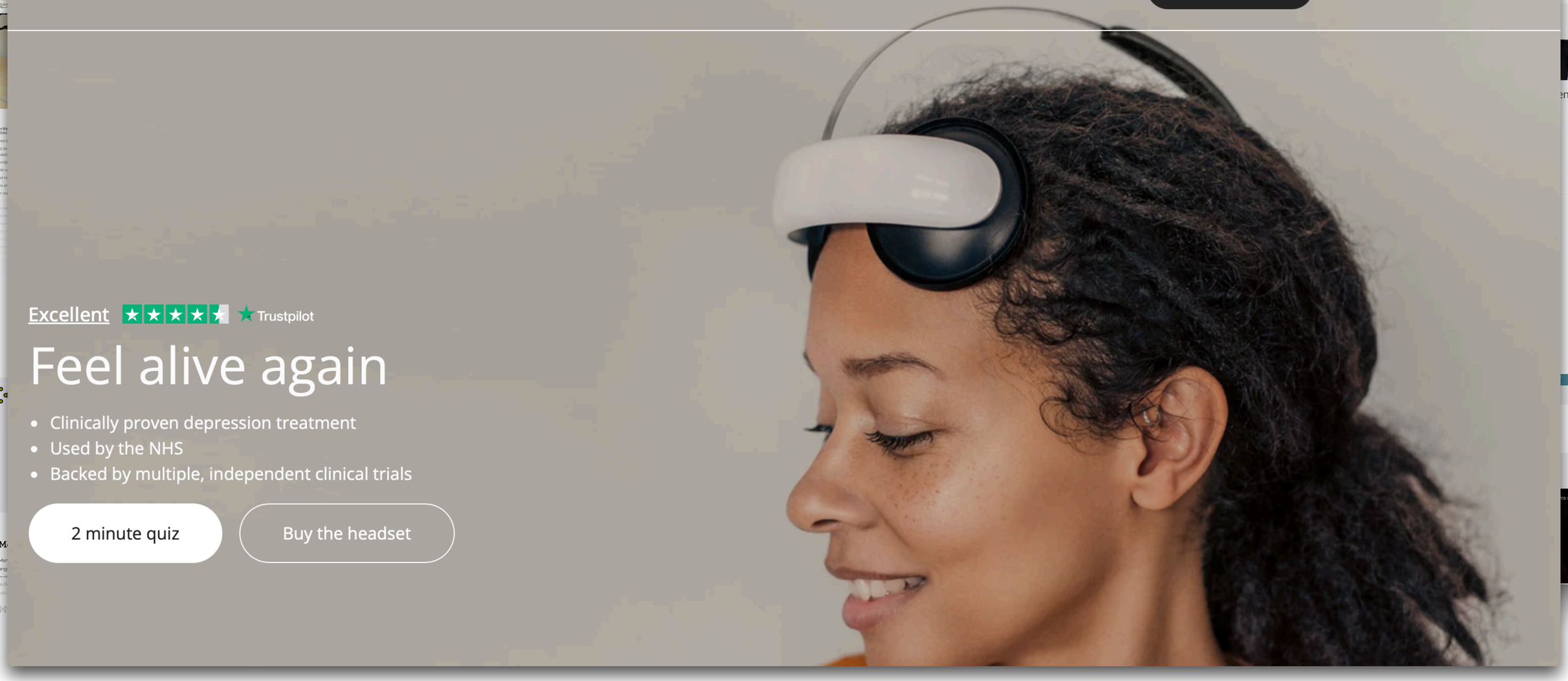

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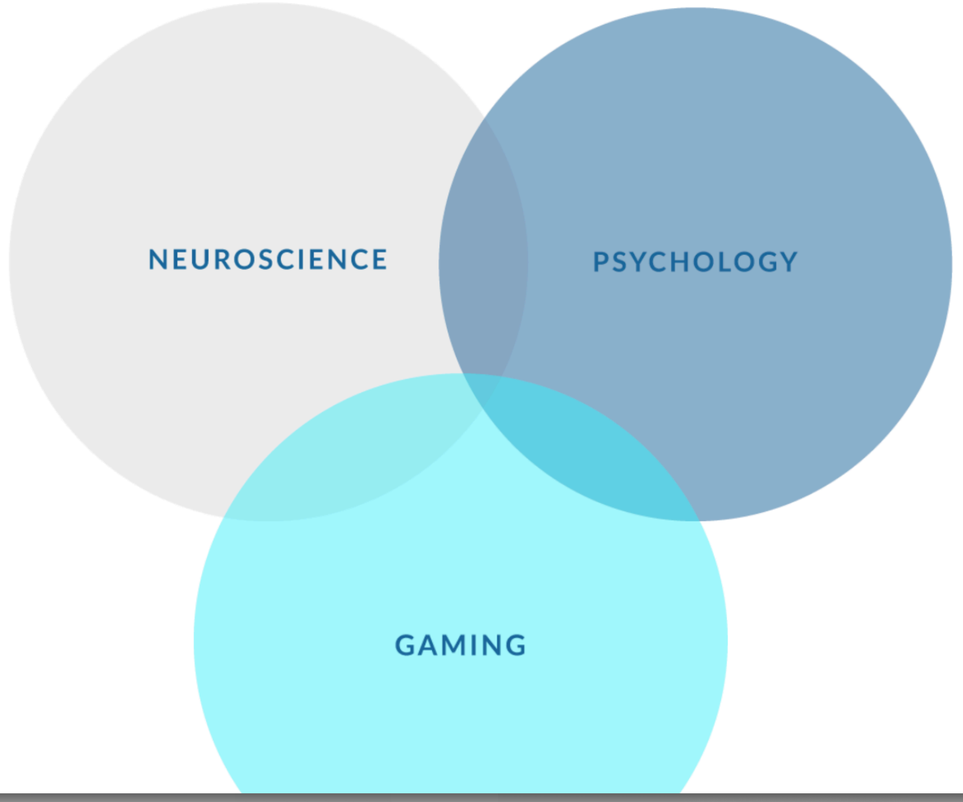


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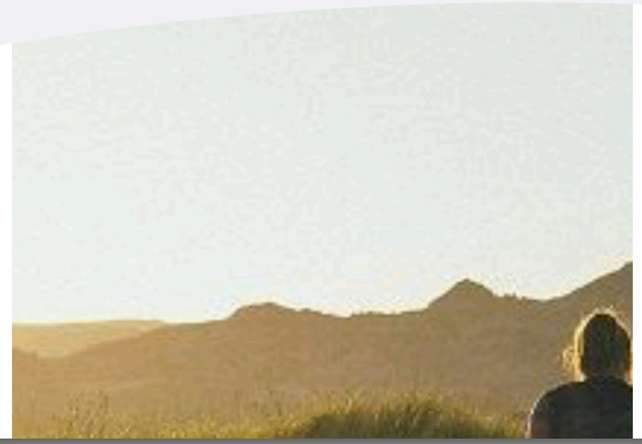
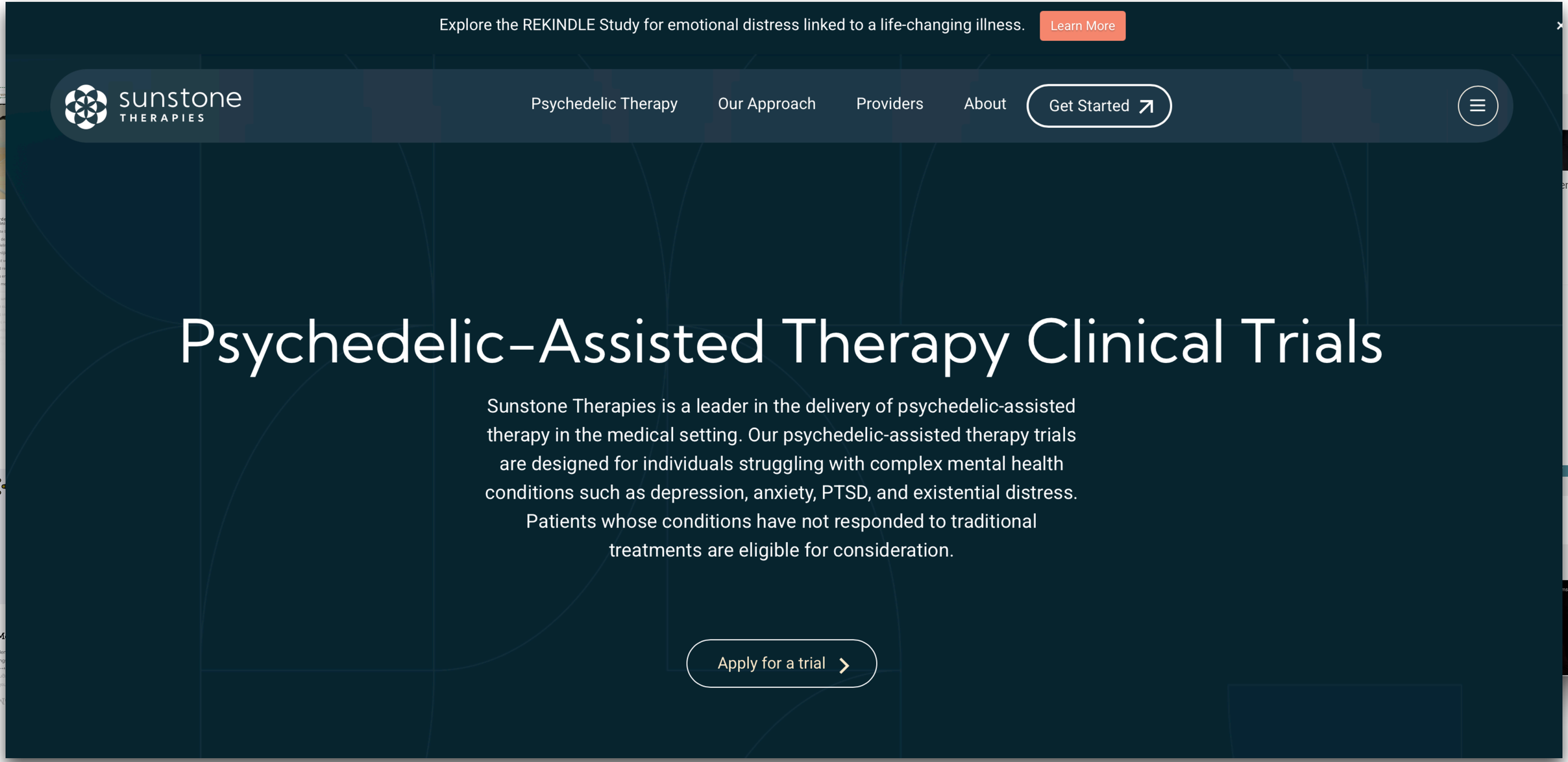


## Memrec in het kort

Memrec is een vorm van cognitieve gedragstherapie voor de behandeling van irreële angst. Memrec staat voor *memory reconsolidation*, (heropslag van angstgeheugen). De methode is ontwikkeld aan de Universiteit van Amsterdam, door Prof. dr. Merel Kindt. Zij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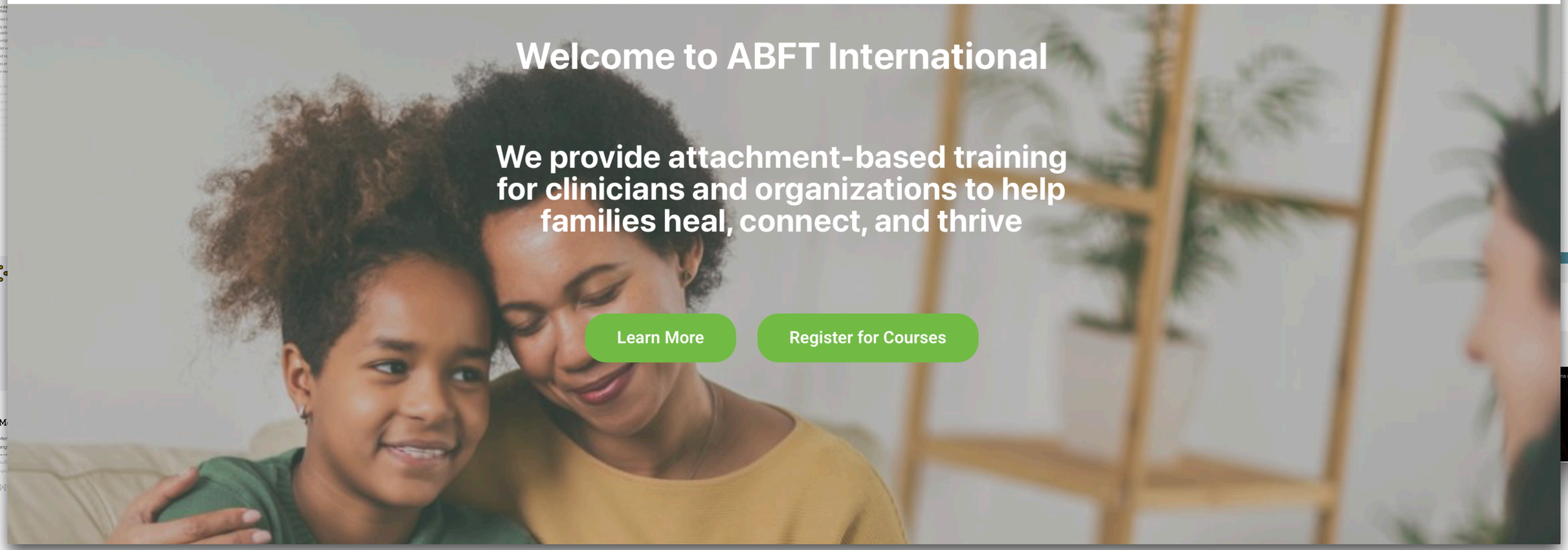

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# What is Internal Family Systems?

> Transformative psychotherapy... and empowering paradigm.

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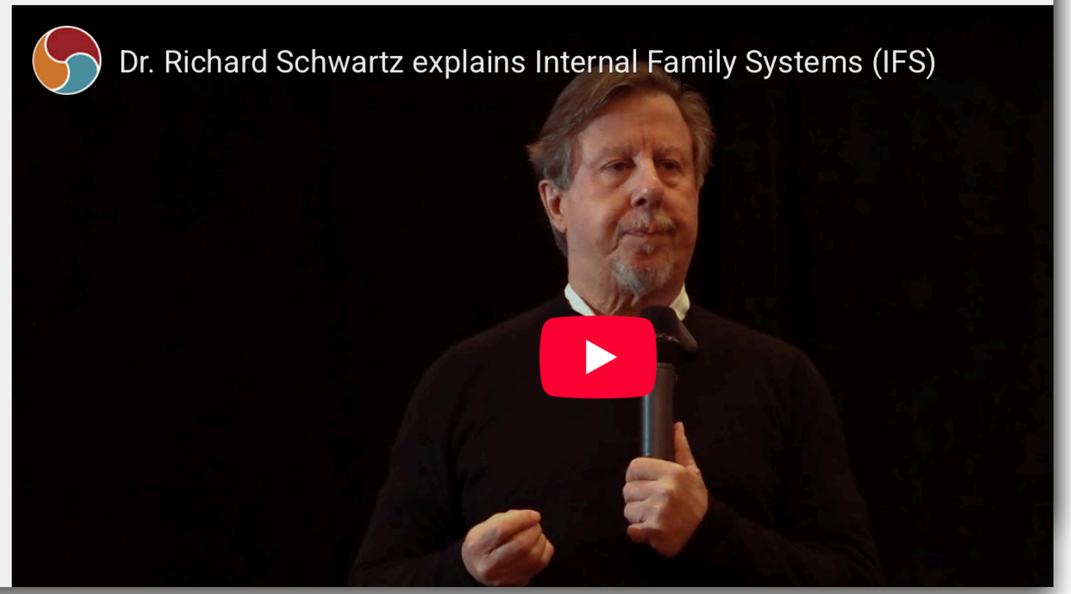

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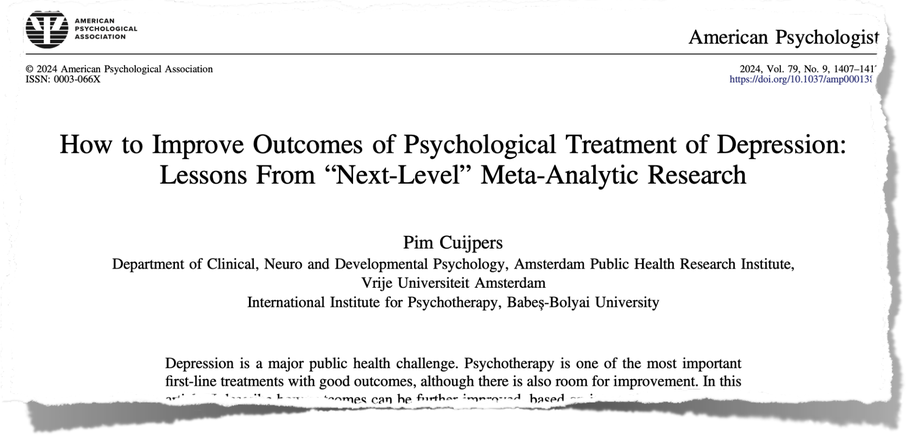
research on sequential treatments and on those who do not respond to a therapy is very much needed. Another important finding is that none of the new therapies that have been introduced over the past 50 years are more effective than previous treatments. It is important, therefore, not to embrace new therapies too easily but to focus on other innovations that will result in better outcomes, such as increased frequency of sessions, feedback to patients, and better matching the



American Psychologist

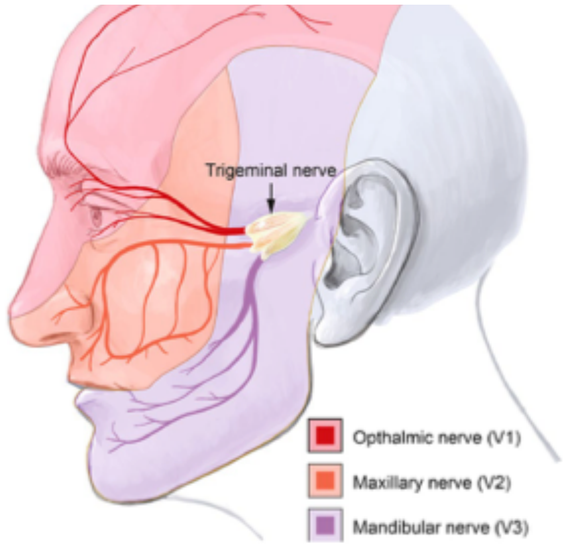

ISSN: 0003-066X
2024, Vol. 79, No. 9, 1407–141
https://doi.org/10.1037/amp00013

# How to Improve Outcomes of Psychological Treatment of Depression: Lessons From "Next-Level" Meta-Analytic Research

Pim Cuijpers
Department of Clinical, Neuro and Developmental Psychology, Amsterdam Public Health Research Institute, Vrije Universiteit Amsterdam
International Institute for Psychotherapy, Babeş-Bolyai University

Depression is a major public health challenge. Psychotherapy is one of the most important first-line treatments with good outcomes, although there is also room for improvement. In this

# Reden 1: Fikse placebo-effecten




Journal of the American Academy of Child & Adolescent Psychiatry
Volume 58 / Number 4 / April 2019


NEW RESEARCH

Check for updates

# Double-Blind, Sham-Controlled, Pilot Study of Trigeminal Nerve Stimulation for Attention-Deficit/ Hyperactivity Disorder

James J. McGough, MD, Alexandra Sturm, PhD, Jennifer Cowen, PhD, Kelly Tung, BS, Giulia C. Salgari, MS, Andrew F. Leuchter, MD, Ian A. Cook, MD, Catherine A. Sugar, PhD, Sandra K. Loo, PhD

**Objective:** Trigeminal nerve stimulation (TNS), a minimal-risk noninvasive neuromodulation method, showed potential benefits for attention-deficit/hyperactivity disorder (ADHD) in an unblinded open study. The present blinded sham-controlled trial was conducted to assess the efficacy

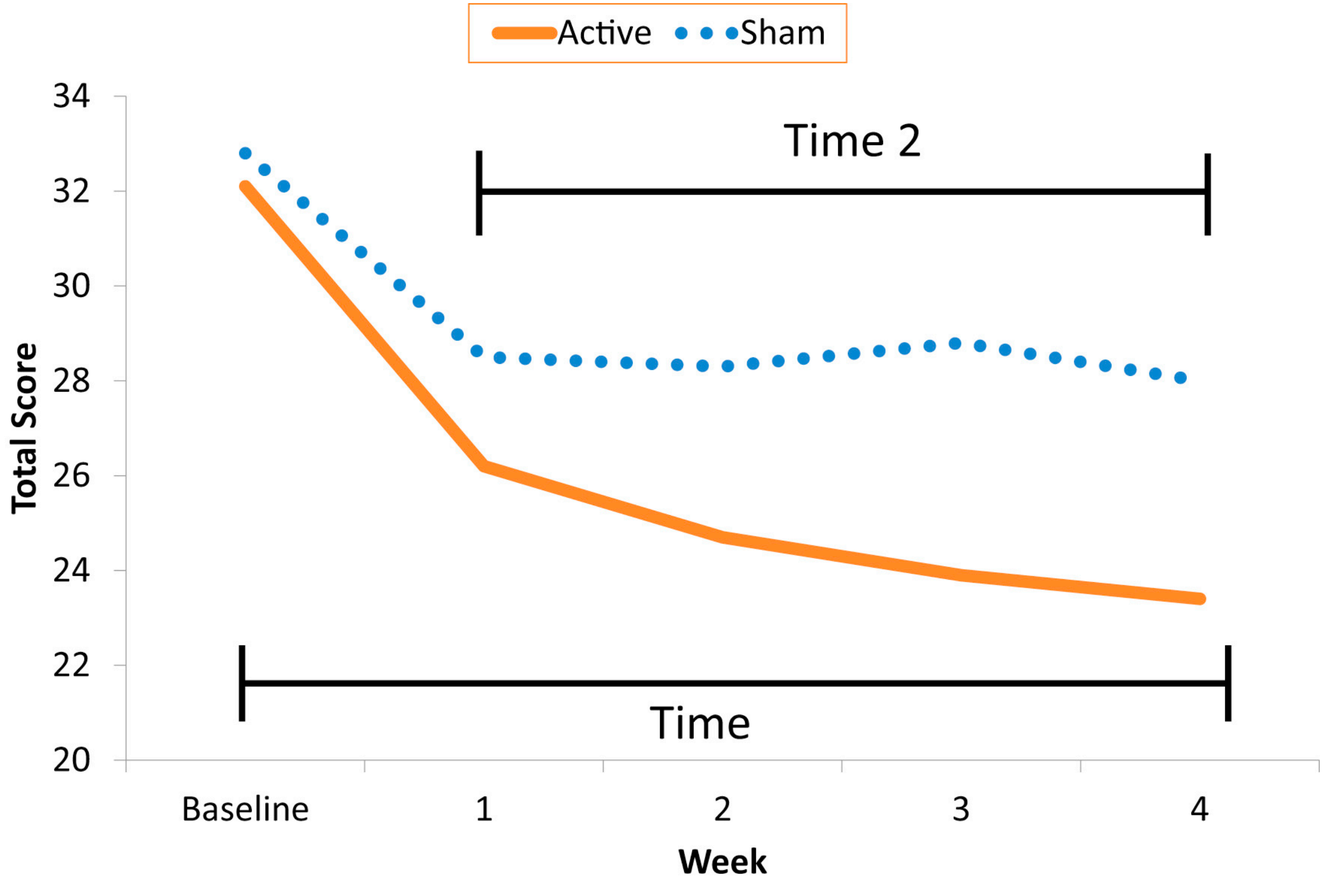
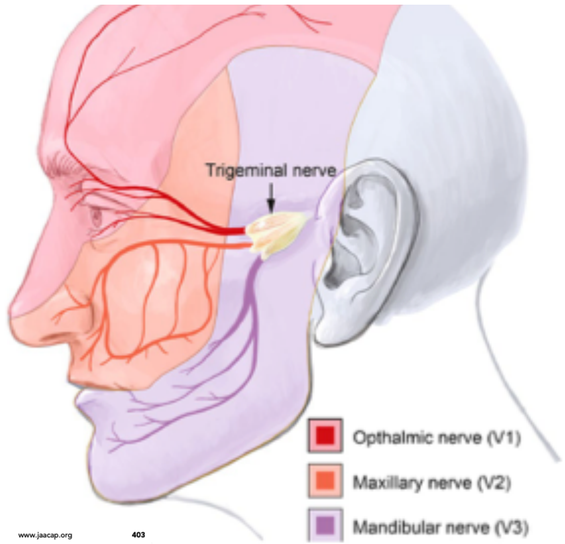



**FIGURE 1** Attention-Deficit/Hyperactivity Disorder Rating Scale Total Scores Over 4-Week Blinded Trial: Active Versus Sham Trigeminal Nerve Stimulation




Journal of the American Academy of Child & Adolescent Psychiatry
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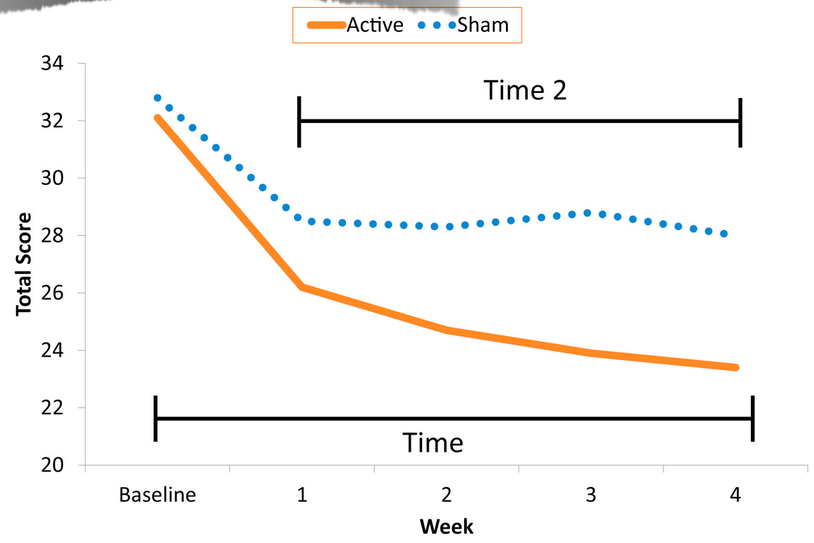


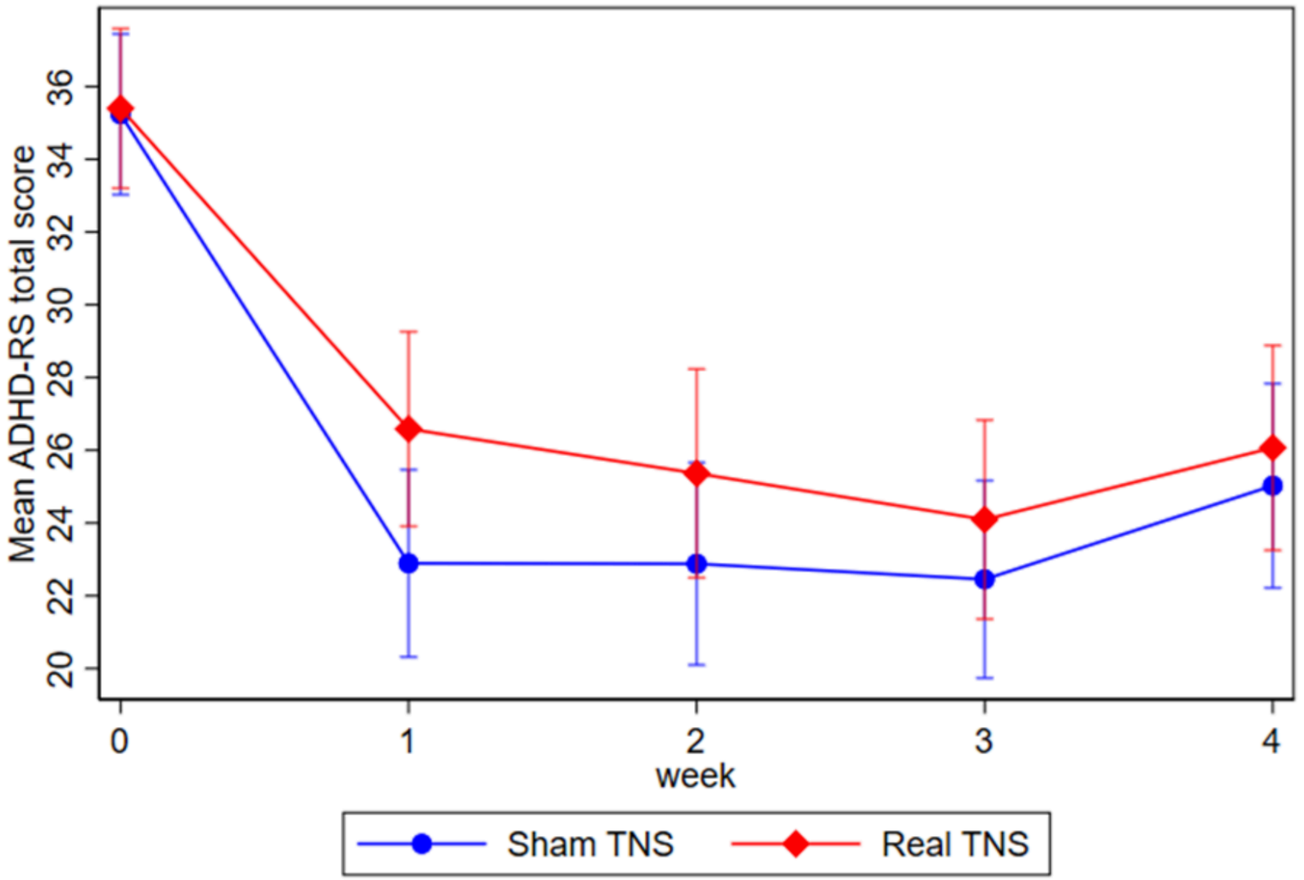


**External Trigeminal Nerve Stimulation in youth with ADHD: a randomized, sham-controlled, phase 2b trial**

Aldo Alberto Conti[1,2*], Natali Bozhilova[1*], Irem Ece Eraydin[3,4 *], Dominic Stringer[5,6], Lena Johansson[1], Robert Marhenke[3], Andrea Bilbow[7], Sahid El Masri[1,8], Joshua Hyde[3], Giovanni Giaroli[9], Holan Liang[10,11], Federico Fiori[1,12,13], Mitul Ashok Mehta[14], Paramala Santosh[1,12,13], Ben Carter[5,6], Samuele Cortese[3,15,16,17,18], Katya Rubia[1,8]

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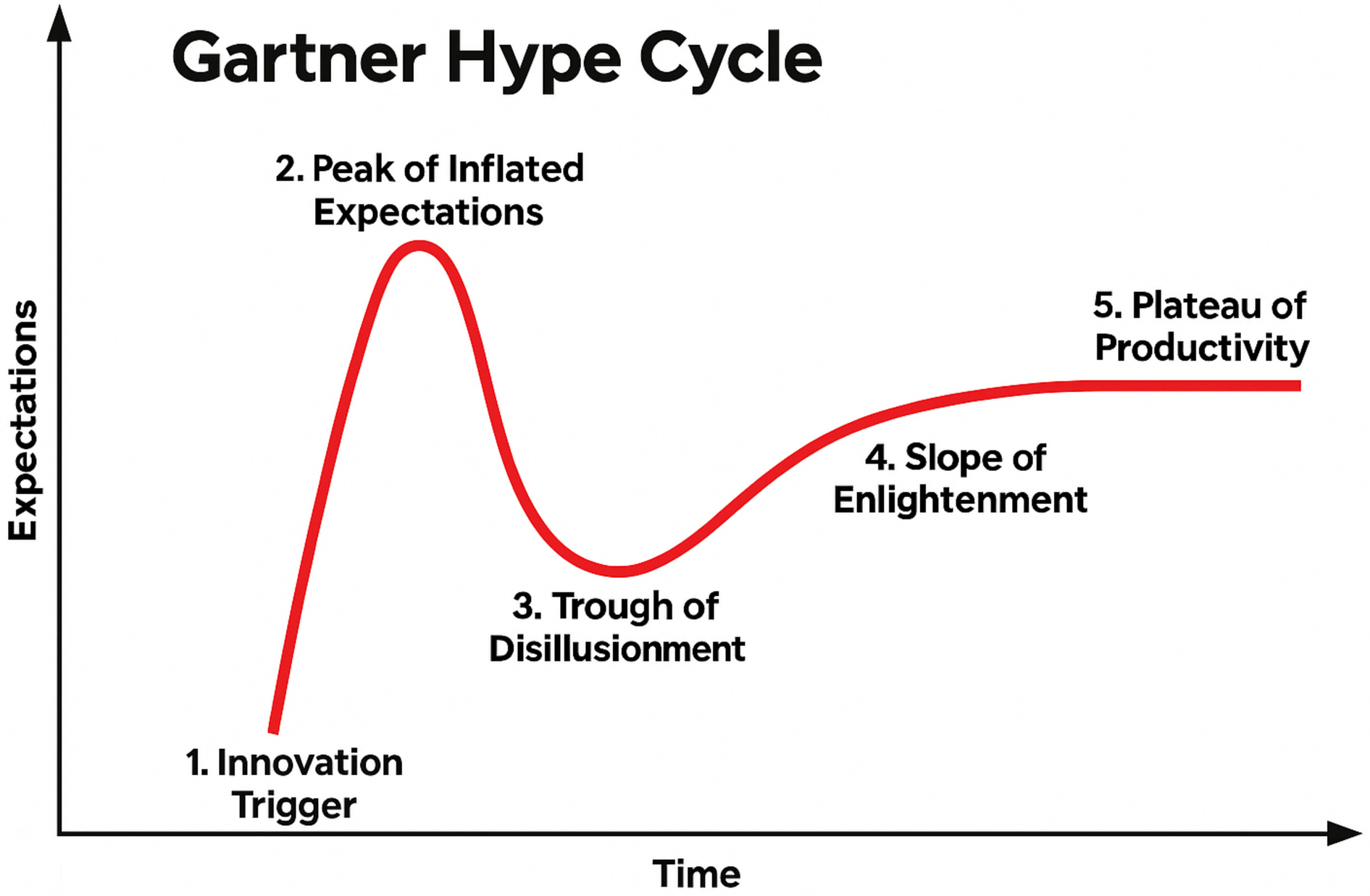
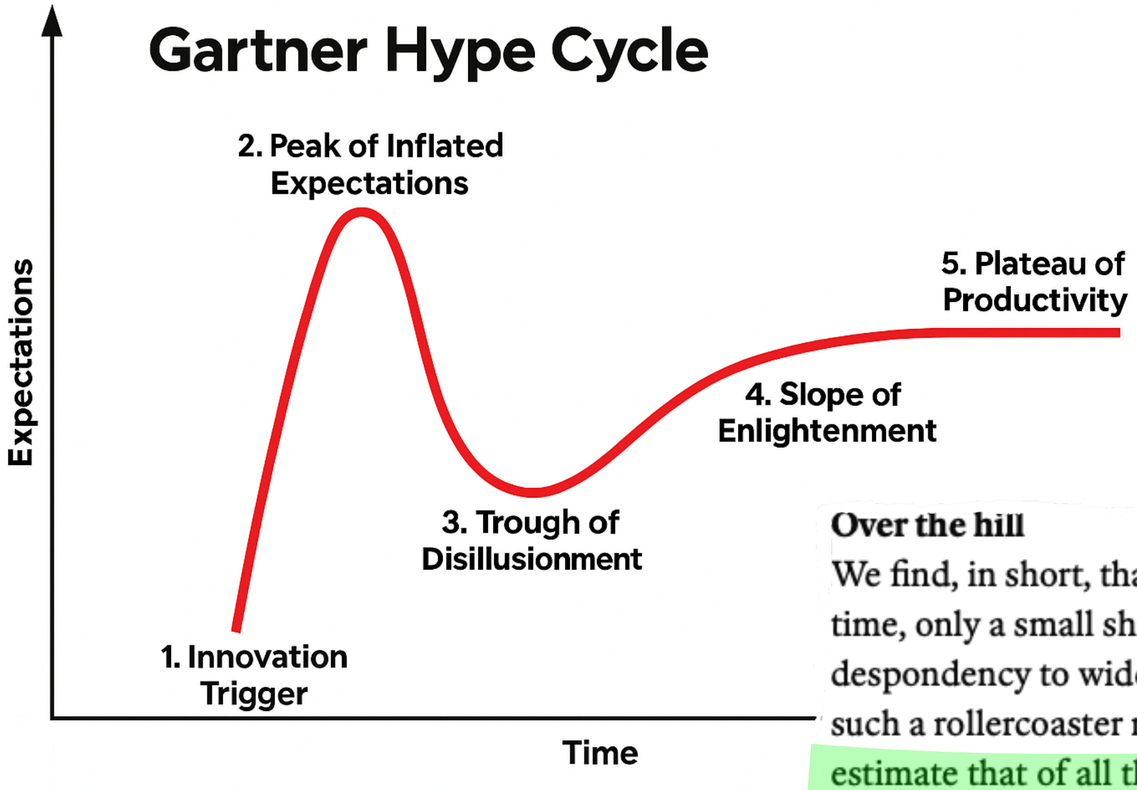

Gartner Hype Cycle
2. Peak of Inflated Expectations
5. Plateau of Productivity
4. Slope of Enlightenment
3. Trough of Disillusionment
1. Innovation Trigger
Expectations
Time



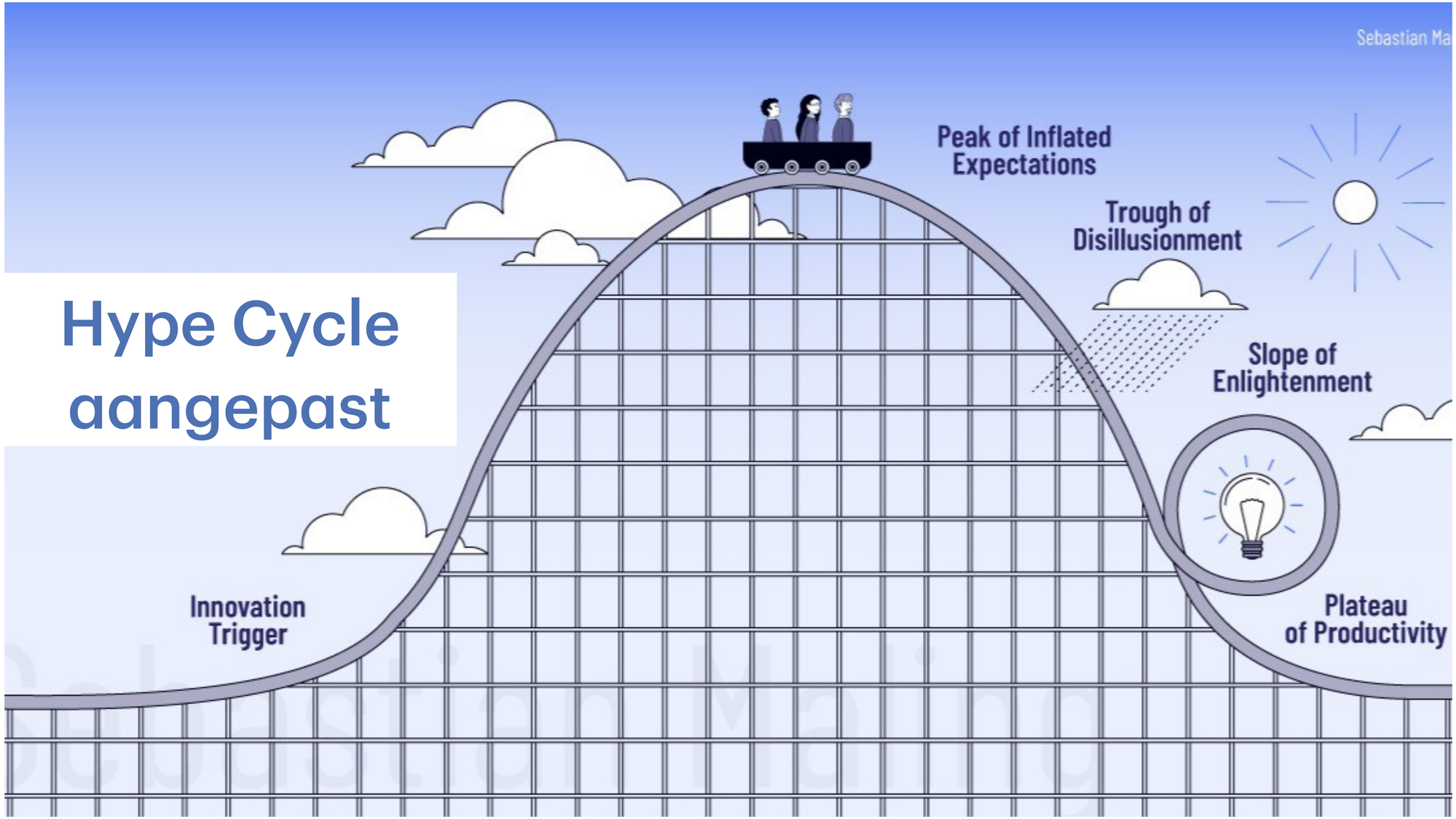

**Over the hill**

We find, in short, that the cycle is a rarity. Tracing breakthrough technologies over time, only a small share—maybe a fifth—move from innovation to excitement to despondency to widespread adoption. Lots of tech becomes widely used without such a rollercoaster ride. Others go from boom to bust, but do not come back. We estimate that of all the forms of tech which fall into the trough of disillusionment, six in ten do not rise again. Our conclusion is similar to that of Mr Mullany: "An alarming number of technology trends are flashes in the pan."

AI could still revolutionise the world. One of the big tech firms might make a breakthrough. Businesses could wake up to the benefits that the technology offers them. But for now the challenge for big tech is to prove that AI has something to offer the real economy. There is no guarantee of success. If you must turn to the history of technology for a sense of AI's future, the hype cycle is an imperfect guide. A better one is "easy come, easy go".

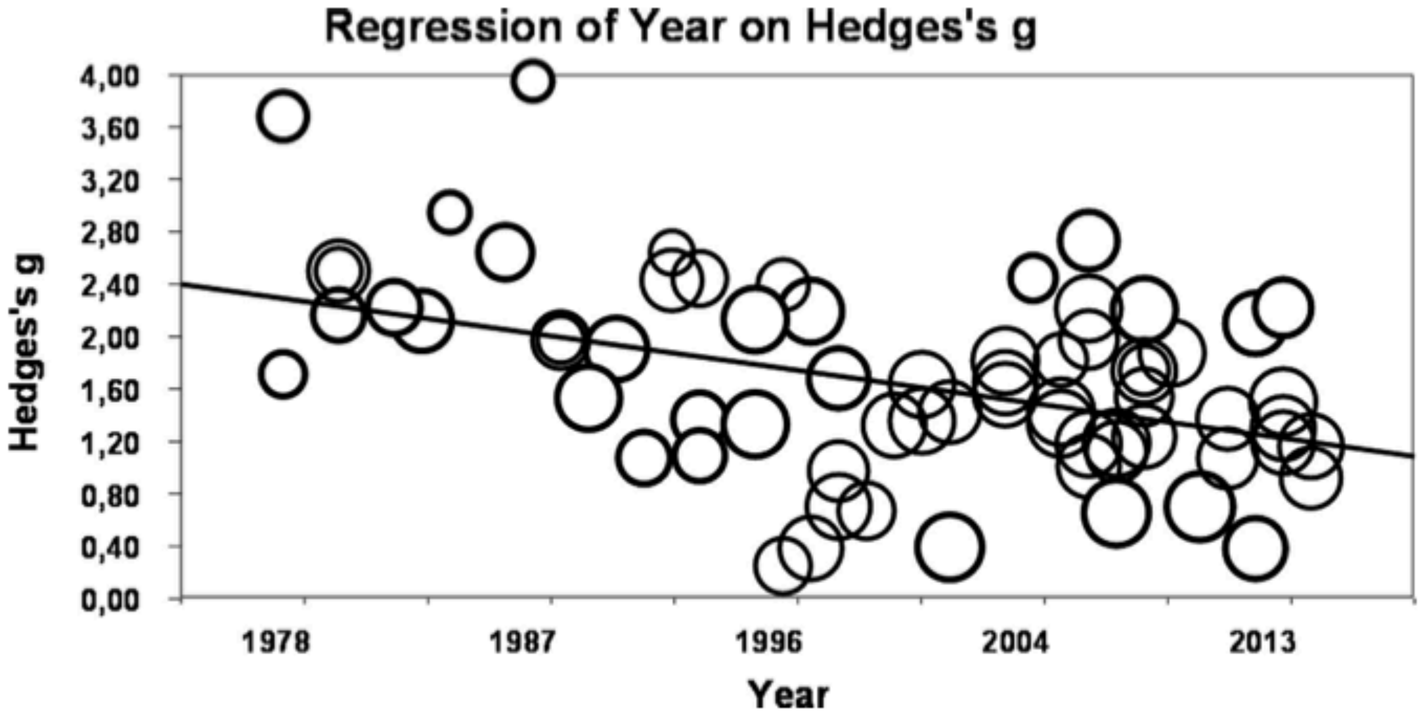
*The Economist*, Aug 24, 2024

# Hype Cycle aangepast



“You should treat as many patients as possible with the new drugs while they still have the power to heal”

– Armand Trousseau (1833) as quoted in Benson & McCallie (1979)




Psychological Bulletin
2015, Vol. 141, No. 4, 747–768


0033-2909/15/$12.00 http://dx.doi.org/10.1037/bul0000015

# The Effects of Cognitive Behavioral Therapy as an Anti-Depressive Treatment is Falling: A Meta-Analysis

Tom J. Johnsen and Oddgeir Friborg
UiT the Arctic University of Norway, University of Tromsø

A meta-analysis examining temporal changes (time trends) in the effects of cognitive behavioral therapy (CBT) as a treatment for unipolar depression was conducted. A comprehensive search of psychotherapy trials yielded 70 eligible studies from 1977 to 2014. Effect sizes (ES) were quantified as Hedge's $g$ based on the Beck Depression Inventory (BDI) and the Hamilton Rating Scale for Depression (HRSD). Rates of remission were also registered. The publication year of each study was examined as a linear metaregression predictor of ES, and as part of a 2-way interaction with other moderators (Year × Moderator). The average ES of the BDI was 1.58 (95% CI [1.43, 1.74]), and 1.69 for the HRSD (95% CI [1.48, 1.89]). Subgroup analyses revealed that women profited more from therapy than did men ($p <$ .05). Experienced psychologists ($g = 1.55$) achieved better results ($p < .01$) than less experienced student therapists ($g = 0.98$). The metaregressions examining the temporal trends indicated that the effects of CBT have declined linearly and steadily since its introduction, as measured by patients' self-reports (the BDI, $p < .001$), clinicians' ratings (the HRSD, $p < .01$) and rates of remission ($p < .01$). Subgroup analyses confirmed that the declining trend was present in both within-group (pre/post) designs ($p <$ .01)

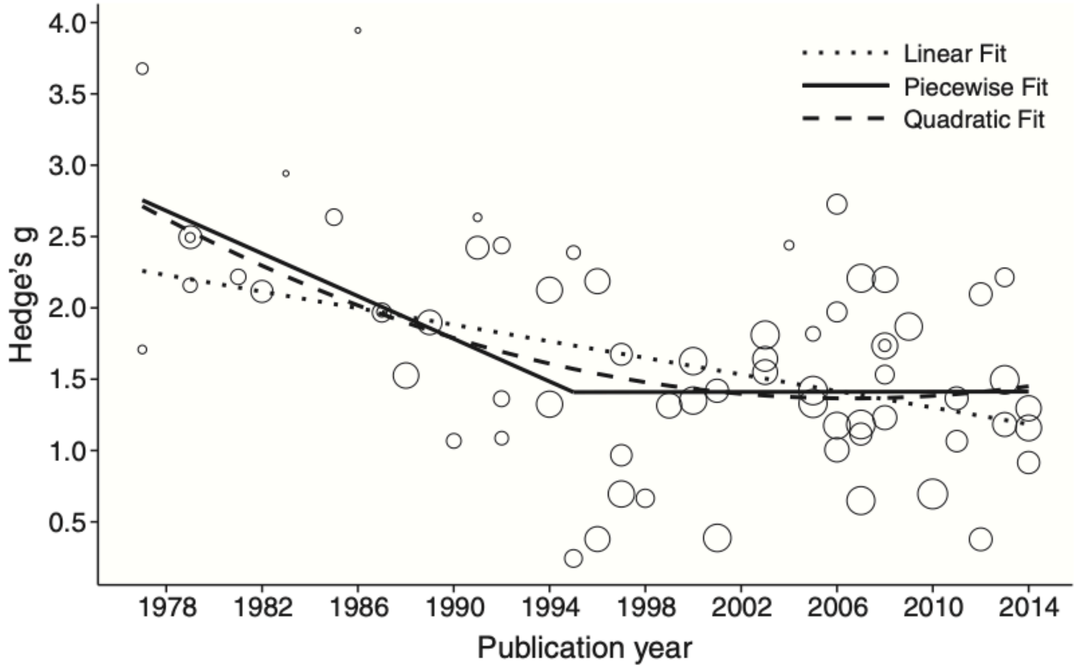



*Figure 1.* Effect sizes on the Beck Depression Inventory per study and estimated effects of publication year for different metaregression models. Disk sizes indicate relative weight of studies.

Psychological Bulletin
2017, Vol. 143, No. 3, 321–325


0033-2909/17/$12.00 http://dx.doi.org/10.1037/bul0000055

COMMENT

# The Effects of Cognitive–Behavioral Therapy for Depression Are Not Falling: A Re-Analysis of Johnsen and Friborg (2015)

Brjánn Ljótsson, Erik Hedman, Simon Mattsson, and Erik Andersson
Karolinska Institutet

Cognitive–behavioral therapy (CBT) has a solid evidence base as an effective treatment for depression. However, a recent meta-analysis (Johnsen & Friborg, 2015) including 70 studies, showed that the effect sizes of CBT for depression have been falling between 1977 and 2014. A possible important limitation in the Johnsen and Friborg (2015) study was that they did not investigate a leveling off in the decline over time of the effectiveness of CBT for depression. We therefore reanalyzed the data reported by Johnsen and Friborg (2015) using meta-analytic regression models that allowed for a curvilinear effect of publication year and also modeled separate estimates of the decline of treatment effect before and after 1995. Our analyses showed that adding a quadratic effect of time to a linear effect of time significantly improved the meta-analytic regression models ($p$ = .017–.027). Furthermore, significant declines were only observed between 1977 and 1995 ($p$ = .001–.009) and not between 1995 to 2014 ($p$ = .987–.785). We conclude that the declining effect of CBT for depression observed by Johnsen and Friborg (2015) was

5, Vol. 141, No. 4, 747–768
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# The Effects of Cognitive Behavioral Therapy as an Anti-Depressive Treatment is Falling: A Meta-Analysis

Tom J. Johnsen and Oddgeir Friborg
UiT the Arctic University of Norway, University of Tromsø

A meta-analysis examining temporal changes (time trends) in the effects of cognitive behavioral therapy (CBT) as a treatment for unipolar depression was conducted. A comprehensive search of psychotherapy trials yielded 70 eligible studies from 1977 to 2014. Effect sizes (ES) were quantified as Hedge's $g$ based on the Beck Depression Inventory (BDI) and the Hamilton Rating Scale for Depression (HRSD). Rates of remission were also registered. The publication year of each study was examined as a linear metaregression predictor of ES, and as part of a 2-way interaction with other moderators (Year × Moderator). The average ES of the BDI was 1.58 (95% CI [1.43, 1.74]), and 1.69 for the HRSD (95% CI [1.48, 1.89]). Subgroup analyses revealed that women profited more from therapy than did men ($p$ < .05). Experienced psychologists ($g$ = 1.55) achieved better results ($p$ < .01) than less experienced student therapists ($g$ = 0.98). The metaregressions examining the temporal trends indicated that the effects of CBT have declined linearly and steadily since its introduction, as measured by patients' self-reports (the BDI, $p$ < .001), clinicians' ratings (the HRSD, $p$ < .01) and rates of remission ($p$ < .01). Subgroup

# Reden 2: Oude wijn in nieuwe zakken

## Wat zijn de 5 P's van interne familiesystemen?


Een belangrijk onderdeel van IFS is de **ontwikkeling van het Zelf**, dat wordt omschreven met de vijf P's: Presence, Patience, Perspective, Persistence, en Playfulness. Deze vijf kwaliteiten helpen om een staat van balans en kalmte te bereiken.

1. **Presence** (Aanwezigheid): het vermogen om aanwezig en bewust te zijn in het huidige moment, zonder oordeel.
2. **Patience** (Geduld): Geduld om je delen met compassie te benaderen en te accepteren dat verandering tijd kost.
3. **Perspective** (Perspectief): Het Zelf biedt een breder perspectief, wat toelaat om situaties van meerdere kanten te bekijken.
4. **Persistence** (Doorzettingsvermogen): IFS moedigt aan om volhardend te zijn, zelfs wanneer het moeilijk is.
5. **Playfulness** (Speelsheid): Speelsheid en nieuwsgierigheid helpen cliënten om hun interne wereld met openheid en lichtheid te verkennen.

# Reden 3: Mechanistisch drijfzand

*Journal of Comparative and Physiological Psychology*
1967, Vol. 63, No. 1, 12–19

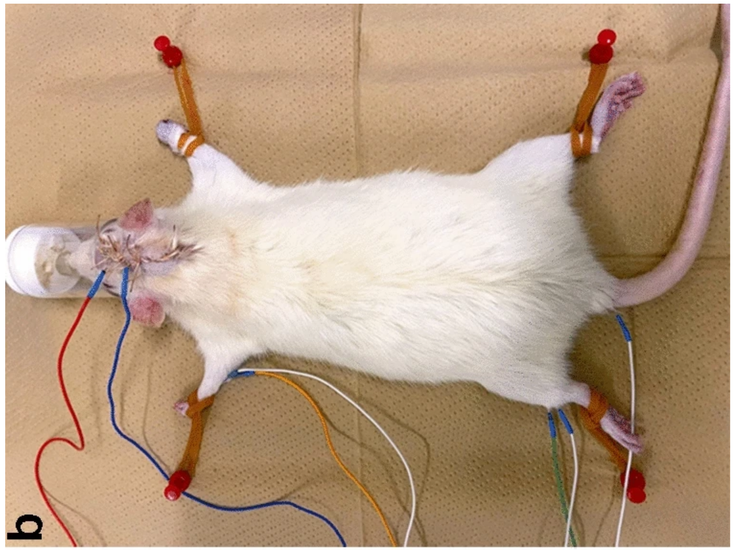
# INSTRUMENTAL LEARNING OF HEART RATE CHANGES IN CURARIZED RATS:

## SHAPING, AND SPECIFICITY TO DISCRIMINATIVE STIMULUS[1]

NEAL E. MILLER AND LEO DICARA[2]

*Yale University*

Artificially respirated rats with skeletal muscles completely paralyzed by curare were rewarded by electrical stimulation of the medial forebrain bundle for either increasing or decreasing their heart rates. After achieving the easy criterion of a small change, they were required to meet progressively more difficult criteria for reward. Different groups learned increases or decreases, respectively, of 20%; 21 of 23 rats showed highly reliable changes. The electrocardiogram indicated that decreased rates involved vagal inhibition. Rats learned to respond discriminatively to the stimuli signaling that cardiac changes would be rewarded.



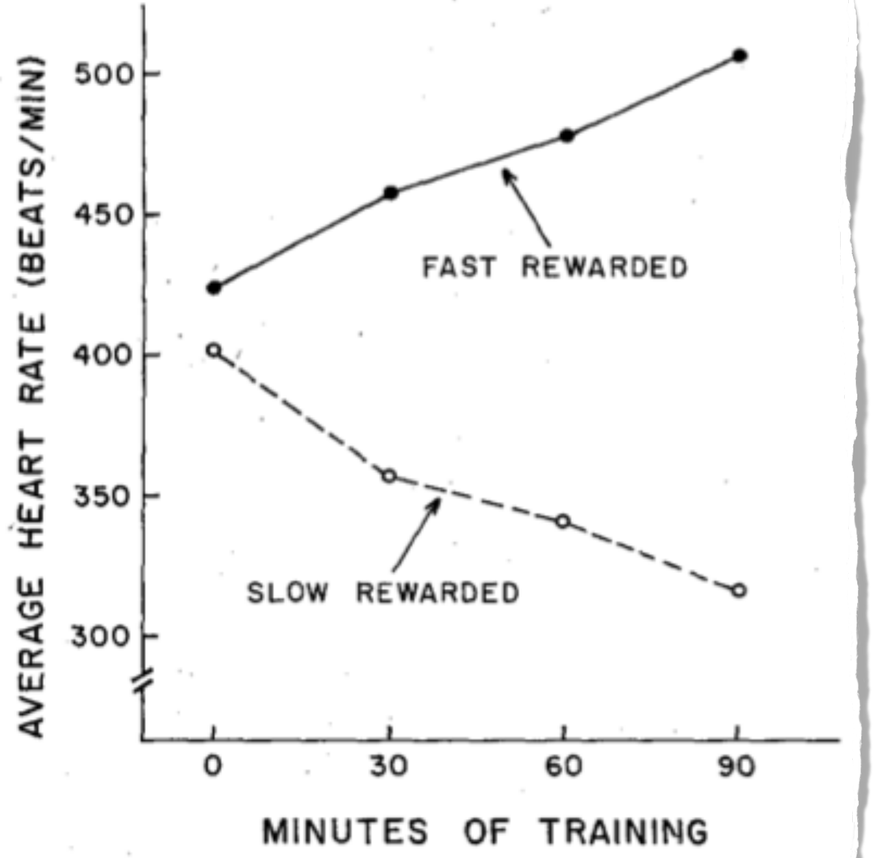
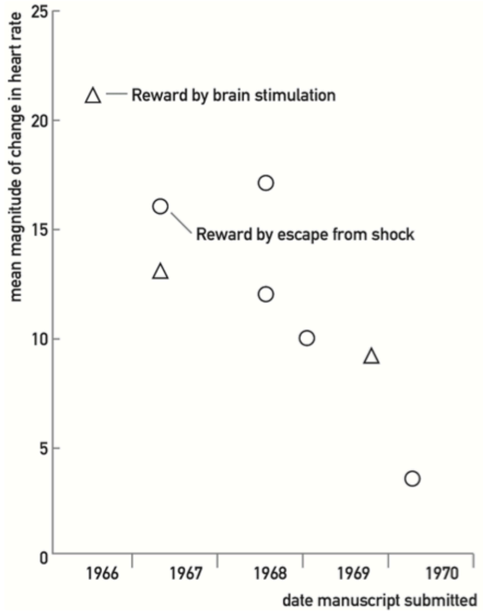
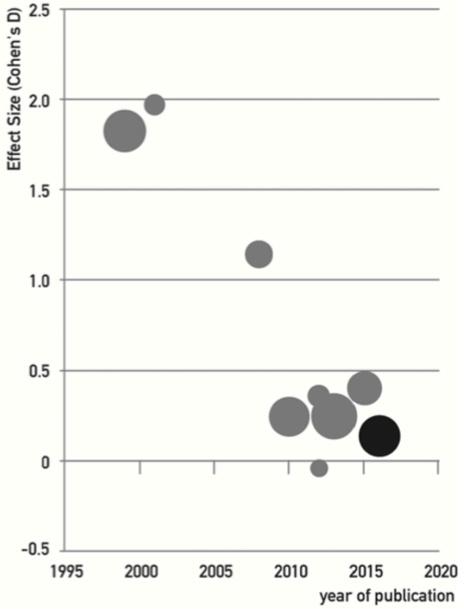
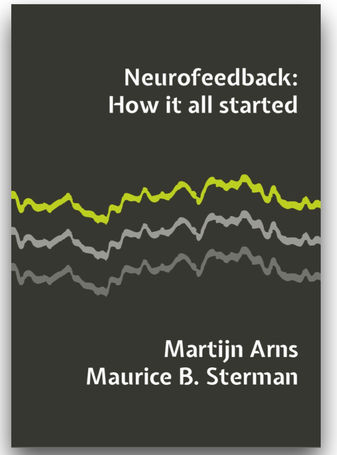



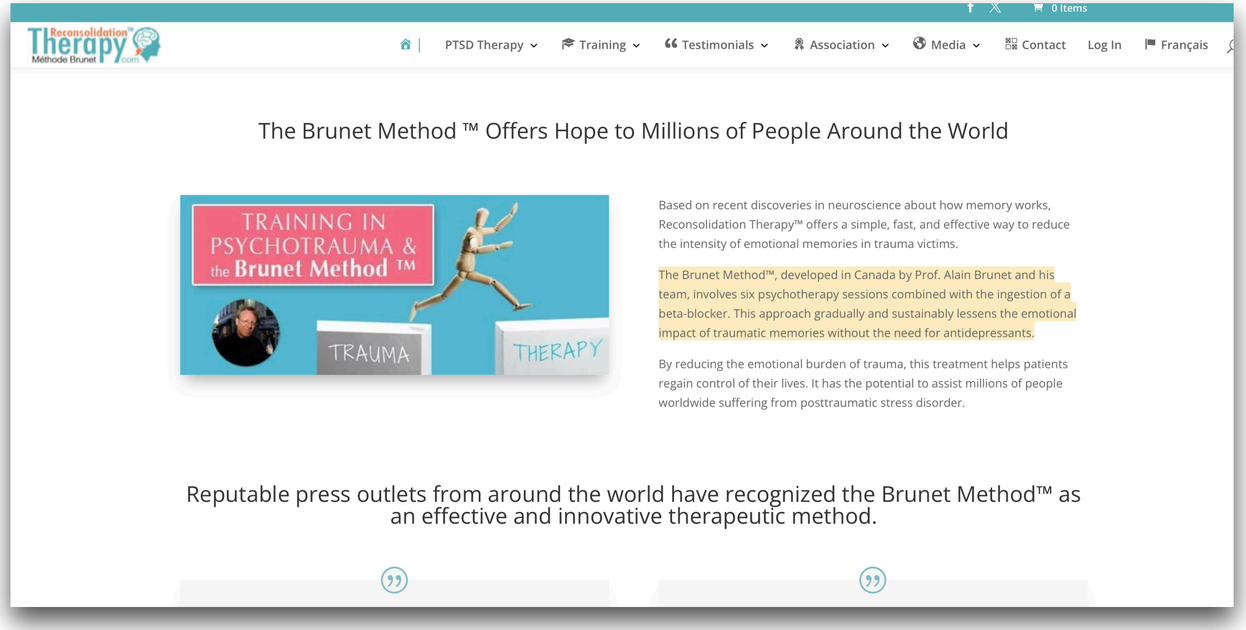

FIG. 1. Instrumental learning by heart in groups rewarded for fast or for slow rates. (Each point represents average of beats per minute during 5 min.)




periments were performed. After asking about those labs, he would often get deviating responses and eventually was told by Miller the responsible post-doctoral student was not there, so he could not show him the curare experiments. During that visit Birbaumer also met Barry Dworkin, with whom he developed a close collaboration on the treatment of scoliosis among others. At that visit, Dworkin shared with Birbaumer they had problems with the replication of the curare experiments, and in the decades to come, Dworkin spent much of his time trying to replicate the earlier curare experiments throughout the 1960's to 1980's but failed to replicate the earlier findings. In the early years some replications were published, but all subsequent replications showed a diminished effect, also visualized in the Figure 21, from Dworkin and Miller's publication *'Failure to Replicate Visceral Learning in the Acute Curarized Rat Preparation.'* [87] Here an almost linear decrement of effect over the years of publication is visible, reminiscent of what is currently very well known as the 'winner's curse', where for example in genetic studies early studies find large effects, and subsequent studies find diminished or no effects anymore. A similar effect was published for the Theta/Beta ratio as a differentiator between ADHD and non-ADHD populations, see right Figure 21. So actually, we could consider this unfortunate finding of

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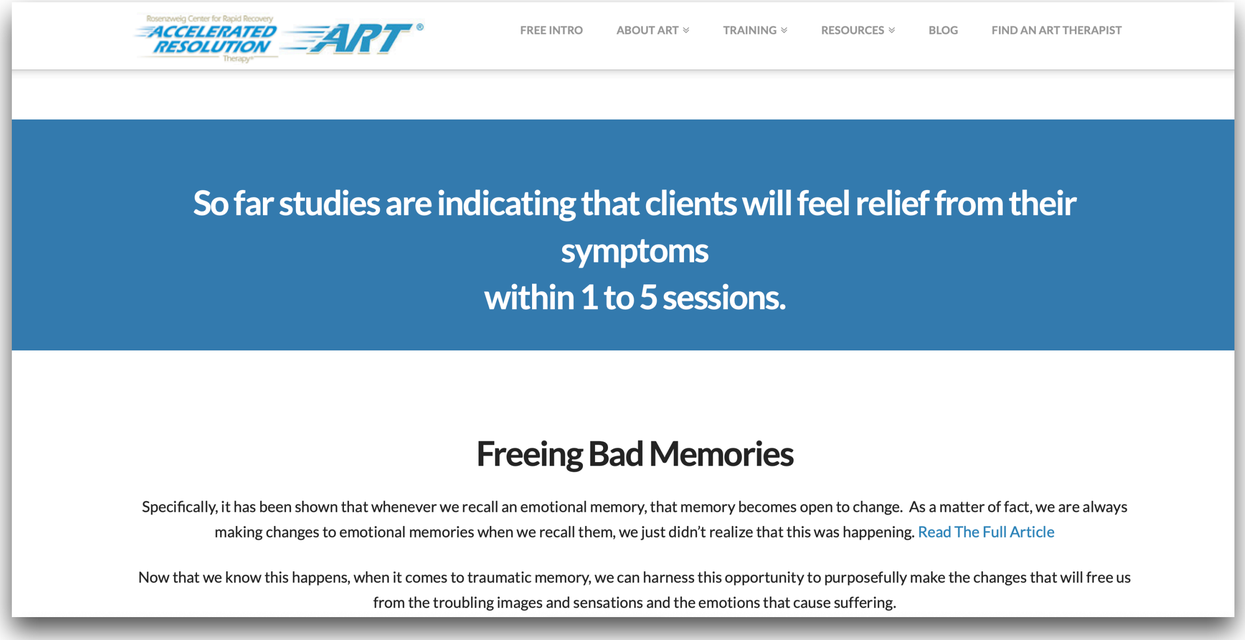
Memrec is een vorm van cognitieve gedragstherapie voor de behandeling van irreële angst. Memrec staat voor memory reconsolidation. (heropslag van angstgeheugen). De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TRAINING
RESOURCES
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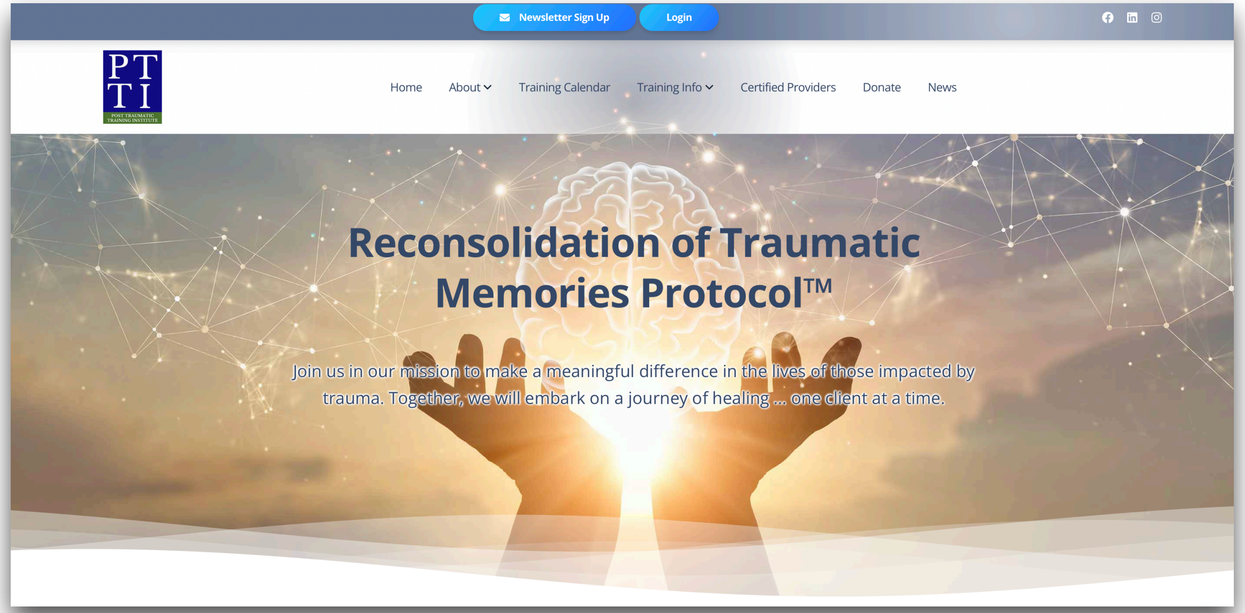
So far studies are indicating that clients will feel relief from their symptoms
within 1 to 5 sessions.
Freeing Bad Memories
Specifically, it has been shown that whenever we recall an emotional memory, that memory becomes open to change. As a matter of fact, we are always making changes to emotional memories when we recall them, we just didn't realize that this was happening. Read The Full Article
Now that we know this happens, when it comes to traumatic memory, we can harness this opportunity to purposefully make the changes that will free us from the troubling images and sensations and the emotions that cause suffering.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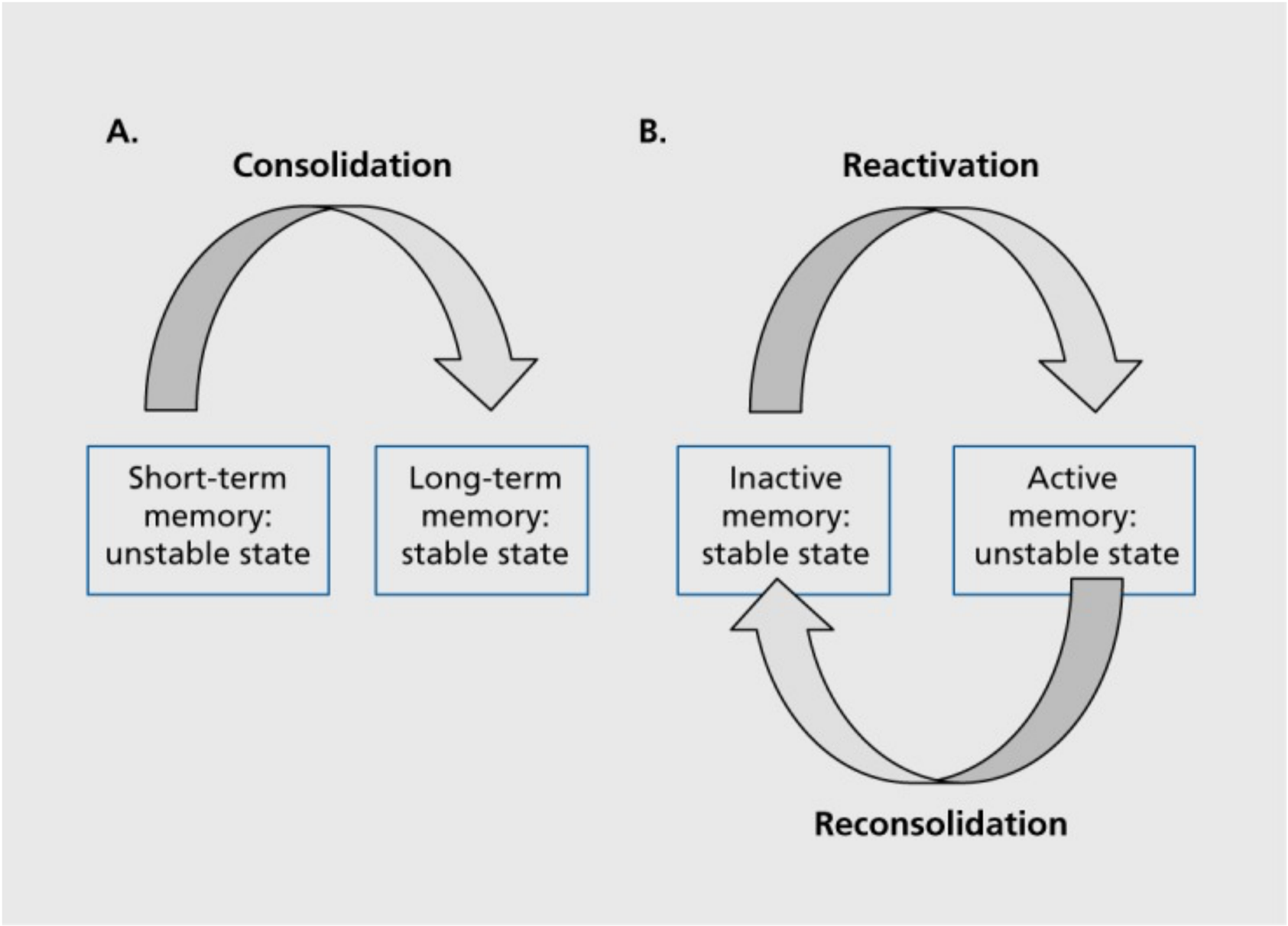
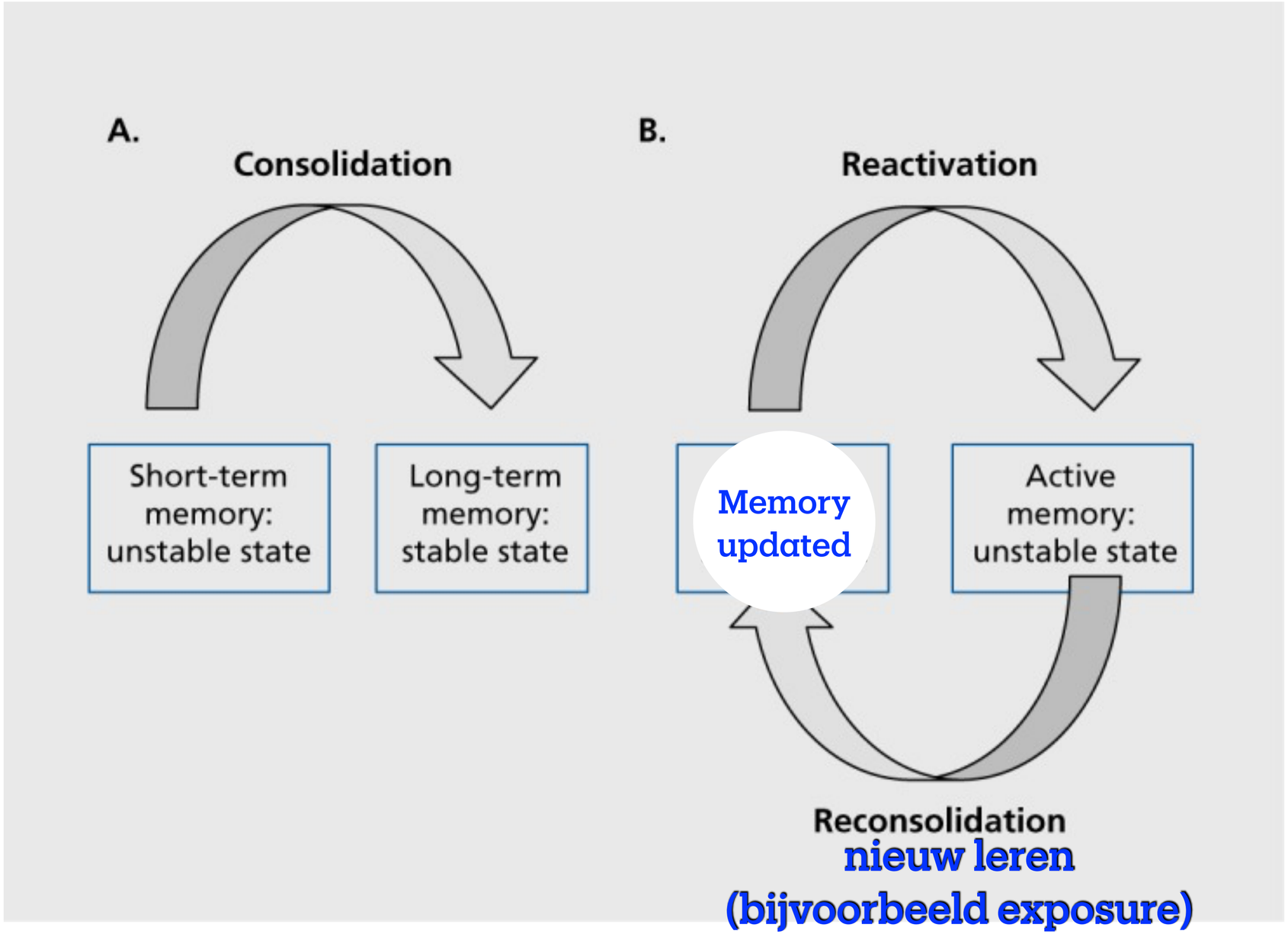
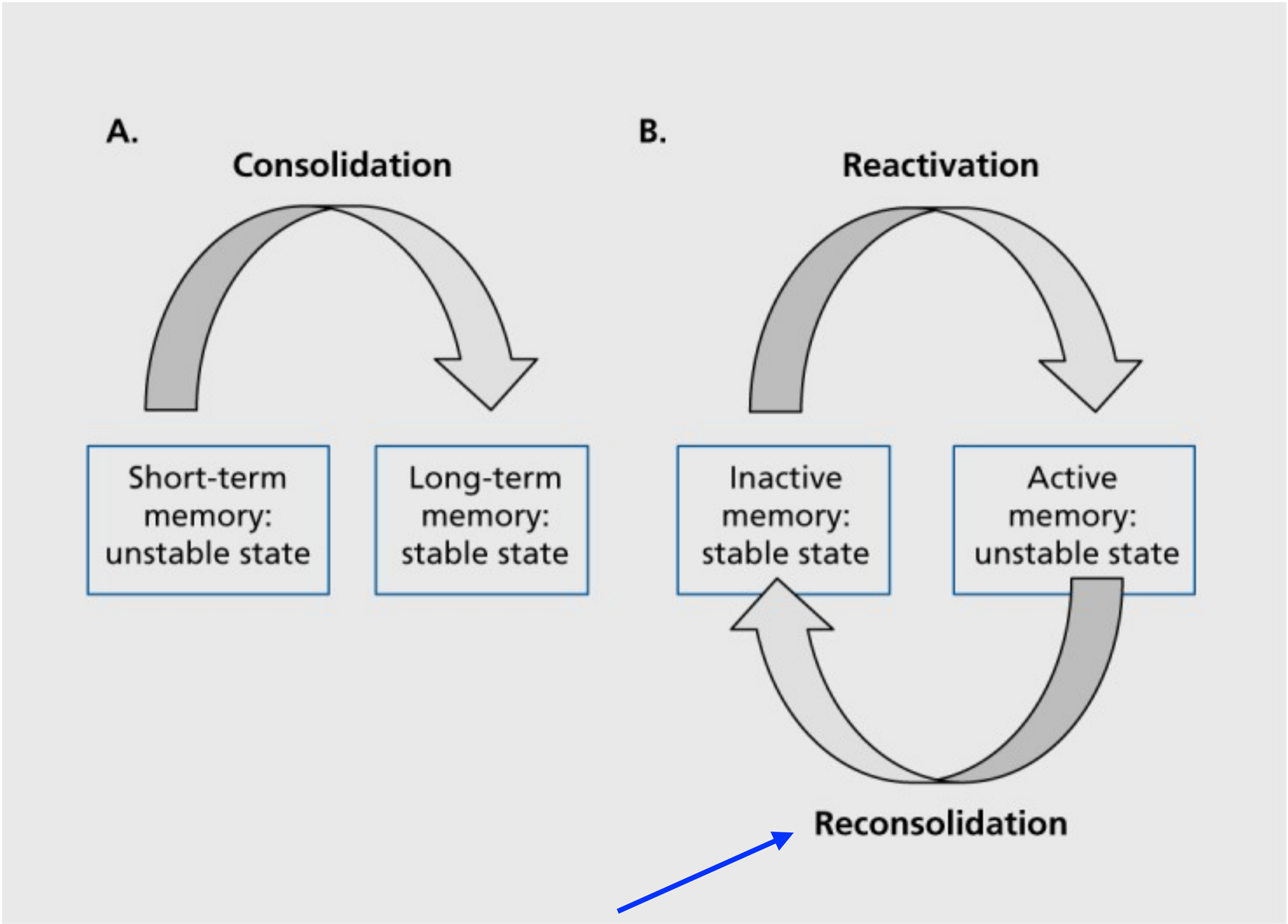



Nader et al., *Dialogues Clin Neurosci* 2013




Nader et al., *Dialogues Clin Neurosci* 2013

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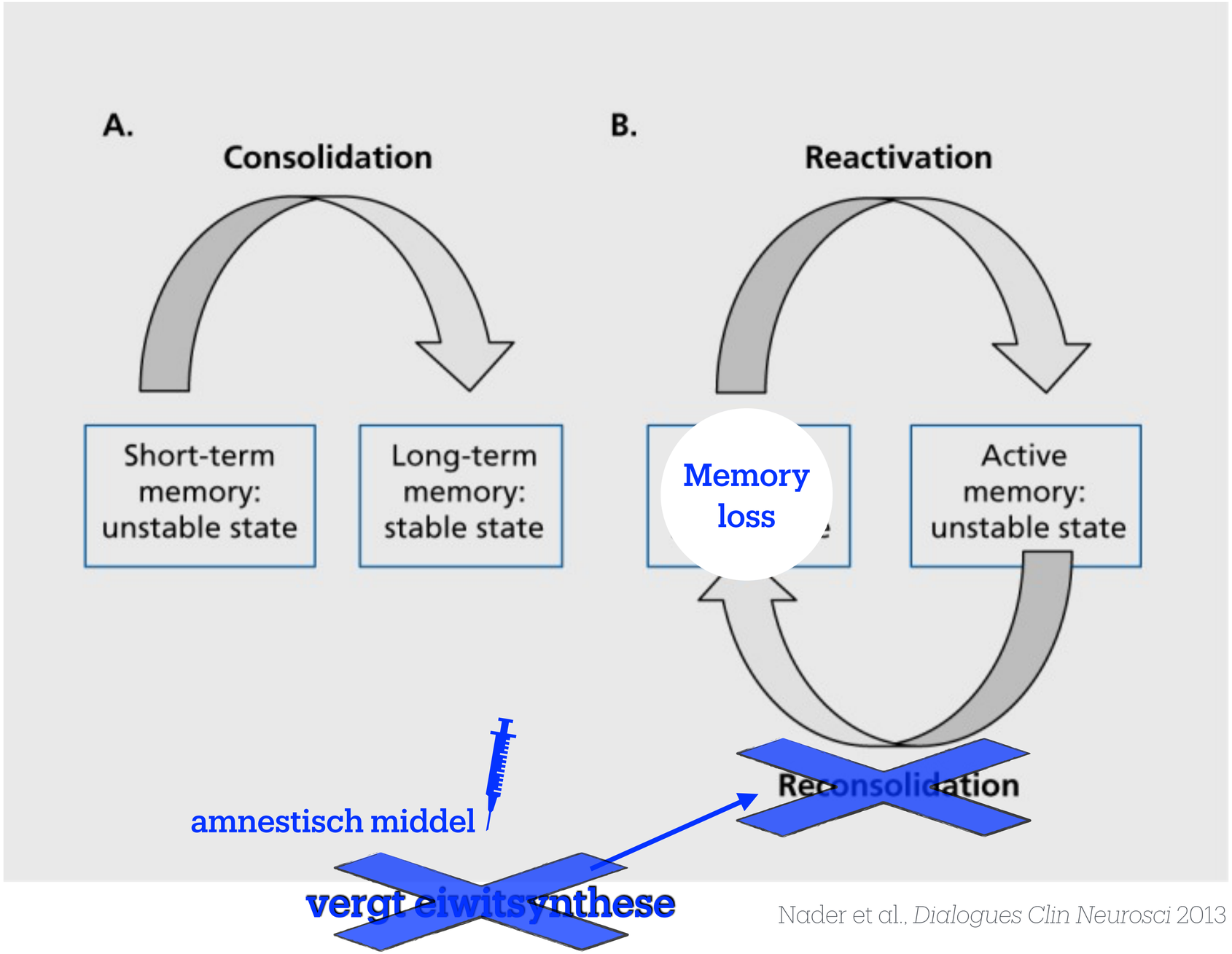
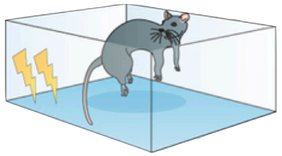
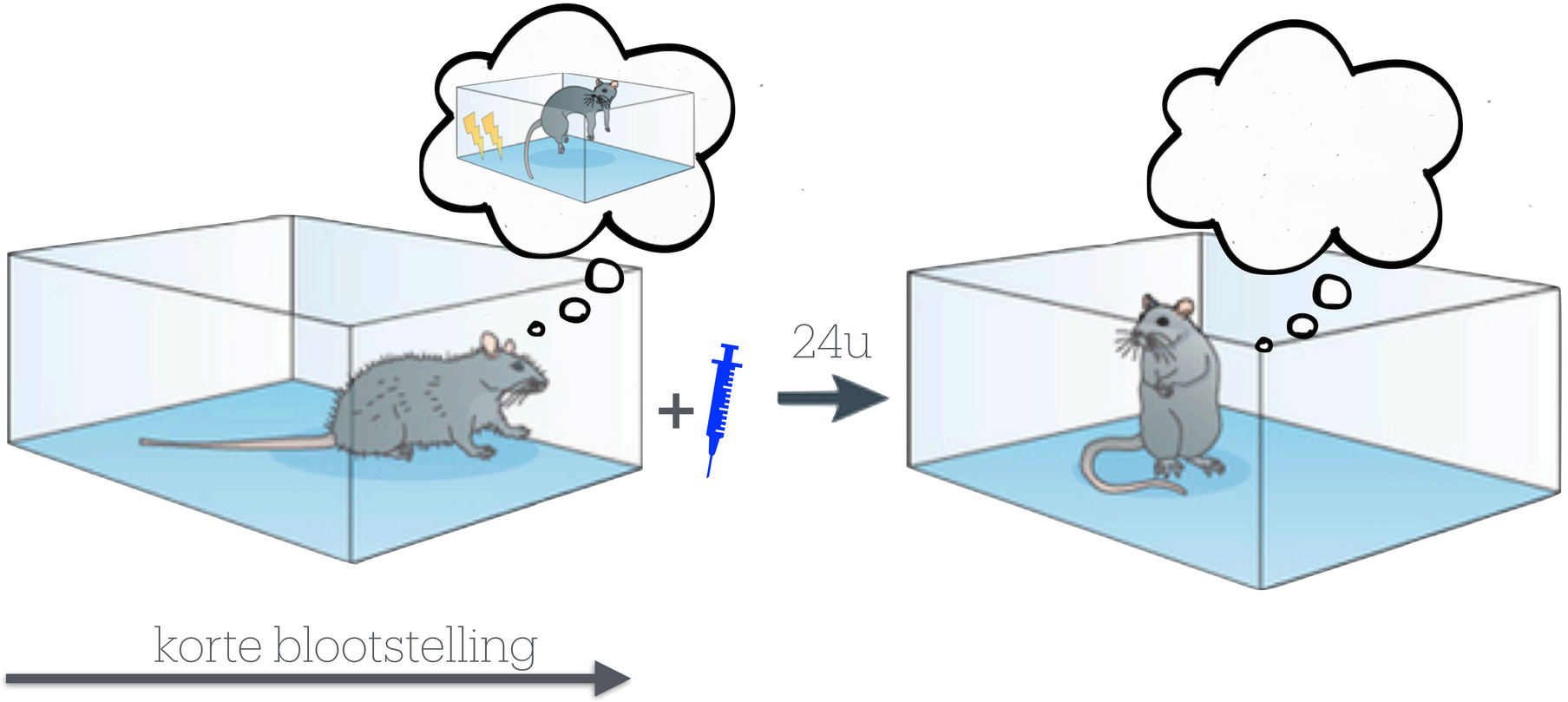
Nader et al., *Dialogues Clin Neurosci* 2013




Nader et al., *Dialogues Clin Neurosci* 2013




24u
korte blootstelling

## Retrograde Amnesia Produced by Electroconvulsive Shock after Reactivation of a Consolidated Memory Trace

Abstract. *Rats had a memory loss of a fear response when they received an electroconvulsive shock 24 hours after the fear-conditioning trial and preceded by a brief presentation of the conditioned stimulus. No such loss occurred when the conditioned stimulus was not presented. The memory loss in animals given electroconvulsive shock 24 hours after conditioning was, furthermore, as great as that displayed in animals given electroconvulsive shock immediately after conditioning. This result throws doubt on the assertion that electroconvulsive shock exerts a selective amnesic effect on recently acquired memories and thus that electroconvulsive shock produces amnesia solely through interference with memory trace consolidation.*

Impaired retention of responses learned shortly before electroconvulsive shock (ECS) stimulation is commonly called retrograde amnesia (RA), and is attributed to interference with consolidation, a process considered re-

event. Our subjects were 100 male Sprague-Dawley rats (220 to 270 g), purchased from a commercial supplier. They were kept in individual cages and fed 12 g of food daily.

Fear conditioning was given in a lick

the inner-wall surface; the subject remained in the chamber until it located the tube and made 110 licks; no gloves were used to handle the subjects; water was available for the next 24 hours.

After the second session, the subjects were randomly divided into five groups of 20 subjects each, and the next day they all received their first treatment, which was the same for all groups except group 1, a "typical RA group" that served as a control. For this treatment, each subject was removed from its home cage with a gloved hand 10 to 15 minutes after feeding and was taken to the lick chamber where earclips were attached. The chamber was modified, with a white panel over the aluminum wall where the tube had been. After 47 seconds, the conditioned stimulus (CS), an 80-db white noise, was presented for 10 seconds. A 1.3-ma shock was delivered [illegible] with noise off

Misanin, Miller, & Lewis, *Science*, 1968

NATURE | VOL 406 | 17 AUGUST 2000 | www.nature.com

# Fear memories require protein synthesis in the amygdala for reconsolidation after retrieval

Karim Nader, Glenn E. Schafe & Joseph E. Le Doux

*W. M. Keck Foundation Laboratory of Neurobiology, Center for Neural Science, New York University, New York, New York 10003, USA*

'New' memories are initially labile and sensitive to disruption before being consolidated into stable long-term memories[1–5]. Much evidence indicates that this consolidation involves the synthesis of new proteins in neurons[6–9]. The lateral and basal nuclei of the amygdala (LBA) are believed to be a site of memory

www.sciencemag.org SCIENCE VOL 324 15 MAY 2009 951

# Extinction-Reconsolidation Boundaries: Key to Persistent Attenuation of Fear Memories

Marie-H. Monfils,[1,2]* Kiriana K. Cowansage,[1] Eric Klann,[1] Joseph E. LeDoux[1,3,4,5]

Dysregulation of the fear system is at the core of many psychiatric disorders. Much progress has been made in uncovering the neural basis of fear learning through studies in which associative emotional memories are formed by pairing an initially neutral stimulus (conditioned stimulus, CS; e.g., a tone) to an unconditioned stimulus (US; e.g., a shock). Despite recent advances, the question of how to persistently weaken aversive CS-US associations, or dampen traumatic memories in pathological cases, remains a major dilemma. Two paradigms (blockade of reconsolidation and extinction) have been used in the laboratory to reduce acquired fear. Unfortunately, their clinical efficacy is limited: Reconsolidation blockade typically requires potentially toxic drugs, and extinction is not permanent. Here, we describe a behavioral design in which a fear memory in rats is destabilized and reinterpreted as safe by presenting an isolated retrieval trial before an extinction session. This procedure permanently attenuates the fear memory without the use of drugs.

duction in fear relative to extinction training conducted outside the reconsolidation window. Specifically, we predicted that an extinction session presented after an isolated retrieval trial would lead to a persistent revaluation of the CS as less threatening, and/or a weakening of the stored trace or access to it, and thus would prevent the return of fear in the three aforementioned tests.

Six experiments were conducted. We first examined whether our behavioral paradigm could prevent the return of fear on a spontaneous recovery test, and if so, whether the observed effect was the result of an update during reconsolidation. We specifically designed this experiment on the basis of the premise that the lability window engaged at the time of retrieval is temporary—in rat fear conditioning, it closes within 6 hours (*4*)—at which time the memory is thought to be reconsolidated (*4*). We posited that if the interval between the isolated retrieval cue and extinction

256 VOLUME 12 | NUMBER 3 | MARCH 2009 NATURE NEUROSCIENCE

BRIEF COMMUNICATIONS

nature neuroscience

# Beyond extinction: erasing human fear responses and preventing the return of fear

Merel Kindt, Marieke Soeter & Bram Vervliet

**Animal studies have shown that fear memories can change when recalled, a process referred to as reconsolidation. We found that oral administration of the β-adrenergic receptor antagonist propranolol before memory reactivation in humans erased the behavioral expression of the fear memory 24 h later and prevented the return of fear. Disrupting the reconsolidation**

In this human study, we tested the hypotheses that the fear response can be weakened by disrupting the reconsolidation process and that disrupting the reconsolidation of the fear memory will prevent the return of fear. To test these hypotheses, we used a differential fear-conditioning procedure with fear-relevant stimuli. Testing included different phases across 3 d: fear acquisition (day 1), memory reactivation (day 2), and extinction followed by a reinstatement procedure and a test phase (day 3) (**Supplementary Figs. 1** and **2** online). The conditioned fear response was measured as potentiation of the eyeblink startle reflex to a loud noise (40 ms, 104 dB) by electromyography of the right orbicularis oculi muscle. Stronger startle responses to the loud noise during the fear-conditioned stimulus ($CS1^+$) as compared with the control stimulus ($CS2^-$) reflects the fearful state of the participant elicited by $CS1^+$. Startle potentiation

Vol 463 | 7 January 2010 | doi:10.1038/nature08637 nature

ARTICLES

# Preventing the return of fear in humans using reconsolidation update mechanisms

Daniela Schiller[1,2], Marie-H. Monfils[1,3], Candace M. Raio[2], David C. Johnson[2], Joseph E. LeDoux[1] & Elizabeth A. Phelps[1,2]

**Recent research on changing fears has examined targeting reconsolidation. During reconsolidation, stored information is rendered labile after being retrieved. Pharmacological manipulations at this stage result in an inability to retrieve the memories at later times, suggesting that they are erased or persistently inhibited. Unfortunately, the use of these pharmacological manipulations in humans can be problematic. Here we introduce a non-invasive technique to target the reconsolidation of fear memories in humans. We provide evidence that old fear memories**

Luyten *et al. BMC Biology* (2021) 19:17
https://doi.org/10.1186/s12915-021-00957-x

BMC Biology

RESEARCH ARTICLE Open Access

# Lack of drug-induced post-retrieval amnesia for auditory fear memories in rats

Laura Luyten[1,2*], Anna Elisabeth Schnell[1,2], Natalie Schroyens[1,2] and Tom Beckers[1,2]

**Abstract**

**Background:** Long-term memory formation is generally assumed to involve the permanent storage of recently acquired memories, making them relatively insensitive to disruption, a process referred to as memory consolidation. However, when retrieved under specific circumstances, consolidated fear memories are thought to return to a labile state, thereby opening a window for modification (e.g., attenuation) of the memory. Several interventions during a critical time frame after this destabilization seem to be able to alter the retrieved memory, for example by

Neurobiology of Learning and Memory 144 (2017) 208–215

Contents lists available at ScienceDirect

Neurobiology of Learning and Memory

journal homepage: www.elsevier.com/locate/ynlme

# A preregistered, direct replication attempt of the retrieval-extinction effect in cued fear conditioning in rats

Laura Luyten *, Tom Beckers

*Centre for the Psychology of Learning and Experimental Psychopathology, KU Leuven, Belgium*

ARTICLE INFO

*Article history:*
Received 11 April 2017
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ABSTRACT

In 2009, Monfils and colleagues proposed a behavioral procedure that was said to result in a permanent attenuation of a previously established fear memory, thereby precluding a possible return of fear after extinction (Monfils, Cowansage, Klann, & LeDoux, 2009). By presenting a single retrieval trial one hour

Scientific Reports | (2022) 12:2285 | https://doi.org/10.1038/s41598-022-06119-5 nature portfolio 1

scientific reports

OPEN

# Demarcating the boundary conditions of memory reconsolidation: An unsuccessful replication

Lotte E. Stemerding✉, Danielle Stibbe, Vanessa A. van Ast & Merel Kindt✉

**Disrupting memory reconsolidation provides an opportunity to abruptly reduce the behavioural expression of fear memories with long-lasting effects. The success of a reconsolidation intervention**

CORTEX 129 (2020) 496–509

Available online at www.sciencedirect.com

ScienceDirect

Journal homepage: www.elsevier.com/locate/cortex

Registered Report

# No persistent attenuation of fear memories in humans: A registered replication of the reactivation-extinction effect

*Anastasia Chalkia [a,b], Natalie Schroyens [a,b], Lu Leng [a], Niels Vanhasbroeck [a], Ann-Kathrin Zenses [a,b], Lukas Van Oudenhove [b,c] and Tom Beckers [a,b,*]*

[a] *Centre for the Psychology of Learning and Experimental Psychopathology, Faculty of Psychology & Educational Sciences, KU Leuven, Belgium*

eNeuro

Research Article: New Research - Registered Report

Cognition and Behavior

# Reactivation-Dependent Amnesia for Contextual Fear Memories: Evidence for Publication Bias

Natalie Schroyens,[1,2] Eric L. Sigwald,[1,3] Wim Van Den Noortgate,[4,5] Tom Beckers,[1,2*] and Laura Luyten[1,2*]

https://doi.org/10.1523/ENEURO.0108-20.2020

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**Abstract**

Research on memory reconsolidation has been booming in the last two decades, with numerous high-impact publications reporting promising amnestic interventions in rodents and humans. However, our own recently-published failed replication attempts of reactivation-dependent amnesia for fear memories in rats suggest that such amnestic

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Verification Report

# Preventing the return of fear in humans using reconsolidation update mechanisms: A verification report of Schiller et al. (2010)

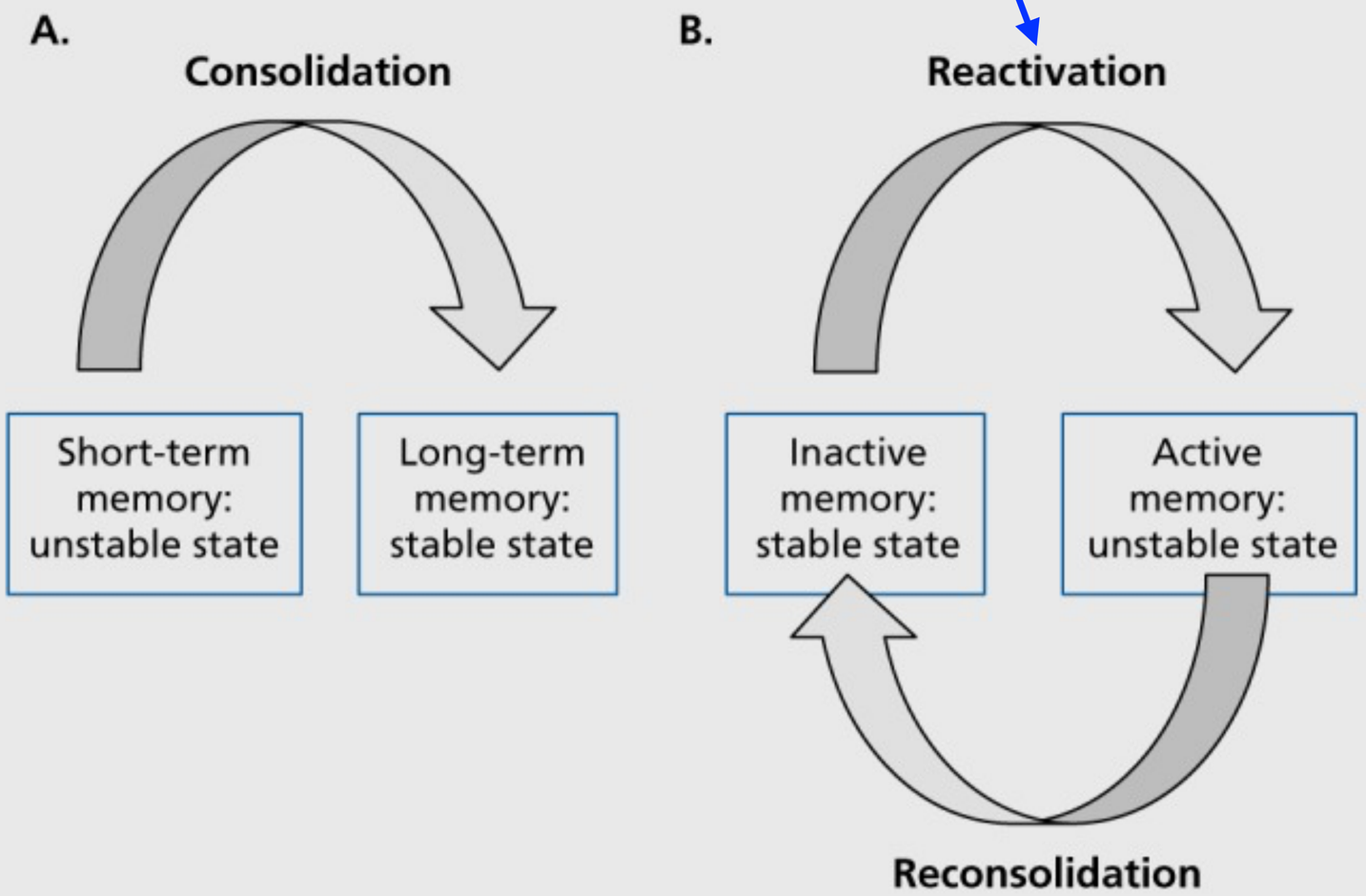
*Anastasia Chalkia* [a,b], *Lukas Van Oudenhove* [b,c] *and Tom Beckers* [a,b,*]

[a] *Centre for the Psychology of Learning and Experimental Psychopathology, Faculty of Psychology & Educational Sciences, KU Leuven, Belgium*

[b] *Leuven Brain Institute, KU Leuven, Belgium*

[c] *Laboratory for Brain-Gut Axis Studies (LaBGAS), Translational Research Centre for Gastrointestinal Disorders (TARGID), Department of Chronic Diseases, KU Leuven, Belgium*

vereist *prediction error*




Nader et al., *Dialogues Clin Neurosci* 2013

Neurobiology of Learning and Memory 97 (2012) 338–345

Contents lists available at SciVerse ScienceDirect

Neurobiology of Learning and Memory

journal homepage: www.elsevier.com/locate/ynlme

## Retrieval per se is not sufficient to trigger reconsolidation of human fear memory

Dieuwke Sevenster [a], Tom Beckers [a,b], Merel Kindt [a,*]

[a] Department of Clinical Psychology, University of Amsterdam, Weesperplein 4, 1018 XA Amsterdam, The Netherlands
[b] Department of Psychology, Katholieke Universiteit Leuven, Tiensestraat 102, 3712 B-3000 Leuven, Belgium

ARTICLE INFO

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ABSTRACT

Ample evidence suggests that consolidated memories, upon their retrieval, enter a labile state, in which they might be susceptible to change. It has been proposed that memory labilization allows for the integration of relevant information in the established memory trace (memory updating). Memory labilization and reconsolidation do not necessarily occur when a memory is being reactivated, but only when there is something to be learned during memory retrieval (prediction error). Thus, updating of a fear memory trace should not occur under retrieval conditions in which the outcome is [illegible] (no prediction

15 FEBRUARY 2013 VOL 339 SCIENCE www.sciencemag.org

## Prediction Error Governs Pharmacologically Induced Amnesia for Learned Fear

Dieuwke Sevenster,[1,2] Tom Beckers,[1,2,3] Merel Kindt[1,2]*

Although reconsolidation opens up new avenues to erase excessive fear memory, subtle boundary conditions put constraints on retrieval-induced plasticity. Reconsolidation may only take place when memory reactivation involves an experience that engages new learning (prediction error). Thus far, it has not been possible to determine the optimal degree of novelty required for destabilizing the memory. The occurrence of prediction error could only be inferred from the observation of a reconsolidation process itself. Here, we provide a noninvasive index of memory destabilization that is independent from the occurrence of reconsolidation. Using this index, we

21:580–584; Published by Cold Spring Harbor Laboratory Press
ISSN 1549-5485/14; www.learnmem.org



**Brief Communication**

## Prediction error demarcates the transition from retrieval, to reconsolidation, to new learning

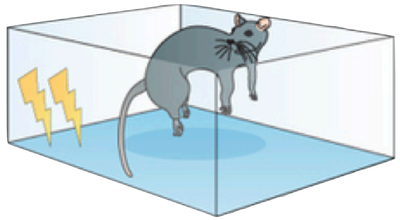
Dieuwke Sevenster,[1,2] Tom Beckers,[1,2,3] and Merel Kindt[1,2]

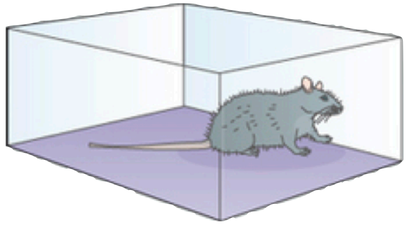
[1]*Department of Clinical Psychology, University of Amsterdam, 1018 WB Amsterdam, The Netherlands;* [2]*Amsterdam Brain and Cognition Center, University of Amsterdam, 1018 WS Amsterdam, The Netherlands;* [3]*Department of Psychology, University of Leuven, B-3000 Leuven, Belgium*

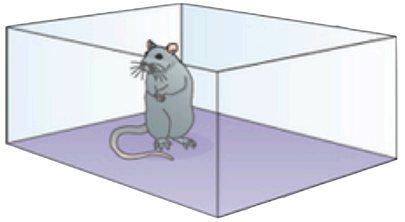
Although disrupting reconsolidation is promising in targeting emotional memories, the conditions under which memory becomes labile are still unclear. The current study showed that post-retrieval changes in expectancy as an index for prediction error may serve as a read-out for the underlying processes engaged by memory reactivation. Minor environmental changes define whether retrieval induces memory reconsolidation or the initiation of a new memory trace even before fear extinction can be observed.

MDZ 3mg/kg or SAL

Conditioning → 24h → Reactivation → 24h → Test







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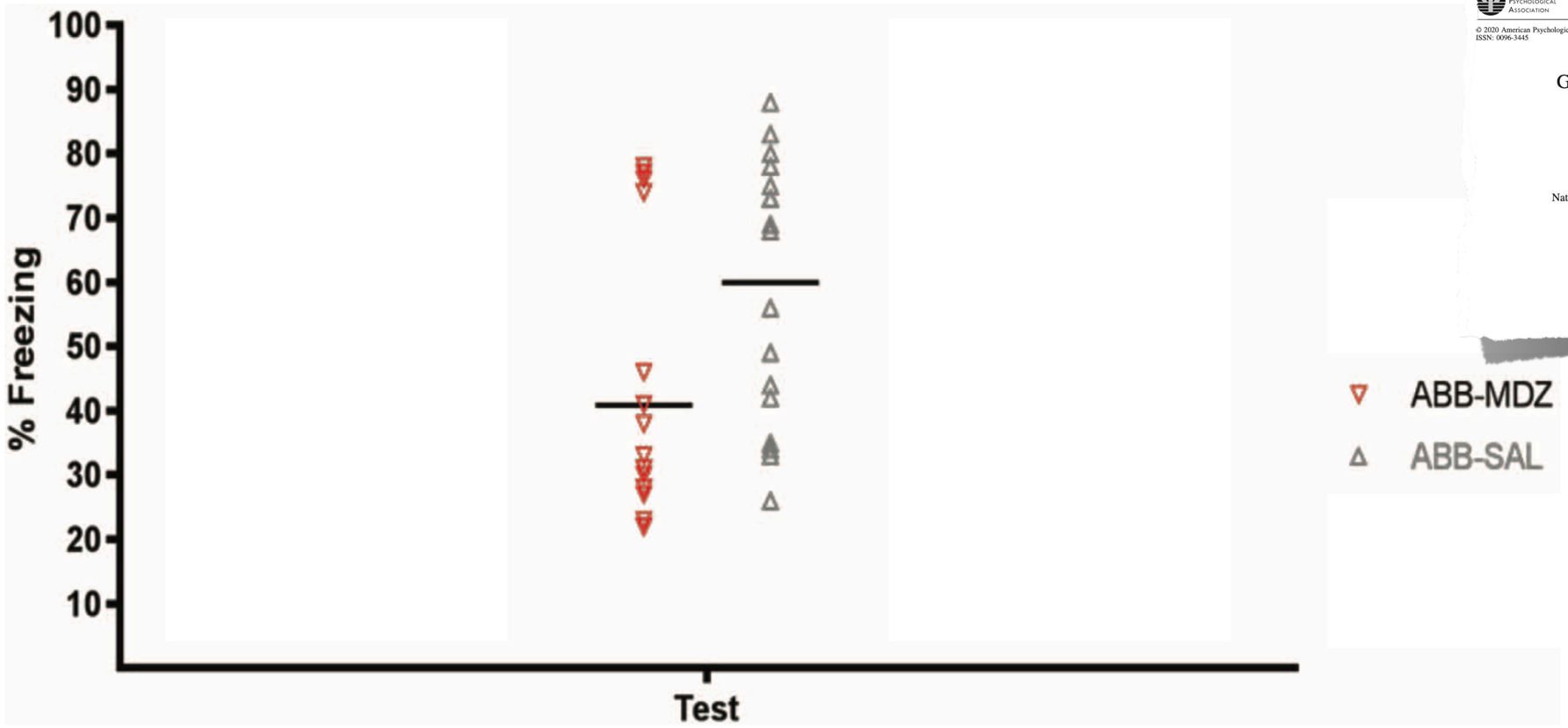


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Journal of Experimental Psychology: General

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http://dx.doi.org/10.1037/xge0000765

## Generalization and Recovery of Post-Retrieval Amnesia

Joaquín M. Alfei
KU Leuven

Roque I. Ferrer Monti
Hebb Institute of Mental Health, Córdoba, Argentina, and National University of Córdoba

Victor A. Molina
National University of Córdoba

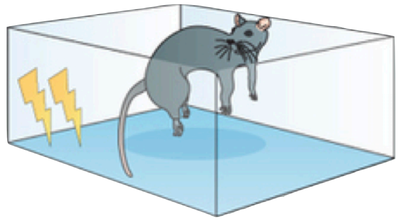
Dimitri De Bundel
Free University of Brussels

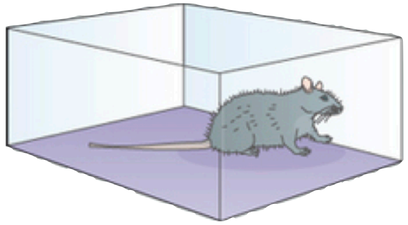
Laura Luyten and Tom Beckers
KU Leuven

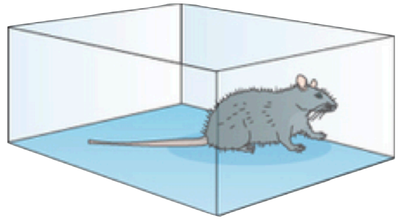
Selective amnesia for previously established memories can be induced by administering drugs that impair protein synthesis shortly after memory reactivation. Competing theoretical accounts attribute this selective post-retrieval amnesia to drug-induced engram degradation (reconsolidation blockade) or to incorporation of sensory features of the reactivation experience into the memory representation, hampering later retrieval in a drug-free state (memory integration). Here we present evidence that critically

MDZ 3mg/kg or SAL

Conditioning → 24h → Reactivation → 24h → Test







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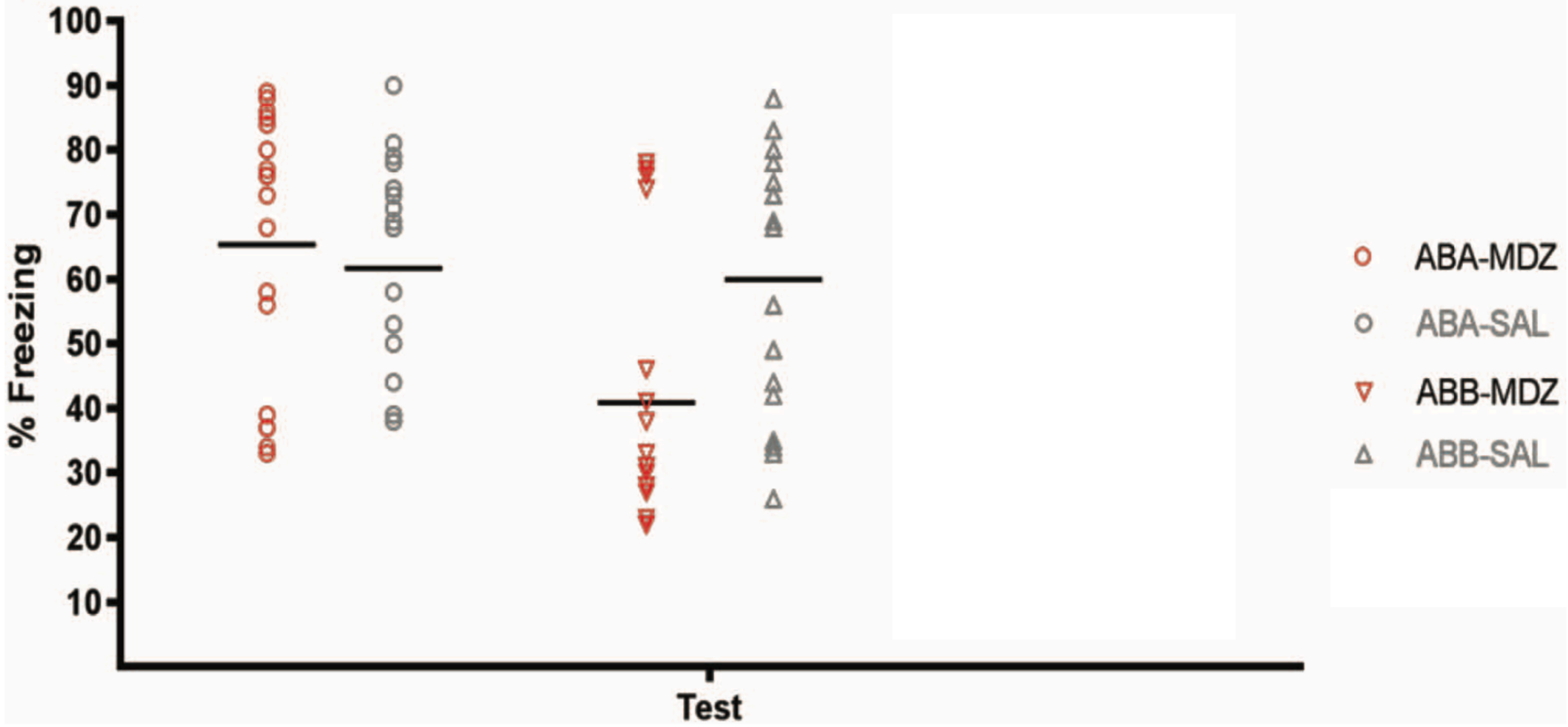


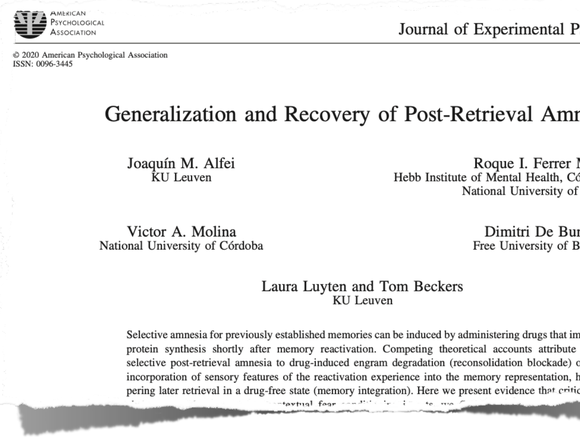

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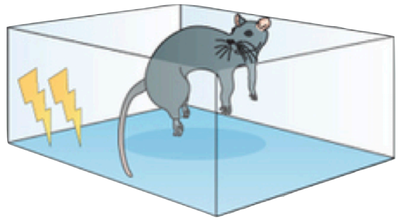

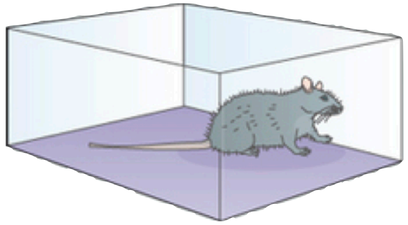

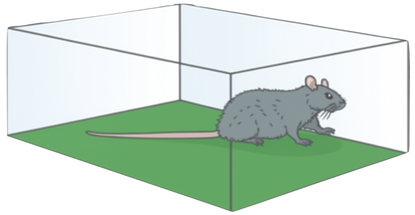

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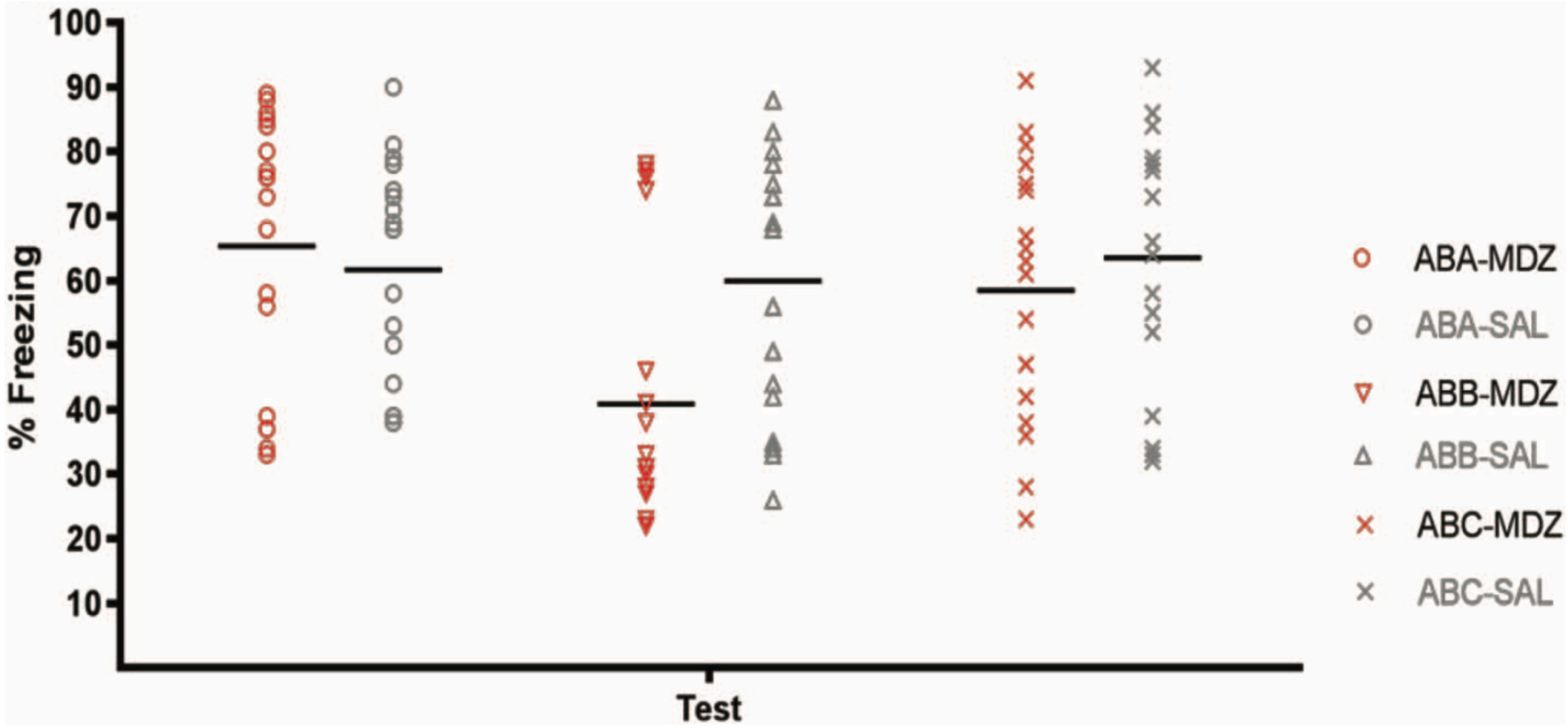


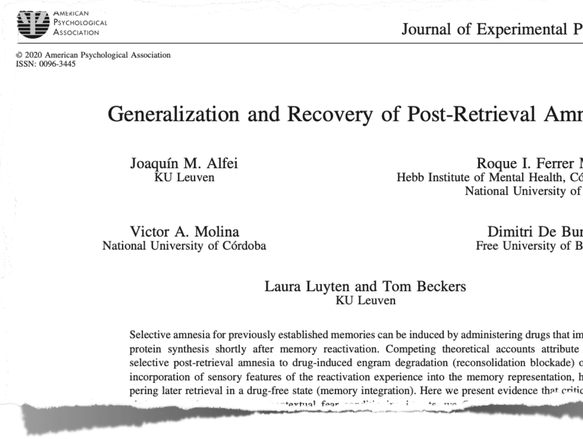

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pering later retrieval in a drug-free state (memory integration). Here we present evidence that

# Kortom, nieuwe behandelingen zijn vaak

- onderhevig aan fikse (maar voorbijgaande) placebo-effecten
- hetzelfde wiel een beetje anders
- gebouwd op wetenschappelijk drijfzand

- en mede daarom geen bron van duurzaam betere behandelresultaten

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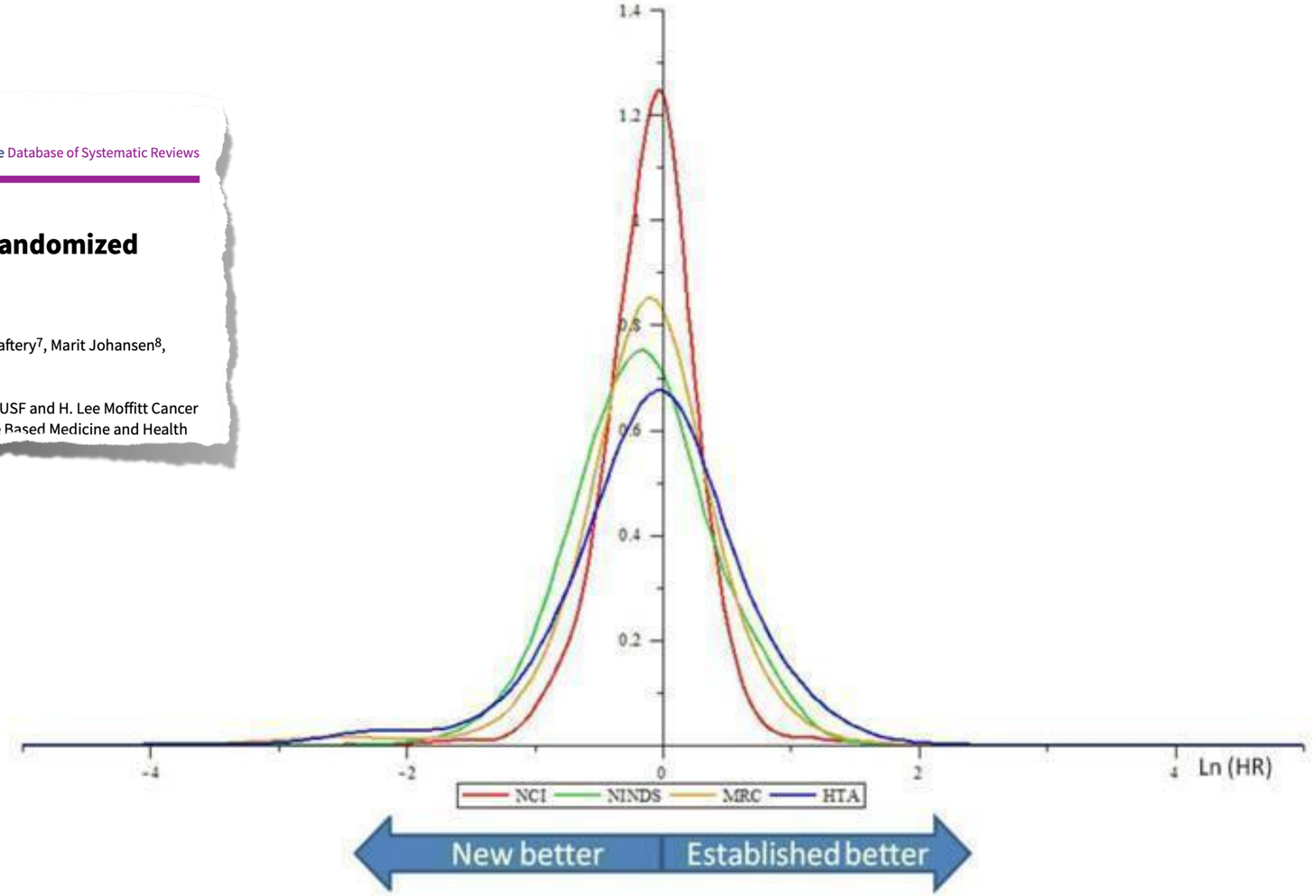
[Methodology Review]

# New treatments compared to established treatments in randomized trials

Benjamin Djulbegovic[1], Ambuj Kumar[2], Paul P Glasziou[3], Rafael Perera[4], Tea Reljic[5], Louise Dent[6], James Raftery[7], Marit Johansen[8], Gian Luca Di Tanna[9], Branko Miladinovic[2], Heloisa P Soares[10], Gunn E Vist[11], Iain Chalmers[12]

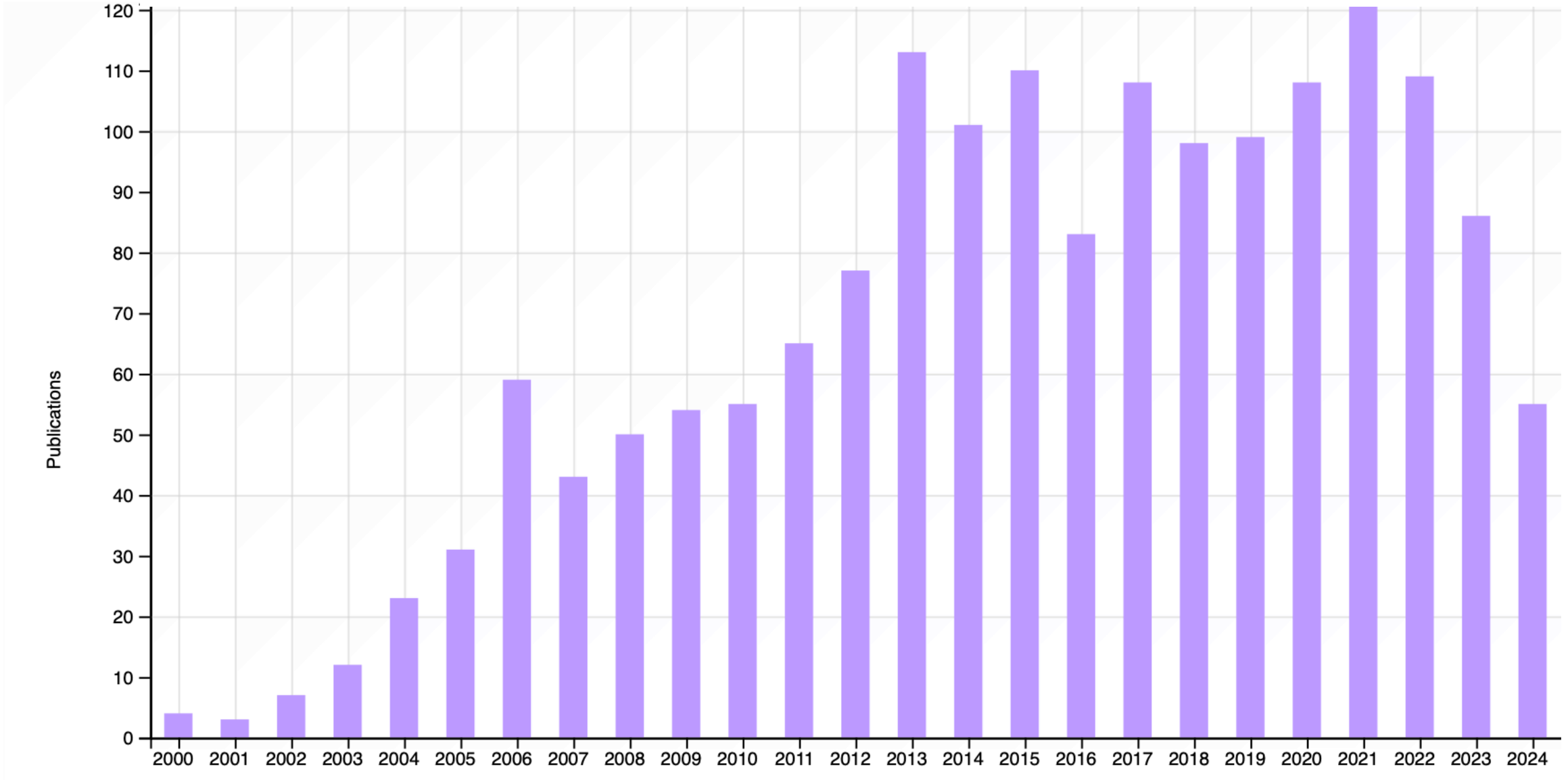
[1]USF Clinical Translational Science Institute, Dpts of Medicine, Hematology and Health Outcome Research, USF and H. Lee Moffitt Cancer Center, USF Health Clinical Research, University of South Florida, Tampa, Florida, USA. [2]Center for Evidence Based Medicine and Health




ndicating unpredictability in the results. This was consistent with the interpretation that new treatments are only slightly superior to established treatments when tested in RCTs. Additionally, meta-regression demonstrated that results have remained stable over time and that the success rate of new treatments has not changed over the last half century of clinical trials. The results were not significantly affected by the choice of comparator (active versus placebo/no therapy).

## Authors' conclusions

Society can expect that slightly more than half of new experimental treatments will prove to be better than established treatments when tested in RCTs, but few will be substantially better. This is an important finding for patients (as they contemplate participation in RCTs),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# Wat dan wel?

The Journal of Child Psychology and Psychiatry

*Journal of Child Psychology and Psychiatry* **:* (2025), pp **–** doi:10.1111/jcpp.70049

# Have parenting programs for disruptive child behavior become less effective?

**Patty Leijten,[1] G.J. Melendez-Torres,[2] Sophia Backhaus,[1] Frances Gardner,[3] Annabeth P. Groenman,[1,4,5] Tycho J. Dekkers,[4,5,6] Barbara J. van den Hoofdakker,[4,5] Liina Björg Laas Sigurðardóttir,[3] Danni Liu,[1] Marjolein Luman,[6,7] Lara Mansur,[1] Merlin Nieterau,[1] Saskia van der Oord,[8] Geertjan Overbeek,[1] Constantina Psyllou,[4,5] Karen Rienks,[1] Susanne Schulz,[1] and John R. Weisz[9]**

[1]Research Institute of Child Development and Education, University of Amsterdam, Amsterdam, The Netherlands; [3]Department of Social Policy and Intervention, ngen, The Netherlands; [5]Department of Child oningen, The Netherlands; [6]Levvel, Academic rlands; [7]Department of Clinical, Neuro and ands; [8]Faculty of Psychology and Educational arvard University, Cambridge, Massachusetts,

y studied over the past five decades. We used effects have evolved over time, and if any time ntion characteristics. **Methods:** We based our

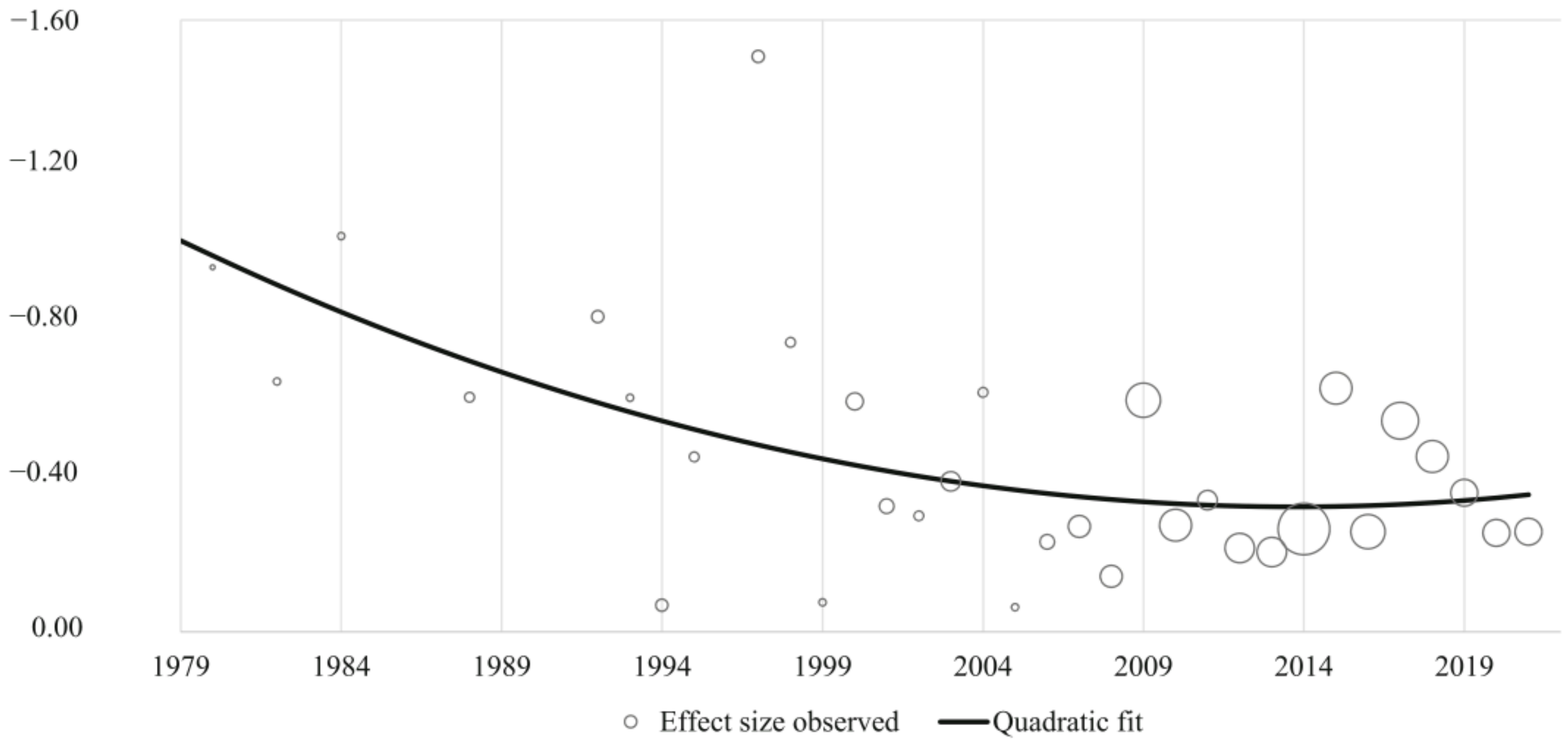
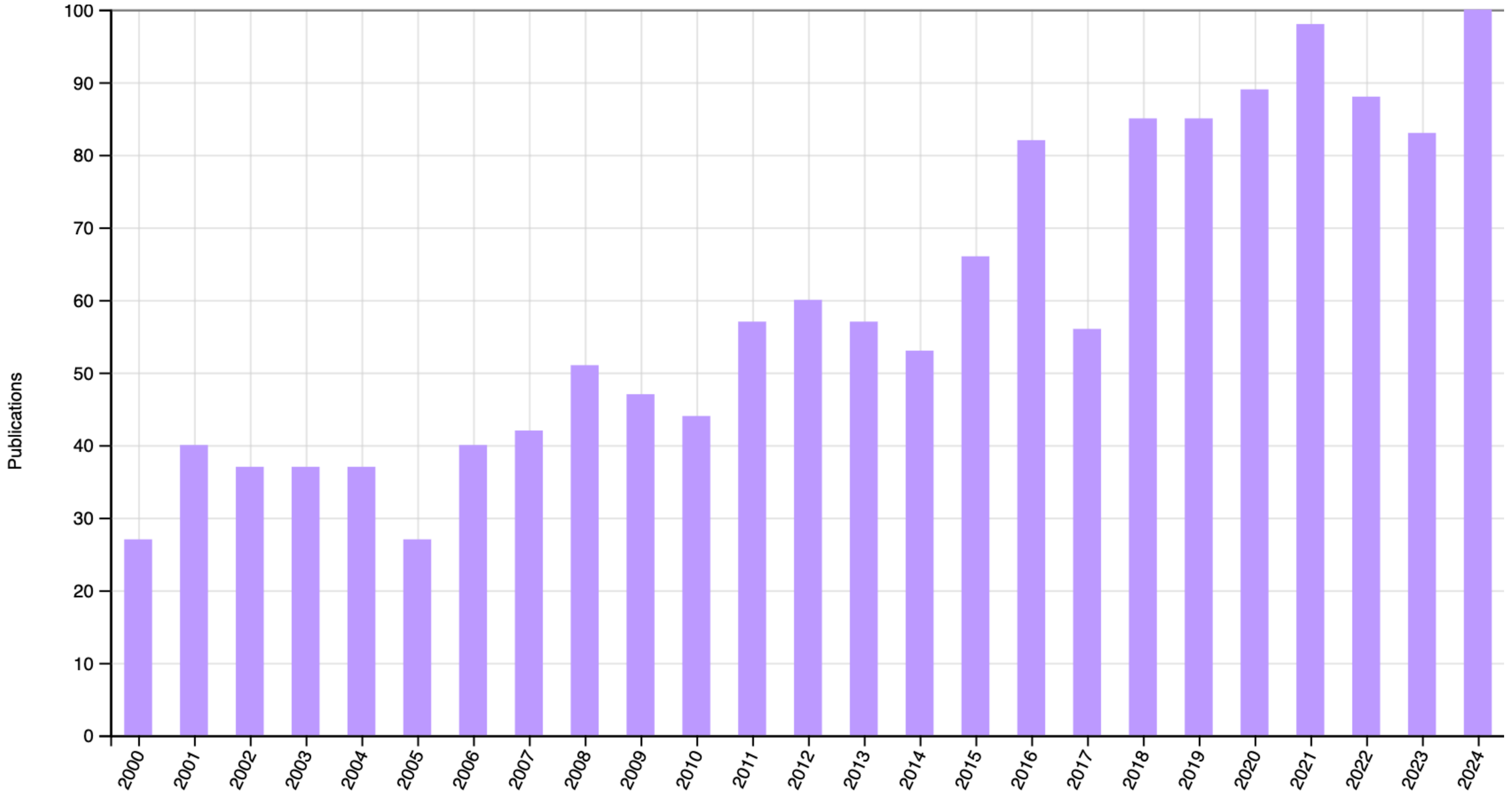



**Figure 2** Time trend in parenting program effects (Cohen's *d*) on disruptive child behavior (bubble size reflects number of trials)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Clinical Psychology Review 45 (2016) 144–156

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# The use of safety-seeking behavior in exposure-based treatments for fear and anxiety: Benefit or burden? A meta-analytic review

Ann Meulders [a,b,*], Tom Van Daele [a,c], Stéphanie Volders [a], Johan W.S. Vlaeyen [a,b,d]

[a] Research Group on Health Psychology, University of Leuven, Leuven, Belgium
[b] Center for Excellence Generalization Research in Health and Psychopathology, University of Leuven, Leuven, Belgium
[c] Applied Psychology, Thomas More University College, Antwerp, Belgium
[d] Department of Clinical Psychological Science, Maastricht University, The Netherlands

## HIGHLIGHTS

- We examined the effect of safety-seeking behavior on exposure-based fear reduction.
- The results of the first meta-analysis on the topic are inconclusive.
- The results provide limited evidence in favor of dropping safety-seeking behavior.
- Due to potential risk of bias in included studies, interpretation warrants caution.
- We suggest that more experimental research based on modern learning theory is needed.

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*Cognitive Behaviour Therapy*, 2014
Vol. 43, No. 1, 83–92, http://dx.doi.org/10.1080/16506073.2013.819376

# Safety Behaviour Enhances the Acceptability of Exposure

Hannah C. Levy and Adam S. Radomsky

*Department of Psychology, Concordia University, Montreal, QC, Canada*

**Abstract.** Compulsive washing and contamination fears are among the most common symptoms of obsessive-compulsive disorder (OCD). Research suggests that exposure and response prevention (ERP) is effective for OCD. However, ERP is prone to dropouts and refusals, and a substantial proportion of clients therefore do not receive the care they need. A proposed solution involves the judicious use of safety behaviour to enhance the acceptability of exposure-based interventions. The current study aimed to test this proposed solution. Participants were 70 undergraduate students who completed two exposure exercises for contamination fear, one with safety behaviour and one without.

Clinical Psychology Review 45 (2016) 144–156

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# The use of safety-seeking behavior in exposure-based treatments for fear and anxiety: Benefit or burden? A meta-analytic review

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Cognitive Therapy and Research
https://doi.org/10.1007/s10608-025-10667-1

ORIGINAL ARTICLE

# Testing Judicious Use of Safety Behaviors During Exposure: A Randomized Controlled Trial Examining when and for whom Safety Behaviors Improve Fear Reduction

Samantha Meckes[1,2] · Anna Cole[3] · Kristen Gee[4] · Cynthia Lancaster[3]

Received: 10 June 2025 / Accepted: 18 September 2025


## Abstract

**Background** Safety behaviors (SBs), or unnecessary protective actions, are thought to play a key role in the development and maintenance of pathological fear and anxiety. However, their impact on exposure therapy outcomes is debated, with empirical studies yielding inconsistent findings. Thus, rather than continuing to test whether safety behaviors impact exposure therapy outcomes, we aimed to examine under which conditions safety behaviors may interfere with or facilitate expo-

Behaviour Research and Therapy 47 (2009) 716–720

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Behaviour Research and Therapy

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Shorter communication

# Safety behaviours preserve threat beliefs: Protection from extinction of human fear conditioning by an avoidance response

Peter F. Lovibond [a,*], Christopher J. Mitchell [a], Erin Minard [a], Alison Brady [a], Ross G. Menzies [b]

[a] School of Psychology, University of New South Wales, Sydney NSW 2052, Australia
[b] Discipline of Behavioural and Social Sciences in Health, University of Sydney, Australia

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ABSTRACT

A laboratory autonomic conditioning procedure was used to establish fear conditioning in human participants by pairing neutral stimuli with electric shock. Participants were also trained to make a button-press response to avoid shock. A target fear stimulus was then extinguished by presenting it without shock. The experimental group was given the opportunity to make the avoidance response during extinction whereas the control group was not. When the fear stimulus was tested without the response available, the control group showed normal extinction of both shock expectancy ratings and skin conductance responses, but the experimental group showed "protection from extinction": they continued to give high expectancy ratings and strong skin conductance responses. We interpret this effect as analogous to the role of within-situation safety behaviours in preserving threat beliefs during exposure therapy for anxiety disorders. The results support a cognitive account of learning and anxiety. The procedure provides a potential laboratory model for further examination of the cognitive and neural mechanisms underlying anxiety and its reduction.

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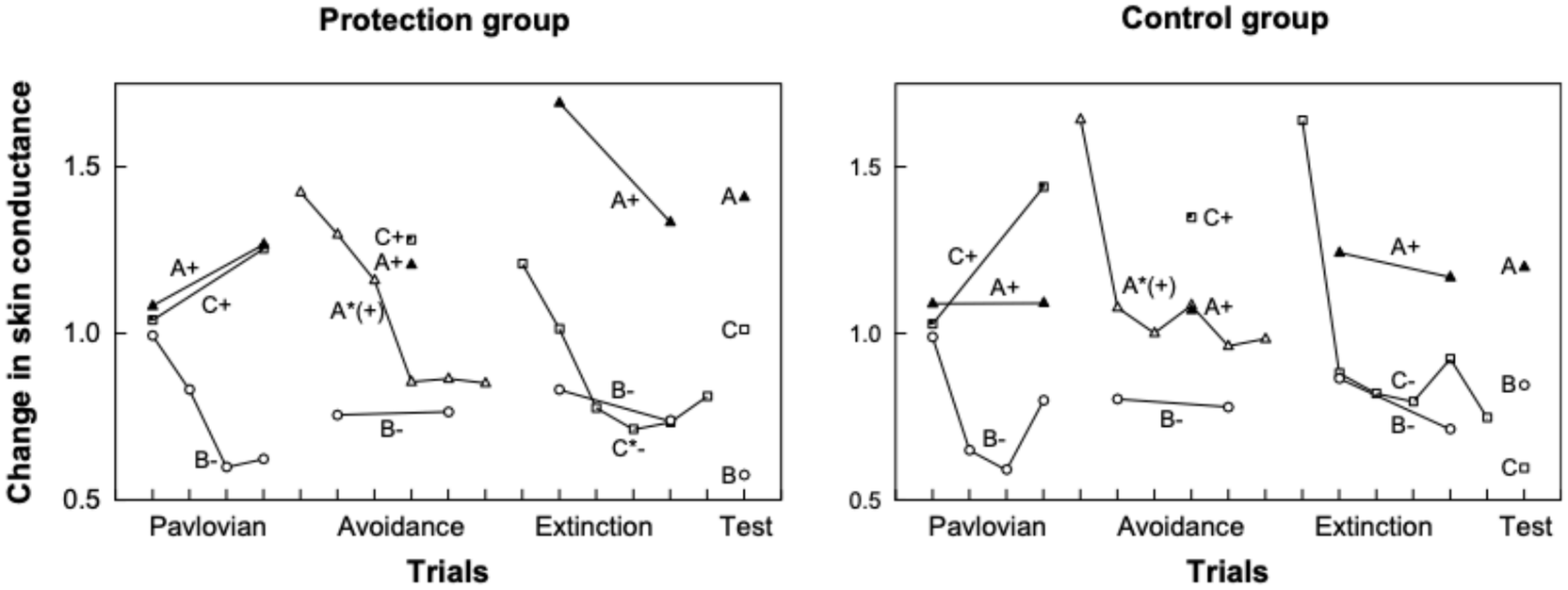

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Article

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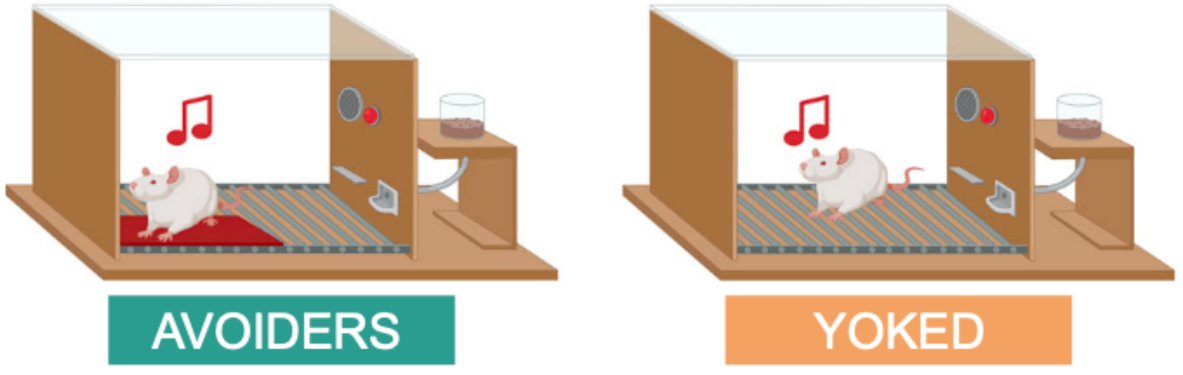
https://doi.org/10.1038/s41539-024-00223-z

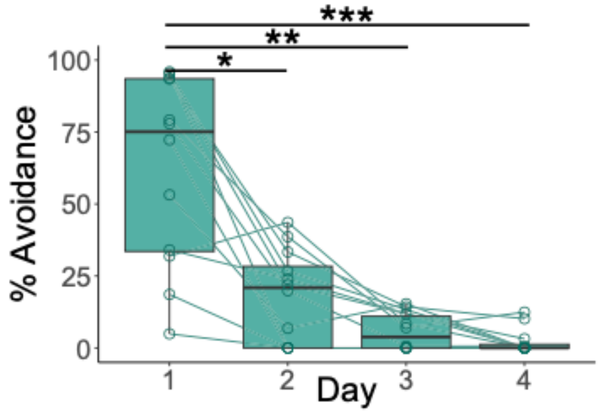
# A history of avoidance does not impact extinction learning in male rats

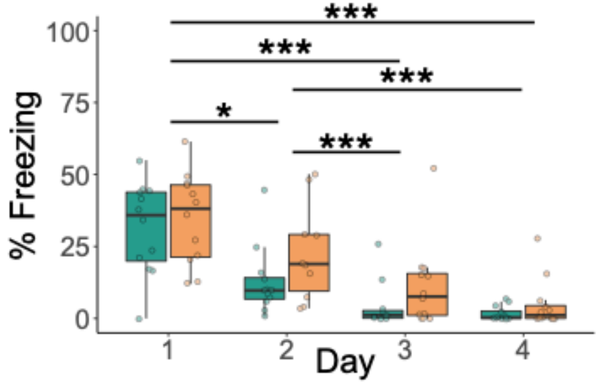
Check for updates

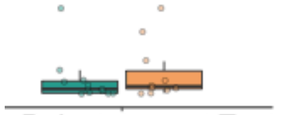
Alba López-Moraga [1,2] ✉, Laura Luyten [1,2,3] ✉ & Tom Beckers [1,2,3] ✉

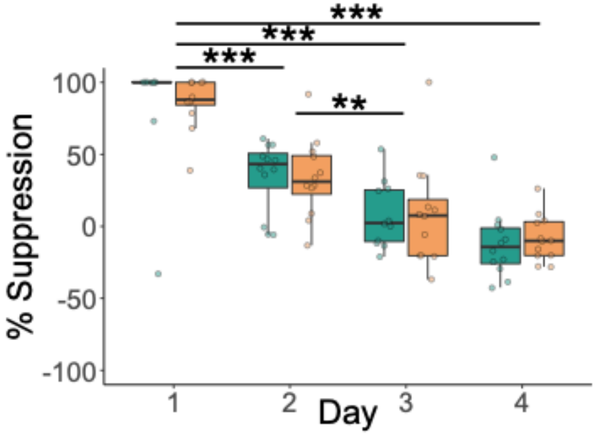
Pervasive avoidance is one of the central symptoms of all anxiety-related disorders. In treatment, avoidance behaviors are typically discouraged because they are assumed to maintain anxiety. Yet, it is not clear if engaging in avoidance is always detrimental. In this study, we used a platform-mediated avoidance task to investigate the influence of avoidance history on extinction learning in male rats. Our results show that having the opportunity to avoid during fear acquisition training does not significantly influence the extinction of auditory-cued fear in rats subjected to this platform-mediated avoidance procedure, which constitutes a realistic approach/avoidance conflict. This holds true irrespective of whether or not avoidance was possible during the extinction phase. This suggests that imposing a realistic cost on avoidance behavior prevents the adverse effects that avoidance has been claimed to

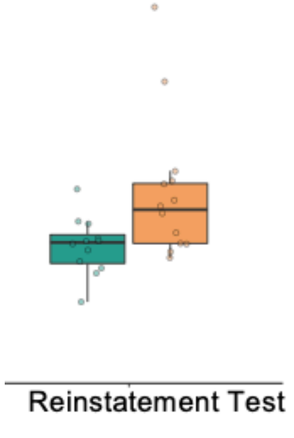


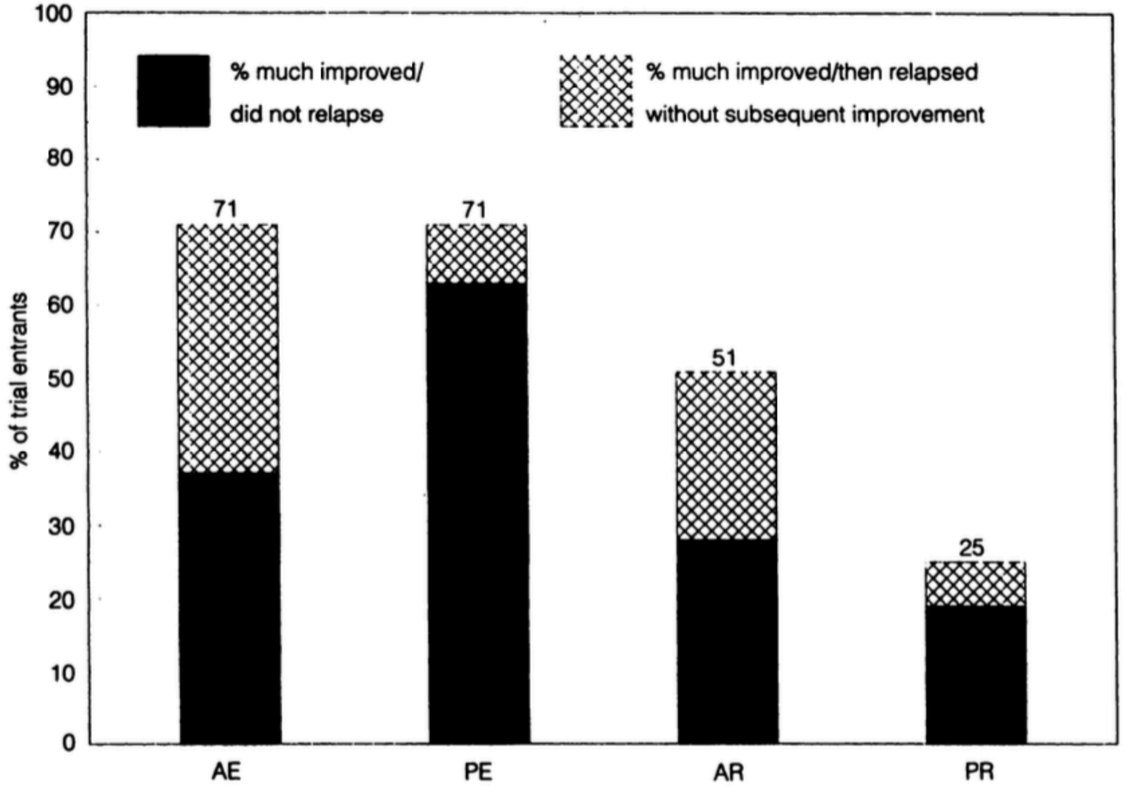
*British Journal of Psychiatry* (1993), **162**, 776–787

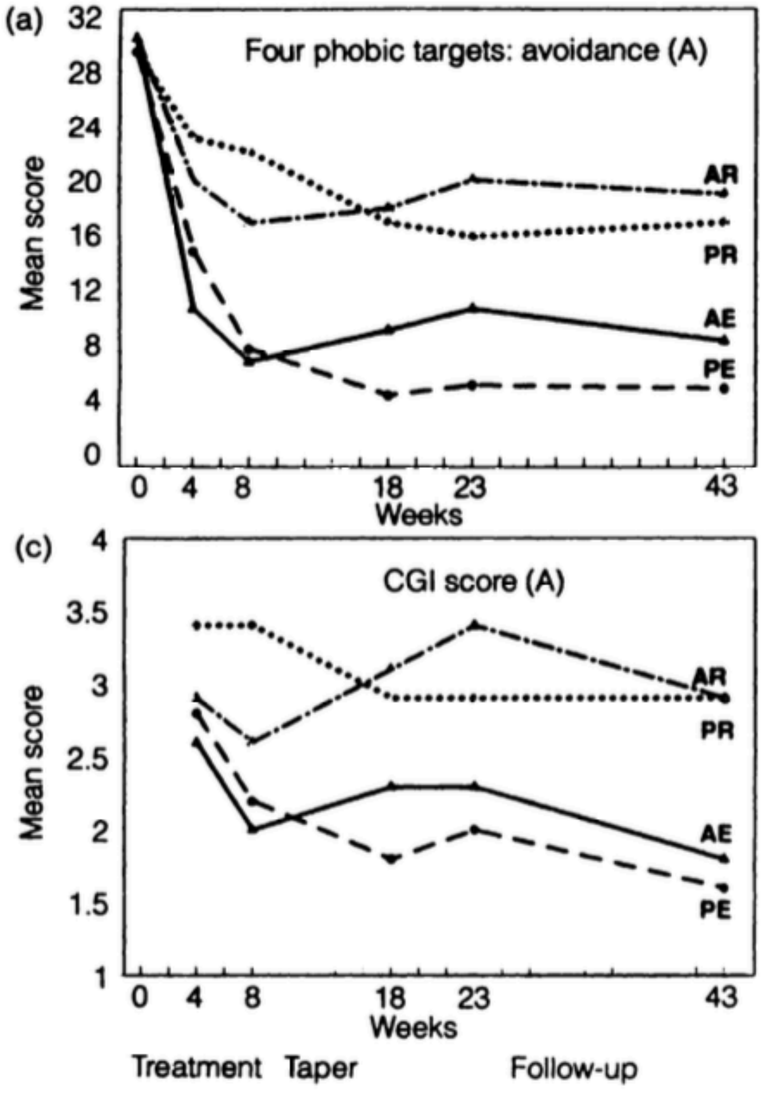
# Alprazolam and Exposure Alone and Combined in Panic Disorder with Agoraphobia

## A Controlled Study in London and Toronto

ISAAC M. MARKS, RICHARD P. SWINSON, METIN BAŞOĞLU, KLAUS KUCH, HOMA NOSHIRVANI, GERALDINE O'SULLIVAN, PAUL T. LELLIOTT, MARLENE KIRBY, GARY McNAMEE, SEDA SENGUN and KIM WICKWIRE

A cross-national randomised trial of alprazolam for chronic panic disorder with agoraphobia was run. Compared with previous trials it had three new features: an exposure therapy contrast group, a six-month treatment-free follow-up, and a low rate of early placebo drop-outs ('non-evaluables'). The dose of alprazolam was high (5 mg/day). The 154 patients had eight weeks of: alprazolam and exposure (combined treatment); or alprazolam and relaxation (a psychological placebo); or placebo and exposure; or placebo and relaxation (double placebo).



Journal of Anxiety Disorders 104 (2024) 102870

Contents lists available at ScienceDirect

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# No harmful effect of propranolol administered prior to fear memory extinction in rats and humans

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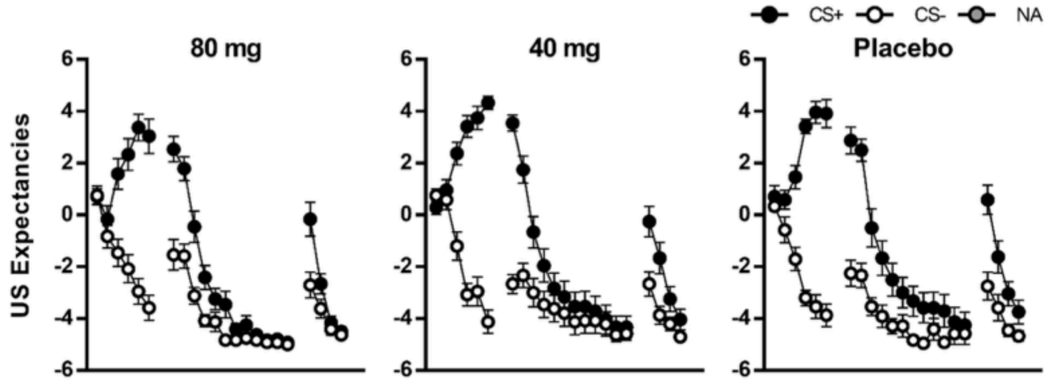
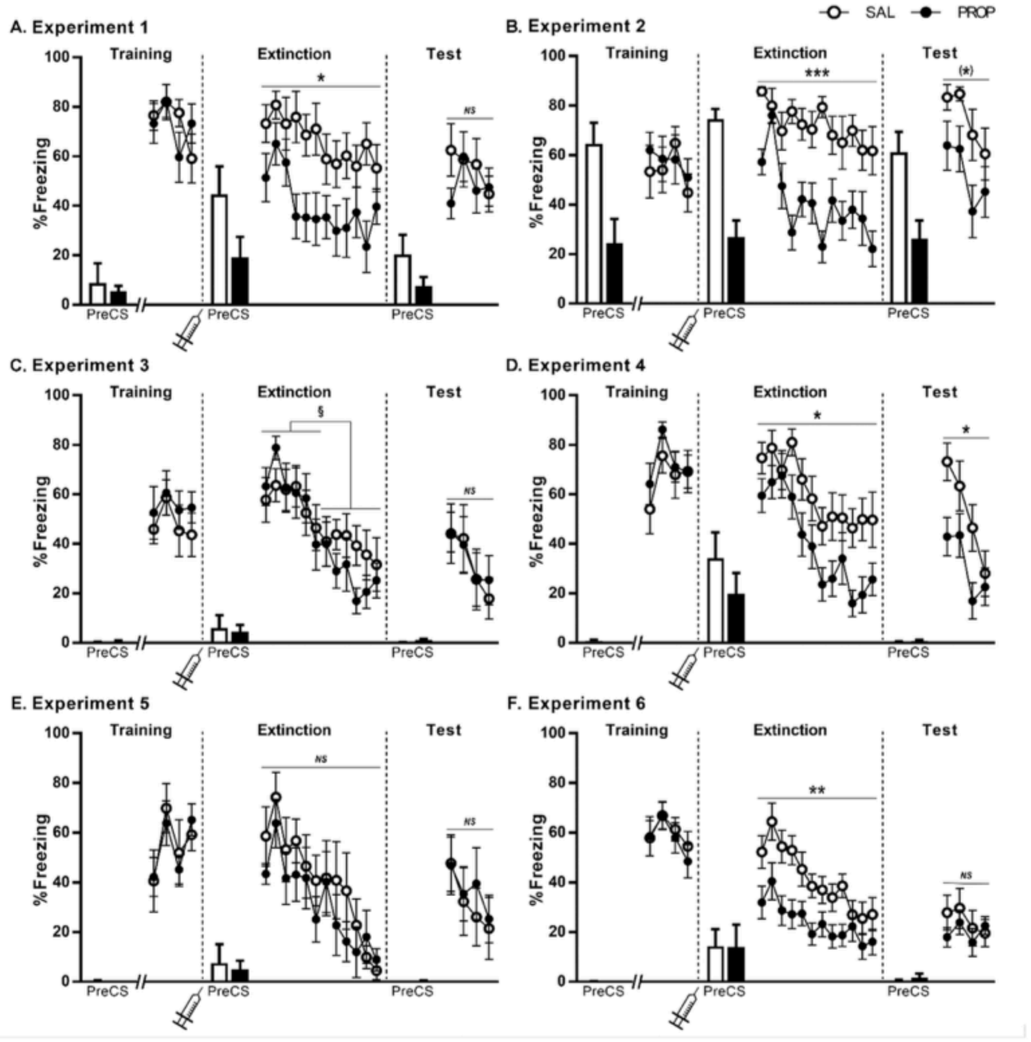
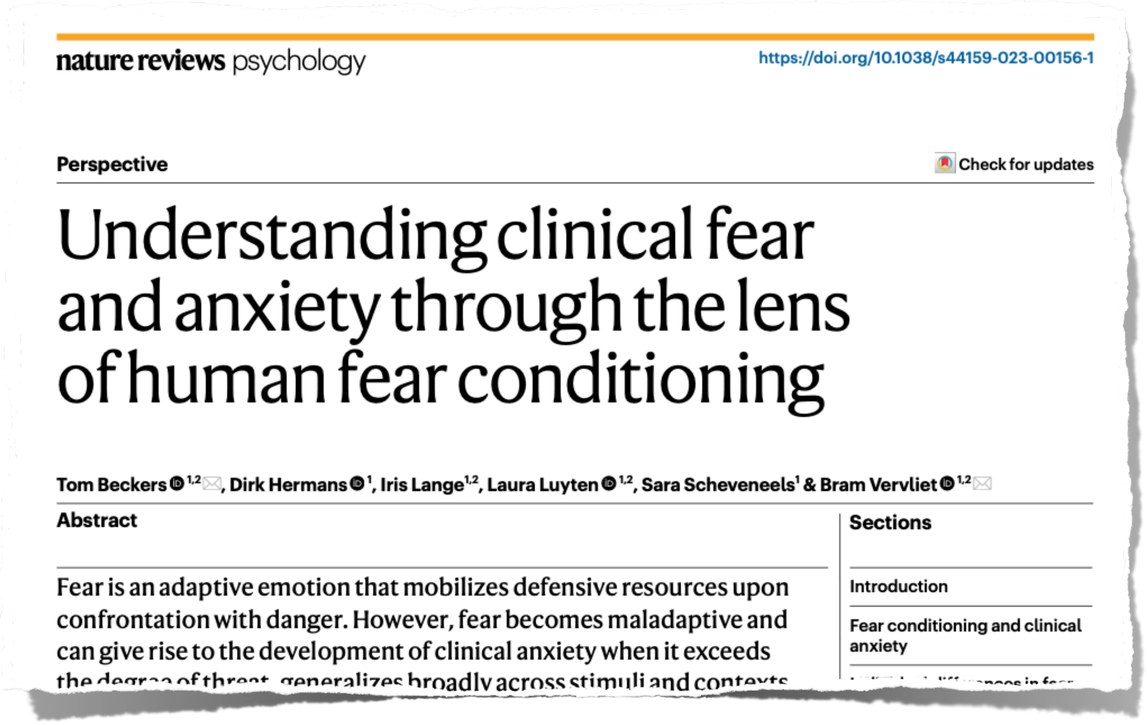
ABSTRACT

Exposure therapy is an evidence-based treatment option for anxiety-related disorders. Many patients also take medication that could, in principle, affect exposure therapy efficacy. Clinical and laboratory evidence indeed suggests that benzodiazepines may have detrimental effects. Large clinical trials with propranolol, a common



- kortom: voor *accepted wisdom* met betrekking tot exposure bestaat soms weinig evidentie vanuit klinische onderzoek
- vooral gebaseerd op basic science met betrekking tot uitdoving
  - ook daar soms weinig evidentie
  - begripsverwarring tussen exposure en uitdoving: uitdoving, als procedure, is een labo-model



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Perspective

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# Understanding clinical fear and anxiety through the lens of human fear conditioning

Tom Beckers[1,2], Dirk Hermans[1], Iris Lange[1,2], Laura Luyten[1,2], Sara Scheveneels[1] & Bram Vervliet[1,2]

**Abstract**

Fear is an adaptive emotion that mobilizes defensive resources upon confrontation with danger. However, fear becomes maladaptive and can give rise to the development of clinical anxiety when it exceeds the degree of threat, generalizes broadly across stimuli and contexts

**Sections**

unconditioned stimuli (US), resulting in a decreased conditioned response (CR) [5]. Extinction is the major mechanism for the large evidence of exposure-based psychological interventions in treating threat- and trauma-related disorders clinically [6, 7].

Klosko, 1989; Craske, Brown, & Barlow, 1991; Gould, Otto, & Pollack, 1995). Exposure therapy is based on principles of fear extinction, in which classically conditioned stimuli gradually lose their phobic quality through repeated exposure without the feared negative consequences (Myers

**regularities in routine care settings. Extinction has emerged as the key mechanism of exposure treatment in anxiety disorders. Examining exposure treatment processes from the perspective of**

iology measures, and event-related potentials. Because exposure therapy, the first-line treatment for anxiety disorders, is largely based on principles of extinction learning, the study also examined the link between extinction

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# Maximizing exposure therapy: An inhibitory learning approach

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ABSTRACT

Exposure therapy is an effective approach for treating anxiety disorders, although a substantial number of individuals fail to benefit or experience a return of fear after treatment. Research suggests that anxious individuals show deficits in the mechanisms believed to underlie exposure therapy, such as inhibitory learning. Targeting these processes may help improve the efficacy of exposure-based procedures. Although evidence supports an inhibitory learning model of extinction, there has been little discussion of how to implement this model in clinical practice. The primary aim of this paper is to provide examples to clinicians for how to apply this model to optimize exposure therapy with anxious clients, in ways that distinguish it from a 'fear habituation' approach and 'belief disconfirmation' approach within standard cognitive-behavior therapy. Exposure optimization strategies include 1) expectancy violation, 2) deepened extinction, 3) occasional reinforced extinction, 4) removal of safety signals, 5) variability, 6) retrieval cues, 7) multiple contexts, and 8) affect labeling. Case studies illustrate methods of applying these

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# Generalization of beneficial exposure effects to untreated stimuli from another fear category

Iris Kodzaga[1], Ekrem Dere[1,2] and Armin Zlomuzica[1]✉



Previous research has shown that fear associated with one stimulus often spreads to other stimuli with similar perceptual features as well as across different stimulus categories. Exposure is considered as the most effective intervention to attenuate exaggerated fear. The extent to which exposure treatment effects can generalize to fears not targeted during treatment remains elusive. Previous studies on possible generalization of beneficial effects of exposure used stimuli sharing the same stimulus category and/or stimuli having high perceptual similarity. The current study examined whether exposure treatment generalization can be achieved for untreated stimuli which do not share any perceptual resemblance and belong to a different fear category. An analogue sample

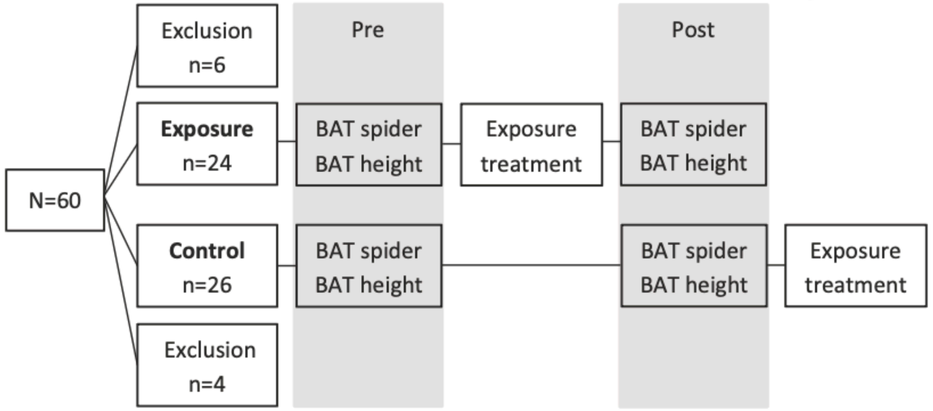


**Fig. 1 Brief outline of the experimental design.** Participants were assigned to the exposure group or control group. Exposure-induced changes in fear and avoidance of spiders were assessed with behavioral approach tests (BATs) prior to (Pre) and after exposure (Post). BATs for heights as the untreated stimulus were conducted to assess exposure treatment generalization. The order of BATs with spiders and heights was counterbalanced across participants. The BAT for spiders was conducted in the treatment room, while the BAT for heights was conducted in a church tower.

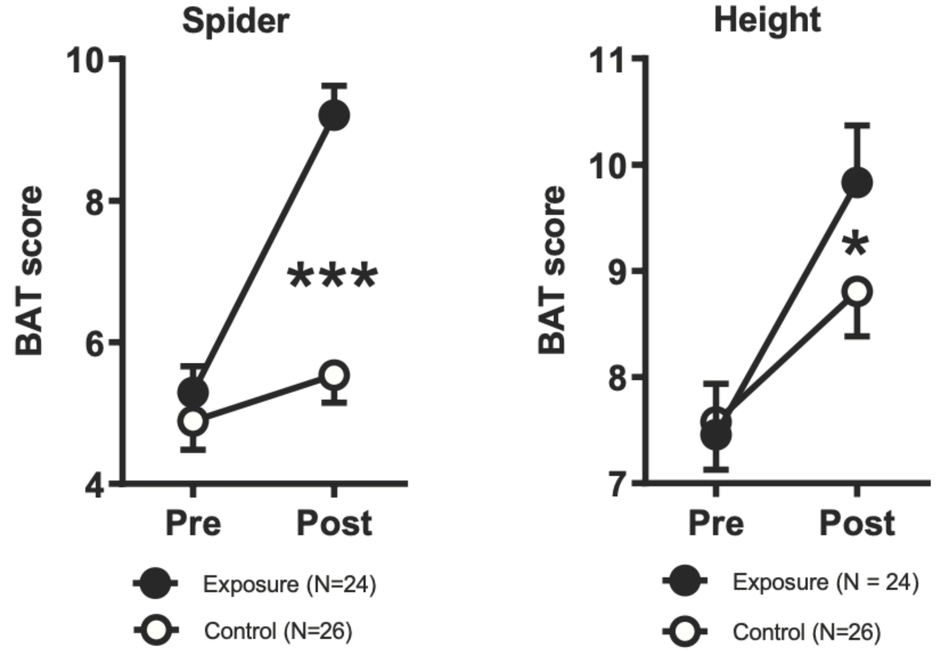


**Fig. 2 Approach distance in the BAT. A** Treatment effectiveness measured with the spider BAT; **B** Generalization measured with the height BAT. Squares represent mean ± SEM. Significant time × group interaction effects, with ***$P < 0.001$, *$P < 0.05$.

# Conclusie: *Beyond belief?*

- Beyond belief blijft er van nieuwe behandelingen en interventies niet altijd veel over
- Wat er *beyond belief* wel van overblijft, zal even goed de effectiviteit van behandeling niet duurzaam verbeteren
- Don’t belief the hype: Geloof de marketeers van de innovatie in de psychotherapie niet te snel, een gezonde dosis scepsis is aangewezen
- Besef dat wetenschappers onder grote druk staan om te innoveren én om impact aan te tonen, druk die hun aanzet om de vertaalbaarheid en het potentieel van de resultaten van hun basisonderzoek te overdrijven
- Zowel clinicus als academicus zouden gebaat zijn bij meer schaven aan wat we al hebben, incrementele ontwikkeling





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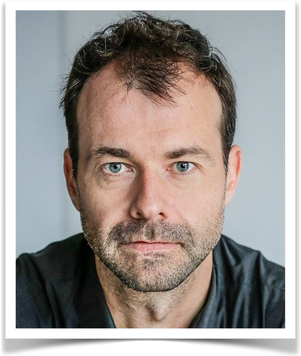



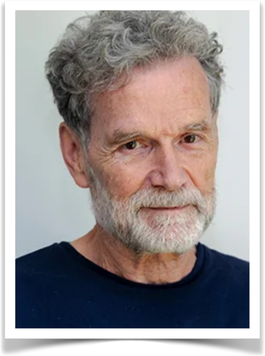

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