'U krijgt van mij een pijnstiller of een onwerkzame stof, dat kan ik u niet vertellen'

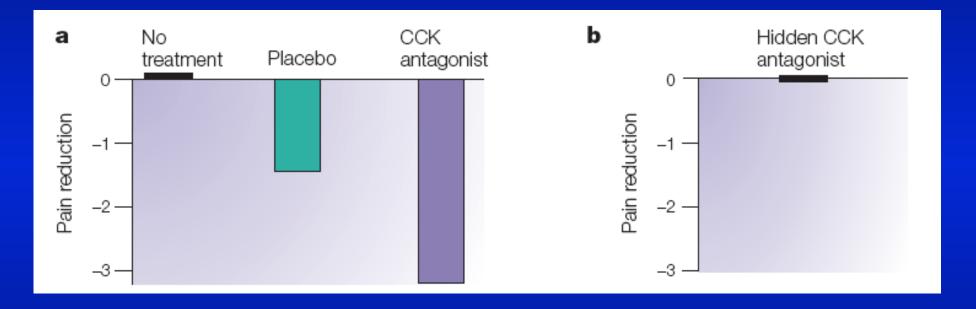
Dokter denkt: Nieuw middel testen in DB RCT

## Proglumide trial 1995

### DB RCT-3 armen: Informed pt

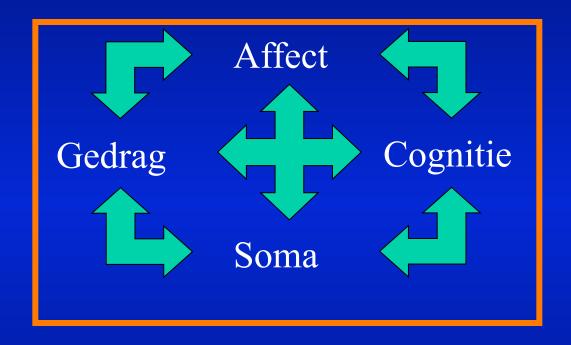
Placebos and painkillers: is mind as real as matter?

NATURE REVIEWS | NEUROSCIENCE | VOLUME 6 | JULY 2005 | 545



# 'Stiekumme' toediening

Patiënt denkt: ik hoop/verwacht dat ik de werkzame stof heb!



Patiënt denkt: ik hoop dat ik de werkzame stof heb!

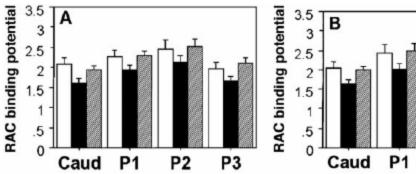
## Raclopride verdringing door dopamine

### **Expectation and Dopamine** Release: Mechanism of the Placebo Effect in Parkinson's

#### Disease

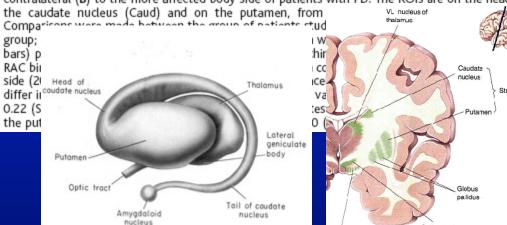
Raúl de la Fuente-Fernández, Thomas J. Ruth Michael Schulzer, Donald B. Calne, A. Jo

The power of placebos has long been recognized for i medical conditions such as Parkinson's disease (PD). Little about the mechanism underlying the placebo effect. Usi dogenous dopamine to compete for [11C]raclopride bink Fig. 1. Placebo-induced changes in RAC binding potential in the striatum ipsilateral (A) and release of endogenous dopamine in the striatum of PD pa placebo. Our findings indicate that the placebo effect in I group; mediated through activation of the damaged nigrostriata



positron emission tomography, we provide in vivo evid contralateral (B) to the more affected body side of patients with PD. The ROIs are on the head of

**P3** 



10 AUGUST 2001

### DB CT analgeticum

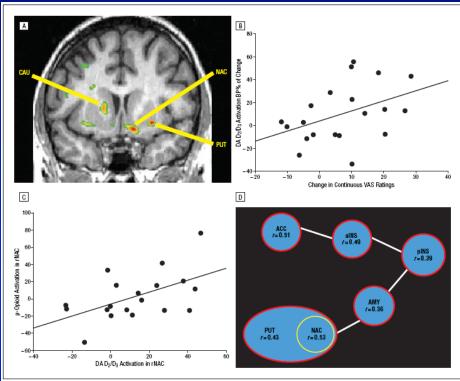


Figure 2. Placebo-induced activation of regional dopaminergic (DA) D<sub>2</sub>/D<sub>3</sub> receptor—mediated neurotransmission. A, Areas in which significant activation of DA neurotransmission during sustained pain were observed after the introduction of a placebo with expectation of analyseis. The z-scores of statistical significance are superimposed over an anatomically standardized magnetic resonance image in a coronal view. B, Postitive correlation between placebo-induced DA Dy/D<sub>2</sub> activation in the right nucleus accumbens (rNAC) (y-axis) and reductions in intensity of pain, reported by means of a visual analog scale (VAS) (x-axis). C, Positive correlations observed between the activation of DA Dy/D<sub>2</sub> (x-axis) and opioid (y-axis) systems in response to placebo administration in the rNAC. D, Schematic representation shows some of the connectivity between the regions in which in-pojoid system activation was detected during placebo administration. The yellow circle represents DA activation; the red circles, endogenous opioid activation. The r values represent the correlation between DA activation in the nucleus accumbens and regional j--poioid system activation. ACC indicates anterior cingulate; alNS, anterior insular cortex; AMY, amygdala; CAU, caudate; plNS, posterior insular cortex; and PUT, putmen.

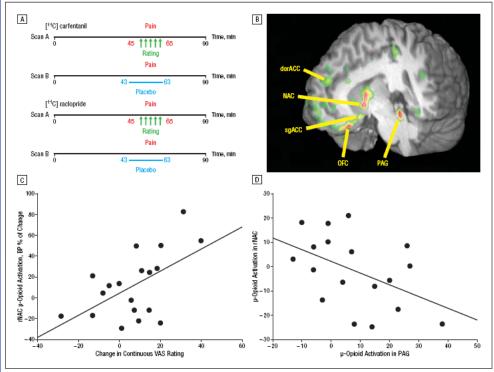


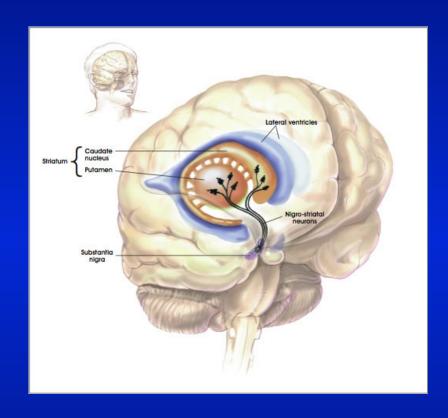
Figure 1. Placebo-induced activation of regional  $\mu$ -opioid receptor—mediated neurotransmission. A, Experimental design. Four scans were obtained in each subject, 2 with administration of carbon 11 [19c]—labeled carfentanii (without and with placebo) and 2 with administration of [19c] received (without and with placebo) and 2 with administration of [19c] received were randomized and counterbalanced in order in each scan series. B, Some of the areas in which significant activation of  $\mu$ -opioid neurotransmission during sustained pain were observed after the introduction of a placebo with expectation of analgesia. The z scores of statistical significance are superimposed over an anatomically standardized magnetic resonance image in a 3-dimensional view. C, Positive correlation between periaqueductal gray matter (PAG) placebo-induced  $\mu$ -opioid system activation in the right nucleus accumbens (rNAC) (y-axis) and reductions in pain report (x-axis). D, Negative correlation between periaqueductal gray matter (PAG) placebo-induced  $\mu$ -opioid activity (x-axis) and that in other supraspinal regions (the rNAC is shown); y(-axis). BP indicates binding potential, don't control of the rostral anterior cinqulate (Bray Siz, and VAS, visual analog scale.

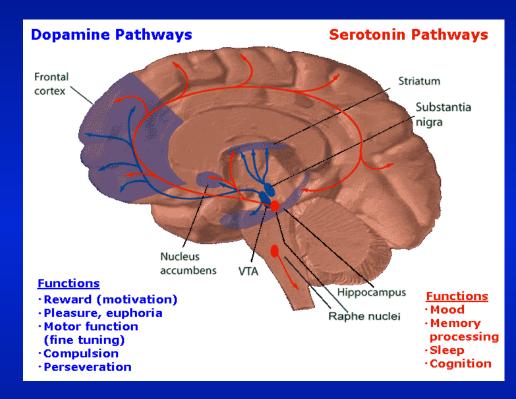
De positieve verwachting activeert dopamine en

endogene opioide banen

Arch Gen Psychiatry. 2008;65(2):220-231

### Placebo effect door positieve verwachting





Tonische avtivatie nigro-striatale dopaminerge neuronen

PFC Nacc PAG

### Placebo effect door positieve verwachting

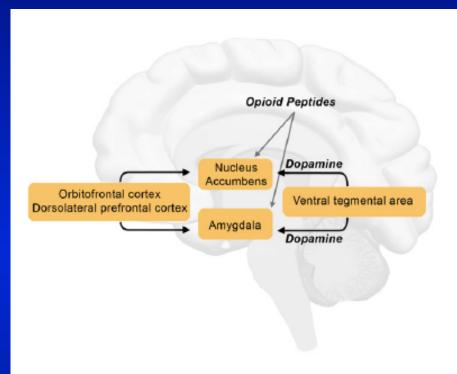
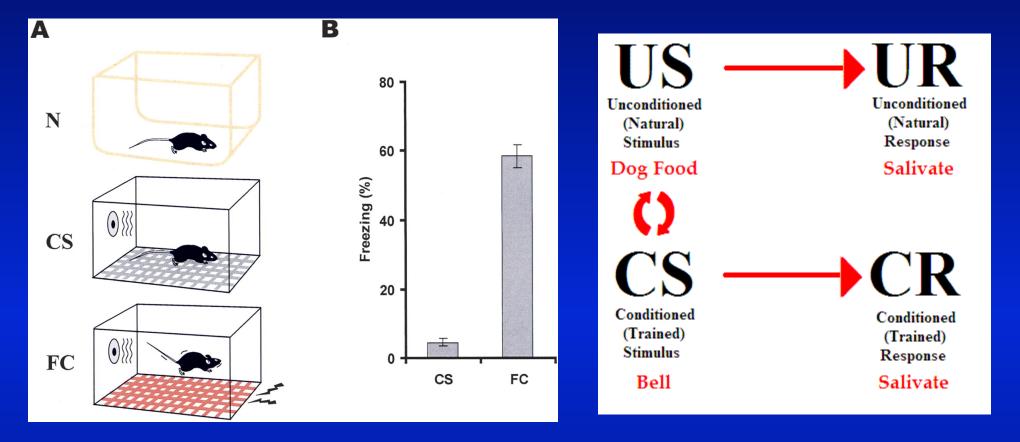


Figure 1. Simplified Scheme of the Reward System

Placebo administration has been found to activate both dopamine and endogenous opioid peptides in the nucleus accumbens, thus suggesting an involvement of reward mechanisms in some types of placebo effects (de la Fuente Fernández et al., 2001; Scott et al., 2008). Note: the main propose of this sketch is to focus on neural substrates of the reward system in the context of the placebo response which, in this case, takes precedence over anatomical accuracy. Verbaal verwachting wekken Opioide bijwerkingen Te remmen door naloxon

Neuron *59*, July 31, 2008



Placebo effect door associatief leren (Pavloviaanse conditionering)

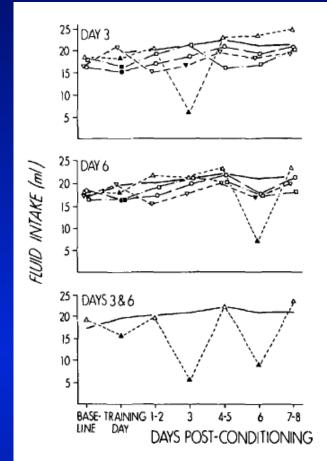


Fig. 1. Mean intake of plain water (open symbols) and saccharin (filled symbols) for placebo (——) and nonconditioned (▼) animals, and conditioned animals that received saccharin (△), cyclophosphamide (□), or neither (○) on Day 3, Day 6, or Days 3 and 6. As a point of reference, the placebo-treated animals are shown in each panel.

It was also observed that some of the cyclophosphamide-treated animals died and that mortality rate tended to vary directly with the volume of saccharin originally consumed.

#### **Behaviorally Conditioned Immunosuppression**

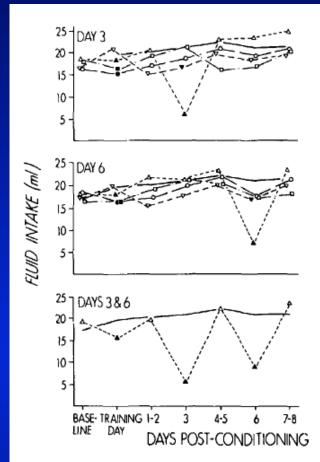


Fig. 1. Mean intake of plain water (open symbols) and saccharin (filled symbols) for placebo (——) and nonconditioned (▼) animals, and conditioned animals that received saccharin (Δ), cyclophosphamide (□), or neither (○) on Day 3, Day 6, or Days 3 and 6. As a point of reference, the placebo-treated animals are shown in each panel.

#### **Behaviorally Conditioned Immunosuppression**

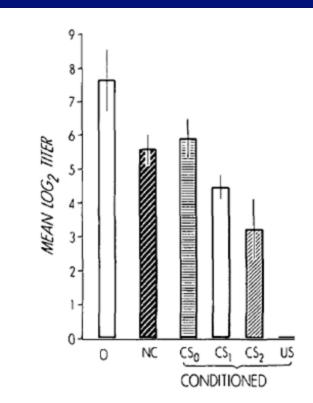


Fig. 2. Hemagglutination titers (means ± SE) obtained 6 days after ip injection of antigen (SRBC). NC = nonconditioned animals provided with saccharin on Day 3 or Day 6; CSo = conditioned animals that did not receive saccharin following antigen treatment; CS1 = conditioned animals given one exposure to saccharin on Day 3 or Day 6; CS2 = conditioned animals exposed to saccharin on Days 3 and 6; US = conditioned animals injected with cyclophosphamide following treatment with antigen.