Modality	Suggestions about	Subjective experience	Autonomic	Endocrine	Immune	Explanation of effects
Verbal suggestions alone						
Inflammatory skin reactions ¹	skin reactions		Yes (HR)		No (skin wheal size)	Reduced HR with placebo
Gastric motility ²	gastric activity		Mixed(effects on EGG; No effect on HRV, SCR)			Placebo effects on gastric slow-wave activity in direction of suggestions
Blood pressure (BP) ³	blood pressure	Yes	Mixed (effects on SCR; no effect on BP or HRV)			SCR increase and subjective drug effect with suggested effective drug
Buprenorphine analgesia ⁴	pain		Yes (Resp)			Reduced respiration with suggested effective drug
Electrical pain in clinic; Ischemic arm pain in lab ⁵	pain	Yes	Yes (HR)			Reduced pain and reduced HR with placebo
Airway resistance ⁶	airway constriction	No	Yes (Resp)			Increased airway resistance with suggested bronchoconstrictor
Tourniquet pain ⁷	pain	Yes		Cortisol, ACTH		Nocebo increases endocrine responses
Ischemic pain ⁸	pain	Mixed (placebo effect only; no nocebo effect)		Mixed (Cortisol: Nocebo effect, no placebo effect; No effects on beta- endorphins)		Nocebo increases endocrine responses; Placebo reduces pain reports
Thermal pain ⁹	pain	Mixed	Mixed (effects on LF/HF HRV ratio; no effects on HR or total HRV)	. ,		Placebo reduces low/high frequency HRV ratio, not total HRV; Placebo effects of pain intensity and stress; No placebo effect on pain unpleasantness, mood, or arousal
Conditioned pain modulation ¹⁰	pain	Yes (females only)	No (HR)			Gender-specific effects on pain, no physio effects

Modality	Suggestions about	Subjective experience	Autonomic	Endocrine	Immune	Explanation of effects
Suggestion including possible effects of learned associations						
Caffeine ¹¹	arousal	No	Mixed (effects on SCR, startle eye blink; no effects on BP, HR)			Decaf coffee increases SCR and startle eye blink
Hormone responses to milkshakes ¹²	calorie content	No		Ghrelin		Ghrelin increases with "sensible" vs. "indulgent" milkshake
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Caffeine ¹³	arousal	Mixed				Decaf coffee increases HR subjective arousal; no effect on stress, calmness, SCL, systolic BP
Muscle relaxant ¹⁴	arousal	Yes	Yes (blink)			Low-arousal suggestions reduce blink reflexes
Responses to propanalol (β- blocker) and atropine (Ach-m agonist) ⁵	drug effects (Open vs hidden drug)		Yes (HR)			Open admin of propranolo reduces HR, open atropino increases HR
Advertising effects on allergen challenge ¹⁵	allergic responses (via advertisements)	Yes			Yes (skin wheal size)	Advertisement effects on skin wheals and beliefs in non-allergic subjects only
Hormonal responses ¹⁶	hormone changes			No (Growth hormone, cortisol)		Growth hormone, cortisol changes with pharmacological conditioning but no effects of suggestion
Electrical pain ¹⁷	pain*	Yes	No (SCR)			Effects on pain only wher suggestion is combined with response conditioning; no effects of SCR

Electrical pain ¹⁸	pain*	Yes	Yes (pupil, SCR)	Dose-dependent placebo effects on pain, SCR and pupil size
Thermal pain ¹⁹	pain*	Yes	Yes (SCR)	"Strong" placebo reduces pain and SCR
Thermal pain ²⁰	pain*	Yes	Yes (SCR)	Placebo reductions in pain and SCR, blocked by naloxone
Secondary hyperalgesia ²¹	pain*	Yes	No (HR, BP)	Effects on pain and secondary hyperalgesia but not physio

Note. Autonomic and neurendocrine effects of verbal suggestions about treatment effects. "Yes" indicates significant effects, "No" indicates null findings. Empty cells indicate a lack of available information. Studies manipulating verbal suggestions about pain or other stimulus/response features have shown effects on autonomic responses and hormone levels, though they do not always mirror the suggestions themselves. Other studies have combined suggestions with previously learned cues, or independently manipulated (crossed) learned cues with suggestion. Combined suggestion and learning has produced strong autonomic effects in some, but not all, studies. In some cases, effects were driven by learning. The effects of suggestion on autonomic and endocrine responses may depend on interactions with learning processes or their ability to engage strong affective responses. Abbreviations: ACTH: adrenocorticotropic hormone; Blink: Startle blink reflex magnitude; BP, blood pressure;EGG: electrogastrogram; HR, heart rate; HRV, heart-rate variability; SCL, skin conductance level; SCR, skin conductance response. *: includes response conditioning.

- 1. Darragh, M., Booth, R.J., Koschwanez, H.E., Sollers III, J., Broadbent, E. Expectation and the placebo effect in inflammatory skin reactions A randomised-controlled trial. Journal of psychosomatic research 74, 439-43 (2013).
- 2. Meissner, K. Effets of placebo interventions on gastric motility and general autonomic activity. Journal of psychosomatic research 66, 391-98 (2009).
- 3. Zimmermann-Viehoff, F., Meissner, K, Koch, J., Weber, C.S., Richter, S., Deter, H-C. Autonomic effects of suggestive placebo interventions to increase or decrease blood pressure: A randomized controlled trial in healthy subjects. Journal of psychosomatic research 75, 32-5 (2013).
- 4. Benedetti, F., Amanzio, M., Baldi, S., Casadio, C. & Maggi, G. Inducing placebo respiratory depressant responses in humans via opioid receptors. The European journal of neuroscience 11, 625-31 (1999).
- 5. Pollo, A., Vighetti, S., Rainero, I. & Benedetti, F. Placebo analgesia and the heart. Pain 102, 125-33 (2003).

- Wigal, J.K., Kotses, H., Rawson, J.C., Creer, T.L. The Effects of Suggestion on the Total Respiratory Resistance of Nonasthmatic Female Subjects. Journal of psychosomatic research 32, 409-416 (1988).
- Benedetti, F., Amanzio, M., Vighetti, S. & Asteggiano, G. The biochemical and neuroendocrine bases of the hyperalgesic nocebo effect. The Journal of neuroscience : the official journal of the Society for Neuroscience 26, 12014-22 (2006).
- 8. Johansen, O., Brox, J. & Flaten, M.A. Placebo and Nocebo Responses, Cortisol, and Circulating Beta-Endorphin. Psychosomatic Medicine 65, 786-790 (2003).
- 9. Aslaksen, P.M. & Flaten, M.A. The Roles of Physiological and Subjective Stress in the Effectiveness of a Placebo on Experimentally Induced Pain. Psychosomatic Medicine 70, 811-818 (2008).
- Aslaksen, P.M., Bystad, M., Vambheim, S.M. & Flaten, M.A. Gender differences in placebo analgesia: event-related potentials and emotional modulation. Psychosomatic Medicine 73, 193-9 (2011).
- 11. Flaten, M., Aasli, O. & Blumenthal, T. Expectations and placebo responses to caffeine-associated stimuli. Psychopharmacology 169, 198-204 (2003).
- 12. Crum, A.J., Corbin, W.R., Brownell, K.D. & Salovey, P. Mind over milkshakes: mindsets, not just nutrients, determine ghrelin response. Health psychology : official journal of the Division of Health Psychology, American Psychological Association 30, 424-9; discussion 430-1 (2011).
- 13. Flaten, M.A. & Blumenthal, T.D. Caffeine-associated stimuli elicit conditioned responses: an experimental model of the placebo effect. Psychopharmacology (Berl) 145, 105-12 (1999).
- 14. Flaten, M.A., Simonsen, T. & Olsen, H. Drug-related information generates placebo and nocebo responses that modify the drug response. Psychosomatic Medicine 61, 250-5 (1999).
- 15. Kamenica, E., Naclerio, R. & Malani, A. Advertisements impact the physiological efficacy of a branded drug. Proceedings of the National Academy of Sciences of the United States of America 110, 12931-5 (2013).

- 16. Benedetti, F. et al. Conscious expectation and unconscious conditioning in analgesic, motor, and hormonal placebo/nocebo responses. The Journal of neuroscience : the official journal of the Society for Neuroscience 23, 4315-23 (2003).
- 17. De Jong, P.J., van Baast, R., Arntz, A. & Merckelbach, H. The placebo effect in pain reduction: the influence of conditioning experiences and response expectancies. International Journal of Behavioral Medicine 3, 14-29 (1996).
- 18. Nakamura, Y. et al. Investigating dose-dependent effects of placebo analgesia: a psychophysiological approach. Pain 153, 227-37 (2012).
- 19. Geuter, S., Eippert, F., Attar, C.H. & Büchel, C. Cortical and subcortical responses to high and low effective placebo treatments. Neuroimage 67, 227-236 (2013).
- 20. Eippert, F. et al. Activation of the opioidergic descending pain control system underlies placebo analgesia. Neuron 63, 533-43 (2009).
- 21. Matre, D., Casey, K.L. & Knardahl, S. Placebo-induced changes in spinal cord pain processing. The Journal of neuroscience : the official journal of the Society for Neuroscience 26, 559-63 (2006).