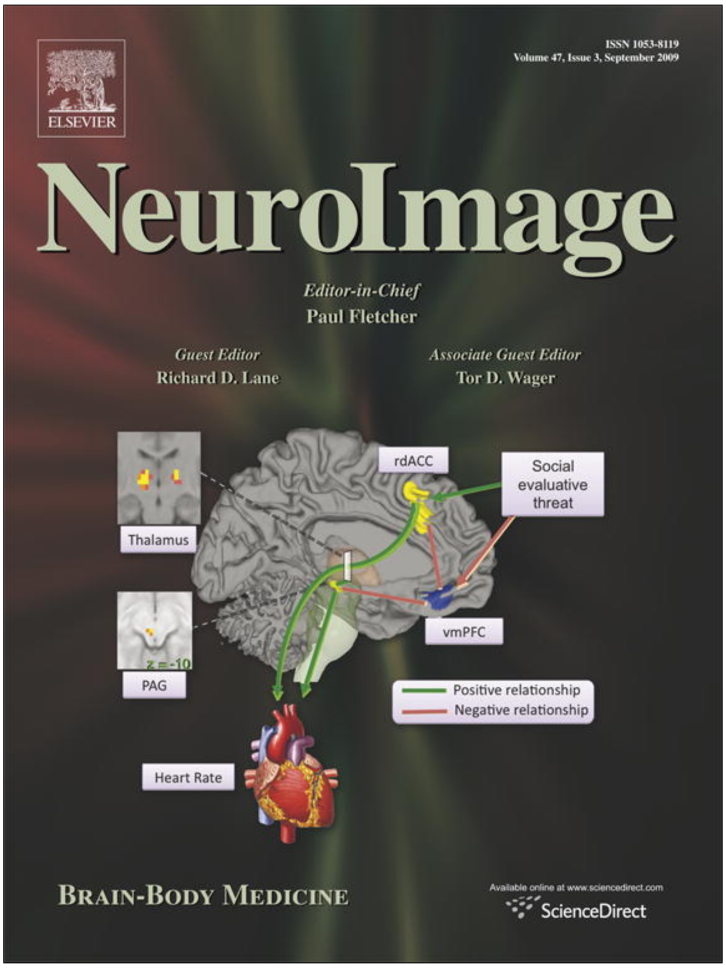
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Editorial

# Introduction to a Special Issue of Neuroimage on Brain–Body Medicine

## Context and purpose of the Special Issue

This Special Issue of *Neuroimage* on Brain–Body Medicine introduces the neuroimaging community to a new domain in which the study of brain structure and function can have an important influence on health — that domain of clinical medicine dealing with bodily disease. To date, the major clinical applications of neuroimaging have been in neurology and psychiatry. The first and arguably still dominant clinical area is neurology, in which brain imaging plays a central role in daily clinical care, particularly in diagnosis. In psychiatry, functional brain imaging is not yet clinically applicable, but it is nevertheless contributing to a paradigm shift in which psychiatric disorders are gradually coming to be understood in terms of pathophysiology rather than descriptive syndromes (George et al., 2002). The application of brain imaging to systemic medical disorders constitutes a third clinical domain in which imaging neuroscience can potentially make an important contribution.

Brain–Body Medicine focuses on interactions between the brain, peripheral pathways and bodily end-organs. Bi-directional brain–body pathways can be thought of as the mechanistic substrate that mediates the relationship between psychological and social factors and physical health. As such, Brain–Body Medicine adds a new dimension to research in the fields of mind–body, behavioral, psychosomatic, and integrative medicine[1]. It also creates linkages, by virtue of the focus on the brain, to newer fields such as psychoneuroimmunology, neuro-cardiology and brain–gut research that have as of yet made relatively little use of neuroimaging technology.

Research findings that link psychological and social factors to medical outcomes, and the clinical practices associated with this research, are in the public interest and are often discussed in the popular media. However, they are viewed with skepticism by many physicians (Freeland et al., 2006). One way of understanding this discrepancy is that demonstrating associations between psychological or social variables on the one hand and medical outcomes on the other, even when including peripheral mediators from the autonomic, endocrine and immune systems, provides an incomplete account of the mechanisms linking mind and body. By studying the brain and relating it to bodily processes and disease, a more complete mechanistic account becomes possible within a biomedical framework (Lane et al., 2009). The field of Brain–Body Medicine seeks to advance understanding of the mechanisms by which mental events influence physical health, and vice versa, and to ultimately use such knowledge to improve medical care and facilitate effective disease prevention.

The field of Brain–Body Medicine likely extends to other areas, but the boundaries of the field are still fluid. Conceivably, these include the study of: 1) the brain mechanisms involved in any systemic medical disorder in which autonomic, endocrine or immune factors influence its etiology, onset or course; 2) brain influences on autonomic, endocrine and immune function under normal conditions; 3) brain structure and function within the field of psychophysiology, which traditionally involves surface measurements from the head (EEG/ERP) and body proper; and 4) medical disorders that are not as yet linked to morbid anatomy, such as functional somatic syndromes like fibromyalgia or chronic fatigue syndrome (Wessely et al., 1999). These disorders likely involve brain–body interactions that remain to be elucidated.

Neuroimaging provides an organizing framework that bridges these diverse areas of study. It can provide more explicit information on functional links between brain and other systems than has been previously available. However, the study of brain–body communications is unknown to many in the neuroimaging community. Relatively little work in this area has been presented at brain imaging meetings or published in brain imaging journals. The purpose of this Special Issue is to bring together the work of many of the leading investigators in this field with the hope of raising awareness about what is currently known, and to convey a sense of the enormous potential that lies ahead.

## Organization of the Special Issue

The historical context of the Special Issue is discussed in more detail in an introductory editorial by Rose (2009). The Special

[1] The boundaries of these disciplines are not well defined, and there is much overlap. *Mind–body medicine* focuses on research and practices pertaining to the interrelationships of the mind, brain, bodily organ systems and behavior. Interventions such as relaxation, hypnosis, yoga, visual imagery, tai chi, and spirituality are designed to enhance the mind's capacity to affect bodily function and symptoms and to promote health. *Behavioral medicine* is the interdisciplinary field concerned with the development and integration of behavioral, psychosocial, and biomedical science knowledge and techniques relevant to the understanding of health and illness, and the application of this knowledge and these techniques to prevention, diagnosis, treatment and rehabilitation. *Psychosomatic medicine* seeks to promote and advance the scientific understanding and multidisciplinary integration of biological, psychological, behavioral and social factors in human health and disease, and to foster the application of this understanding in education and improved health care, particularly at the interface of psychiatry and medicine. *Integrative medicine* is the practice of medicine that reaffirms the importance of the relationship between practitioner and patient, focuses on the whole person, is informed by evidence, and makes use of all appropriate therapeutic approaches, healthcare professionals and disciplines to achieve optimal health and healing. Included in this approach are practices that do not fall within the realm of conventional medicine, such as herbalism, chiropractic, homeopathy, and certain mind–body medicine techniques.


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Issue is then organized into six sections, designed to cover a sample of topics relevant to Brain–Body Medicine in which current, cutting-edge research is being done using neuroimaging. These are: (1) the autonomic nervous system; (2) the endocrine and immune systems; (3) brain–peripheral relationships with measures of end-organ function; (4) neuroimaging of clinical disorders with strong central nervous system (CNS) influences; (5) neuroimaging of CNS interventions to treat medical conditions; and (6) methodology relevant for brain–peripheral imaging. The Special Issue concludes with a summary editorial (Lane and Wager, 2009).

Our intent was to be comprehensive in the coverage of topics and to present representative work in each area. The primary focus within each section is empirical reports of new findings, but review articles and commentaries are included to promote an integrative understanding. All papers were invited and went through the rigorous peer review process typical of *Neuroimage*.

As will be apparent in the descriptions below, an important theme running throughout the Special Issue is that of emotion, emotion regulation and stress. Decades of work in mind–body medicine have demonstrated the relevance of emotion and stress to medical outcomes (Glaser and Kiecolt-Glaser, 2005; McEwen 1998; Lane 2008; Schier and Carver, 1992). Thus, they figure prominently in the study of how the brain influences physical disease and related somatic processes.

*Section 1: Autonomic nervous system*

The autonomic nervous system (ANS) section begins with an introductory overview by Cameron (2009) that places the ANS in the context of two other information transfer systems, endocrine and immune, that mediate bidirectional communication between the brain and peripheral end-organs. Cechetto and Shoemaker (2009) then present a review of the brain circuitry involved in regulating the ANS. Williams et al. (2009) examine the neural correlates of negativity bias (the tendency to have negative emotional responses) by examining brain responses to implicit and explicit presentation of fearful faces as a function of serotonin transporter allelic variants and early life stress. The next three papers use variants of a public speaking task, one of the most commonly used and effective laboratory stressors (Kirschbaum et al., 1993), to elicit stress in the neuroimaging environment. Åhs et al. (2009) examine the neural correlates of heart rate variability (vagal tone, an index of activity in one of the two branches of the ANS) during PET imaging as individuals with social phobia perform a public speaking task. Wager et al., 2009a,b present two companion papers on public speech preparation that map cortical–subcortical–cardiovascular pathways involved in the generation of heart rate responses (Wager et al., 2009a) and subjective anxiety (Wager et al., 2009b). Finally, Urry et al. (2009) examine the voluntary regulation of emotional responses to unpleasant pictures, focusing on the relationships between brain and autonomic responses during regulation.

*Section 2: Endocrine and immune systems*

The section on endocrine and immune mechanisms begins with a review article by Dedovic et al. (2009) on the functional neuroanatomy of the regulation of cortisol, a hormone that plays a key role in “stress” responses. King et al. (2009) present a PET study that identifies the neural basis of adrenocorticotropic hormone (ACTH) response to trauma recall. Eisenberger et al. (2009) use fMRI to examine the neural basis of the proinflammatory cytokine response to endotoxin in the context of a social exclusion task, and O'Connor et al. (2009) use fMRI to examine the neural basis of the proinflammatory cytokine response in the context of grief. Next, Ohira et al. (2009) use PET to examine the neural basis of lymphocyte, particularly natural killer cell, redistribution during the performance of a stressful task that manipulated uncertainty. In concluding commentaries, Thayer and Sternberg (2009) discuss the importance of vagal mechanisms in linking the brain and the immune systems bidirectionally, and McEwen (2009) offers an integrative perspective on the brain as the master orchestrator of the stress response, including the regulation of autonomic, endocrine and immune effects.

*Section 3: Relationships between brain and peripheral organ systems*

This section describes brain–periphery relationships with measures of four different end-organ systems, with a focus on processes directly relevant to disease. Three papers deal with the cardiovascular system. Jennings and Zanstra (2009) review evidence suggesting that brain mechanisms may contribute to the etiology of essential hypertension. Gianaros and Sheu (2009) review evidence on the role of functional and structural brain predictors of cardiovascular reactivity and their association with the development of atherosclerosis and coronary artery disease. Beacher et al. (2009) provide evidence that gray matter density (measured using voxel-based morphometry) in the dorsal brainstem is associated with the severity of vasovagal syncope, or simple fainting. Next, Fukudo et al. (2009) use PET to demonstrate that the neural response to colonic or rectal distension, a probe that is commonly used in the study of irritable bowel syndrome (IBS), varies as a function of serotonin transporter allelic variants. Labus et al. (2009) use PET to demonstrate changes in brain connectivity as a function of habituation to repeated rectal distension in patients with IBS. Next, Evans et al. (2009) examine the neural basis of cognitive and emotional influences on spontaneous breathing. Rosenkranz and Davidson (2009) then review evidence that integrates neuroimaging research on emotion circuitry in relation to symptom expression in asthma. This section concludes with an empirical paper by Griffiths et al. (2009) on the brain basis of the sensation of urinary urgency and the changes that occur with aging.

*Section 4: Clinical disorders with strong CNS influences*

The section on neuroimaging of clinical disorders with strong CNS influences focuses on pain and conversion disorder. Wiech and Tracey (2009) review the neuroimaging literature on emotion–pain interactions in the brain. Price et al. (2009) present an integrative review suggesting that synergistic interactions between brain processes (placebo/nocebo effects) and spino-thalamic afferents promote hyperalgesia in IBS. Derbyshire and Osborn (2009) present new evidence regarding offset analgesia, an effect that involves profound de-coupling of somatic input and experienced pain, using fMRI. Seminowicz et al. (2009) use high-field MRI in rats to provide evidence on brain gray matter atrophy following peripheral nerve damage in a rodent model of chronic pain. Next, Nowak and Fink (2009) review the literature on the neural substrates of conversion disorder, and Cojan et al. (2009) present an fMRI study examining the neural basis of conversion paralysis using a go–no go task.

*Section 5: Interventions*

The next section on interventions addresses brain function in relation to a broad range of interventions. First, Lutz et al. (2009) examine the neural correlates of heart rate changes during performance of compassion-based meditation in experts and novices. Vanhaudenhuyse et al. (2009) use fMRI to examine the effect of hypnosis on experimental heat pain. Napadow et al. (2009)

use fMRI to examine the brain correlates of sham acupuncture as a function of the subjective sensations induced. Kong et al. (2009) use fMRI to examine relationships between expectancy (placebo) and acupuncture manipulations in the context of experimental heat pain. Next, Harris et al. (2009) used PET to examine changes in opiate receptor occupancy in response to acupuncture in patients with fibromyalgia. Finally, Rowny et al. (2009) compare the heart rate effects of magnetic seizure therapy to those of electroconvulsive stimulation in a non-human primate model.

*Section 6: Methodology for assessing brain–body relationships*

The final section on methodology addresses topics that will facilitate future work in this area. Given that the fMRI BOLD signal varies as a function of the rate of delivery of oxygenated blood to brain tissue, Birn et al. (2009) provide methods and results on disentangling neurally induced effects on the BOLD signal from certain cardiovascular and respiratory artifacts. Next, Gray et al. (2009) discuss the complexities of peripheral physiological measurement in the fMRI environment, and King and Liberzon (2009) discuss methodological considerations in the study of the neuroendocrine stress response in the fMRI environment. Finally, Bullmore et al. (2009) address approaches to the analysis of complex systems in brain imaging and other data.

## Conclusion

Our hope is that this Special Issue will catalyze interest in Brain–Body Medicine and will serve as a useful reference for empirical research. Although the range of topics covered is considerable, the possibilities for future work appear unlimited.

## References


Åhs, F., Sollers III, J., Furmark, T., Fredrikson, M., Thayer, J.F., 2009. High frequency heart rate variability and cortico-striatal activity in men and women with social phobia. NeuroImage 47, 815–820.

Beacher, F.D.C.C., Gray, M.A., Mathias, C.J., Critchley, H.D., 2009. Vulnerability to simple faints is predicted by regional differences in brain anatomy. NeuroImage 47, 937–945.

Birn, R.M., Murphy, K., Handwerker, D.A., Bandettini, P.A., 2009. fMRI in the presence of task-correlated breathing variations. NeuroImage 47, 1092–1104.

Bullmore, E., Barnes, A., Bassett, D.S., Fornito, A., Kitzbichler, M., Meunier, D., Suckling, J., 2009. Generic aspects of complexity in brain imaging data and other biological systems. NeuroImage 47, 1125–1134.

Cameron, O.G., 2009. Visceral brain-body information transfer. NeuroImage 47, 787–794.

Cechetto, D.F., Shoemaker, J.K, 2009. Functional neuroanatomy of autonomic regulation. NeuroImage 47, 795–803.

Cojan, Y., Waber, L., Carruzzo, A., Vuilleumier, P., 2009. Motor inhibition in hysterical conversion paralysis. NeuroImage 47, 1026–1037.

Dedovic, K., Duchesne, A., Andrews, J., Engert, V., Pruessner, J.C., 2009. The brain and the stress axis: The neural correlates of cortisol regulation in response to stress. NeuroImage 47, 864–871.

Derbyshire, S.W.G., Osborn, J., 2009. Offset analgesia is mediated by activation in the region of the periaqueductal grey and rostral ventromedial medulla. NeuroImage 47, 1002–1006.

Eisenberger, N.I., Inagaki, T.K., Rameson, L.T., Mashal, N.M., Irwin, M.R., 2009. An fMRI study of cytokine-induced depressed mood and social pain: the role of sex differences. NeuroImage 47, 881–890.

Evans, K.C., Dougherty, D.D., Schmid, A.M., Scanell, E., McCallister, A., Benson, H., Dusek, J. A., Lazar, S.W., 2009. Modulation of spontaneous breathing via limbic/paralimbic-bulbar circuitry: an event-related fMRI study. NeuroImage 47, 961–971.

Freedland, K.E., Miller, G.E., Sheps, D.S., 2006. The Great Debate, revisited. Psychosom. Med. 68, 179–184.

Fukudo, S., Kanazawa, M., Mizuno, T., Hamaguchi, T., Kano, M., Watanabe, S., Sagami, Y., Shoji, T., Hongo, M., Itoyama, I., Yanai, K., Tashiro, M., Aoki, M., 2009. Impact of serotonin transporter gene polymorphism on brain activation by colorectal distention. NeuroImage 47, 946–951.

George, M.S., Nahas, Z., Li, X., Kozel, F.A., Anderson, B., Yamanaka, K., Chae, J.H., Foust, M. J., 2002. Novel treatments of mood disorders based on brain circuitry (ECT, MST, TMS, VNS, DBS). Semin. Clin. Neuropsychiatry 7 (4), 293–304.

Gianaros, P.J., Sheu, L.K., 2009. A review of neuroimaging studies of stressor-evoked blood pressure reactivity: emerging evidence for a brain-body pathway to coronary heart disease risk. NeuroImage 47, 922–936.

Glaser, R., Kiecolt-Glaser, J.K., 2005. Stress-induced immune dysfunction: implications for health. Nat. Rev. Immunol. 5 (3), 243–251.

Gray, M.A., Minati, L., Harrison, N.A., Gianaros, P.J., Napadow, V., Critchley, H.D., 2009. Physiological recordings: basic concepts and implementation during functional magnetic resonance imaging. NeuroImage 47, 1105–1115.

Griffiths, D.J., Tadic, S.D., Schaefer, W., Resnick, N.M., 2009. Cerebral control of the lower urinary tract: how age-related changes might predispose to urge incontinence. Neuroimage 47, 981–986.

Harris, R.E., Zubieta, J.-K., Scott, D.J., Napadow, V., Gracely, R.H., Clauw, D.J., 2009. Traditional Chinese acupuncture and placebo (sham) acupuncture are differentiated by their effects on μ-opioid receptors (MORs). NeuroImage 47, 1077–1085.

Jennings, J.R., Zanstra, Y., 2009. Is the brain the essential in hypertension? NeuroImage 47, 914–921.

King, A.P., Liberzon, I., 2009. Assessing the neuroendocrine stress response in the functional neuroimaging context. NeuroImage 47, 1116–1124.

King, A.P., Abelson, J.L., Britton, J.C., Phan, K.L., Taylor, S.F., Liberzon, I., 2009. Medial prefrontal cortex and right insula activity predict plasma ACTH response to trauma recall. NeuroImage 47, 872–880.

Kirschbaum, C., Pirke, K.M., Hellhammer, D.H., 1993. The "Trier Social Stress Test"—a tool for investigating psychobiological stress responses in a laboratory setting. Neuropsychobiology 28, 76–81.

Kong, J., Kaptchuk, T.J., Polich, G., Kirsch, I, Vangel, M., Zyloney, C., Rosen, B., Gollub, R., 2009. An fMRI study on the interaction and dissociation between expectation of pain relief and acupuncture treatment. NeuroImage 47, 1066–1076.

Labus, J.S., Naliboff, B.D., Berman, S.M., Suyenobu, B., Vianna, E.P., Tillisch, K., Mayer, E.A., 2009. Brain networks underlying perceptual habituation to repeated aversive visceral stimuli in patients with irritable bowel syndrome. NeuroImage 47, 952–960.

Lane, R., 2008. Neural substrates of implicit and explicit emotional processes: a unifying framework for psychosomatic medicine. Psychosom. Med. 70, 213–230.

Lane, R, Waldstein, S, Jennings, R, Lovallo, W, Rose, R, Chesney, M, Schneiderman, N, Drossman, D, Thayer, J, Cameron, O., 2009. The rebirth of neuroscience in psychosomatic medicine, part I: historical context, methods and relevant basic science. Psychosom. Med. 71, 117–134. 304.

Lane, R.D., Wager, T.D., 2009. The new field of Brain– Body Medicine: what have we learned and where are we headed? NeuroImage 47, 1135–1140.

Lutz, A., Greischar, L.L., Perlman, D.M., Davidson, R.J., 2009. BOLD signal in insula is differentially related to cardiac function during compassion meditation in experts vs. novices. NeuroImage 47, 1038–1046.

McEwen, B.S., 1998. Protective and damaging effects of stress mediators. N Engl J Med 338 (3), 171–179.

McEwen, B.S., 2009. The brain is the central organ of stress and adaptation. NeuroImage 47, 911–913.

Napadow, V., Dhond, R.P., Kim, J., LaCount, L., Vangel, M., Harris, R.E., Kettner, N., Park, K., 2009. Brain encoding of acupunture sensation — coupling on-line rating with fMRI. NeuroImage 47, 1055–1065.

Nowak, D.A, Fink, G.R., 2009. Psychogenic movement disorders: aetiology, phenomenology, neuro-anatomical correlates and therapeutic approaches. NeuroImage 47, 1015–1025.

O'Connor, M.-F., Irwin, M.R., Wellisch, D.K., 2009. When grief heats up: proinflammatory cytokines predict regional brain activation. NeuroImage 47, 891–896.

Ohira, H., Fukuyamal, S., Kimura, K., Nomura, M., Isowa, T., Ichikawa, N., Matsunaga, M., Shinoda, J., Yamada, J., 2009. Regulation of natural killer cell redistribution by prefrontal cortex during stochastic learning. NeuroImage 47, 897–907.

Price, D.D., Craggs, J.G., Zhou, Q., Verne, N.G., Perlstein, W.R., Robinson, M.E., 2009. Widespread hyperalgesia in irritable bowel syndrome is dynamically maintained by tonic visceral impulse input and placebo/nocebo factors: evidence from human psychophysics, animal models, and neuroimaging. NeuroImage 47, 995–1001.

Rose, R.M., 2009. Embodying the mind: a brief history of the science integrating mind and body. NeuroImage 47, 785–786.

Rosenkranz, M.A., Davidson, R.J., 2009. Affective neural circuitry and mind-body influences in asthma. NeuroImage 47, 972–980.

Rowny, S.B., Cycowicz, Y.M., McClintock, S.M., Truesdale, M.D., Luber, B., Lisanby, S.H., 2009. Differential heart rate response to magnetic seizure therapy (MST) relative to electroconvulsive therapy: a nonhuman primate model. NeuroImage 47, 1086–1091.

Scheier, M.F., Carver, C.S., 1992. Effects of optimism on psychological and physical well-being: theoretical overview and empirical update. Cogn. Ther. Res. 16 (2), 201–228.

Seminowicz, D.A., Laferriere, A.L., Millecamps, M., Yu, J.S.C., Coderre, T.J., Bushnell, M.C., 2009. MRI structural brain changes associated with sensory and emotional function in a rat model of long-tern neuropathic pain. NeuroImage 47, 1007–1014.

Thayer, J.F., Sternberg, E.M., 2009. Neural concomitants of immunity — focus on the vagus nerve. NeuroImage 47, 908–910.

Urry, H.L., van Reekum, C.M., Johnstone, T., Davidson, R.J., 2009. Individual differences in some (but not all) medial prefrontal regions reflect cognitive demand while regulating unpleasant emotion. NeuroImage 47, 852–863.

Vanhaudenhuyse, A., Boly, M., Balteau, E., Schnakers, C., Moonen, G., Luxen, A., Lamey, M., Degueldre, C., Brichant, J.F., Maquet, P., Laureys, S., Faymonville, M.E., 2009. Pain and non-pain processing during hypnosis: a thulium-YAG event related fMRI study. NeuroImage 47, 1047–1054.

Wager, T.D., Waugh, C.E., Lindquist, M., Noll, D.C., Fredrickson, B.L., Taylor, S.F., 2009a. Brain mediators of cardiovascular responses to social threat, part I: reciprocal

dorsal and ventral sub-regions of the medial prefrontal cortex and heart-rate reactivity. NeuroImage 47, 821–835.
Wager, T.D., Van Ast, V.A., Hughes, B.L., Davidson, M.L., Lindquist, M.A., Ochsner, K.N., 2009b. Brain mediators of cardiovascular responses to social threat, part II: prefrontal–subcortical pathways and relationship with anxiety. NeuroImage 47, 836–851.
Wessely, S., Nimnuan, C., Sharpe, M., 1999. Functional somatic syndromes: one or many? Lancet 354 (9182), 936–939.
Wiech, K., Tracey, I., 2009. The influence of negative emotions on pain: behavioral effects and neural mechanisms. NeuroImage 47, 987–994.
Williams, L.M., Gatt, J.M., Schofield, P.R., Olivieri, G., Peduto, A., Gordon, E., 2009. 'Negativity bias' in risk for depression and anxiety: brain–body fear circuitry correlates, 5-HTT-LPR and early life stress. NeuroImage 47, 804–814.

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